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# What's new in Lupus Nephritis: from guidelines to real-world practices

**A promotional symposium organised and funded by Otsuka Pharmaceutical Europe Ltd at the the European League Against Rheumatism (EULAR) 2024 European Congress of Rheumatology**

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The Otsuka-sponsored satellite symposium *"What's new in Lupus Nephritis: from guidelines to real-world practices"* took place on 14 June 2024 at the EULAR 2024 European Congress of Rheumatology in Vienna, Austria.

A leading faculty of European experts in the field of lupus nephritis (LN) discussed the importance of vigilant patient monitoring, examined clinical and real-world evidence for the use of LN therapies, and considered the implications of recent guideline updates for the management of LN, sharing knowledge and expertise from their own clinical practice.

# Faculty

## Professor Clemens Scheinecker (Chair)

Head of the Special Outpatient Clinic for Clinical Immunology at the Department of Rheumatology, Department of Medicine, Medical University of Vienna, Austria

## Dr Josefina Cortés-Hernández

Lupus Research Unit, Vall d'Hebron Research Institute, Barcelona, Spain

## Dr Ravindra Rajakariar

Lead Clinician for Renal Medicine at Barts Health NHS Trust, London, UK

# Hot topics in lupus nephritis: Vigilant monitoring – urgency for screening

**Professor Clemens Scheinecker**

Professor Scheinecker highlighted that around half of patients with systemic lupus erythematosus (SLE) develop renal signs and symptoms and 5–20% will have developed end-stage kidney disease (ESKD) after 10 years.[1] Each LN flare leads to irreversible nephron loss, and this loss of nephrons continues with ongoing LN (**Figure 1**).[1] Predictors for the development of ESKD include gender, kidney function at diagnosis, activity and number of flares.[1]

In patients with LN, the amount of proteinuria, expressed as urine to protein creatinine ratio (UPCR), urinary sediment, and estimated glomerular filtration rate (eGFR) are important parameters to assess disease progression and treatment efficacy, while kidney biopsy remains the gold standard for the evaluation of inflammatory activity and chronic damage. The EULAR recommendations for the management of SLE: 2023 update defines treatment targets for LN as ≥25% reduction in UPCR at 3 months; ≥50% reduction in UPCR to <3 g/day at 6 months and UPCR <0.5–0.7 g/day at 12–24 months (all with eGFR within 10% from baseline).[2]

In clinical trials of LN, rates of complete renal response (CRR) and partial renal response (PRR) are used to evaluate treatment efficacy. Around 60% of patients will fail on a particular therapy and 14–33% are resistant to treatment.[3] Switching therapy should be considered if there is no improvement in symptoms after 3–4 months and PRR has not been achieved after 6–12 months (**Table 1**).

There is no good panel of biomarkers for LN and there remains a need to identify new biomarkers, particularly to assess therapeutic response, predict relapse and determine disease activity. Further research is also needed to better understand (1) the value of repeat kidney biopsy prior to discontinuation of immunosuppression and after 1 year of treatment, to guide decisions on further therapy; and (2) prediction of response to specific therapies, using clinical, cellular and/or molecular markers.[2]

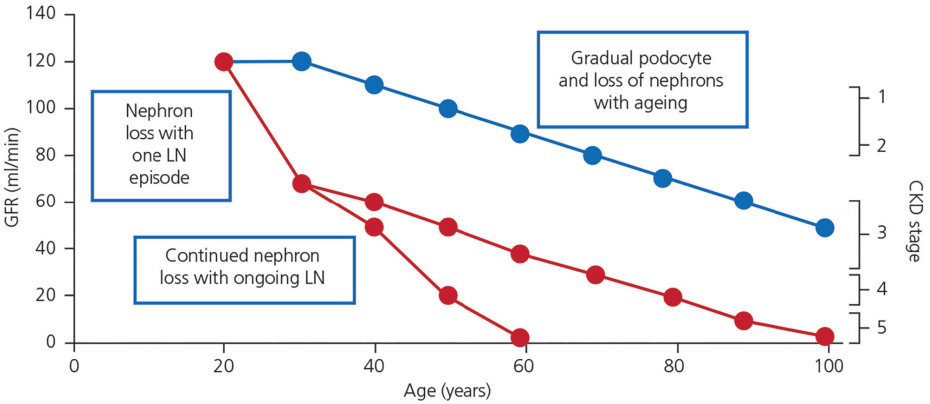


**Figure 1. Lifetime risk of ESKD in patients with LN[4]**

Figure adapted from Anders et al. (2020).[1]
CKD, chronic kidney disease; ESKN, end-stage kidney disease; GFR, glomerular filtration rate; LN, lupus nephritis.

| | Complete renal response (CRR) | Partial renal response (PRR) | Non-responsel refractory |
|---|---|---|---|
| 2023 EULAR | UPCR <500-700 mg/day at 12 months | ≥50% reduction in proteinuria at 6 months | Failure to achieve PRR or CRR |
| KDIGO 2024 | UPCR <0.5 g/g AND stabilisation or improvement of kidney function at 6-12 months | UPCR reduced by ≥50% AND UPCR <3 g/g AND stabilisation or improvement of kidney function at 6-12 months | Failure to achieve PRR or CRR at 6-12 months |

**Table 1. Guideline recommended definitions of treatment goals for LN[2,4]**

EULAR, European League Against Rheumatism; UPCR, urine protein creatinine ratio; CRR, complete renal response; PRR, partial renal response.

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# Key recent trials and guidelines in lupus nephritis

**Dr Josefina Cortés-Hernández**

Dr Cortés-Hernández explained that LN remains a significant contributor to short- and long- term morbidity, and mortality in patients with SLE.[1] Despite improvements in prognosis, better characterisation of the different stages of the disease and development of new therapeutic strategies, unmet needs remain.[5] There is a need to predict the individual risk for LN in patients with SLE. Standard-of-care immunosuppressive therapies achieve poor complete renal response rates, with considerable toxicity so it is important to identify the best therapeutic options for each individual patient. There is also a need to distinguish chronic kidney damage from active immunologic kidney injury and to identify better, more reliable biomarkers to monitor disease.[5]

The treatment of LN has evolved considerably over the past fifty years.[6] Through increased understanding of the pathogenesis of LN, we now know that multiple immune pathways are implicated in this disease, allowing for different treatment targets. Belimumab and voclosporin are the most recently approved therapies for LN, while several other emerging therapies are still under investigation.[6]

Belimumab is an antibody directed against soluble B-cell activating factor (BAFF)/B-lymphocyte stimulator (BlyS) that affects B-cell development, maturation, survival and antibody production.[7–10] In the Phase 3 BLISS-LN trial of patients with active LN (N=448), significantly more patients in the belimumab (plus standard therapy) group than in the placebo (plus standard therapy) group had a primary efficacy renal response (PERR) at Week 104 (43% vs 32%; p=0.03).[7] Secondary endpoint results also favoured belimumab. The safety profile of belimumab was consistent with that in previous trials.[7]

Voclosporin is a calcineurin inhibitor (CNI) that inhibits T-cell activation and stabilises podocytes in the kidney, which decreases proteinuria.[11] Voclosporin has standardised dosing and therapeutic drug monitoring is not mandated in the summary of product characteristics.[11–13] Additionally, co-administration of voclosporin with mycophenolate mofetil (MMF) has no clinically significant impact on mycophenolic acid concentrations.[11–13] In the Phase 3 AURORA 1 trial in patients with active LN (N=357), voclosporin in combination MMF and low-dose glucocorticoids led to a clinically and statistically superior CRR rate compared with MMF and low-dose glucocorticoids alone (41% vs 23%; p<0·0001).[14] The median time to UPCR ≤0.5 mg/mg was 169 days for voclosporin compared with 372 days for placebo (p<0.001).[14] In the AURORA 2 long-term extension trial, reductions in mean UPCR achieved during the first year of treatment in AURORA 1 were maintained (**Figure 2**) and mean corrected eGFR remained stable in both treatment groups over the 3-year study period (**Figure 3**).[15]

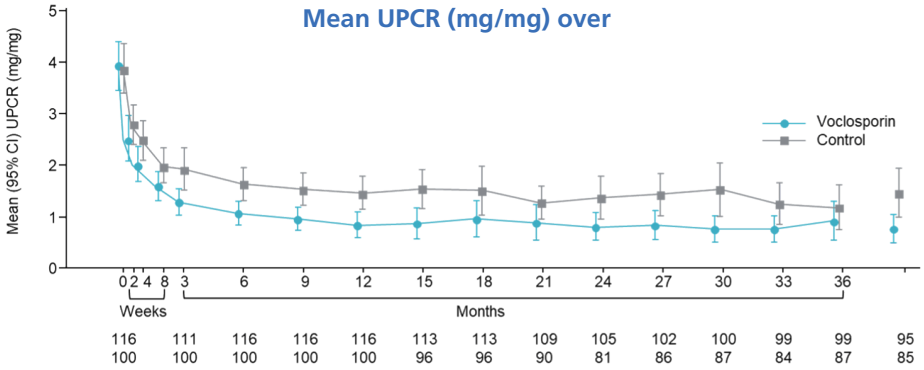


**Figure 2. Mean UPCR over time[15]**

Figure adapted from Saxena *et al*. (2024)15 UPCR, urine to protein creatinine ratio

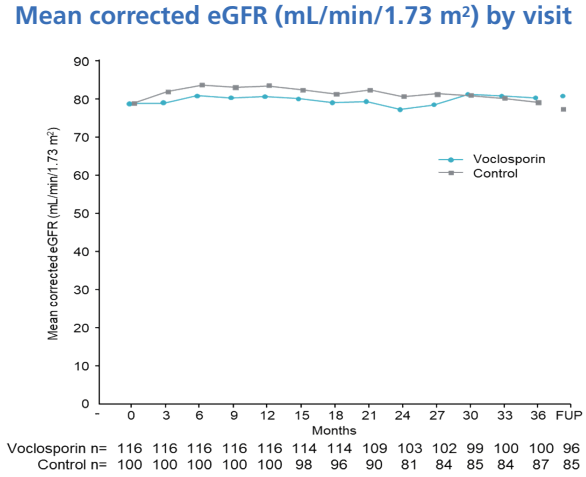


**Figure 3. Mean corrected eGFR over time[15]**

Figure adapted from Saxena *et al*. (2024)15
eGFR, estimated glomerular filtration rate; FUP follow up

# Two years of experience in lupus nephritis with the latest therapies in a real-world setting

**Dr Ravindra Rajakariar**

Dr Rajakariar shared insights from Barts Lupus Centre in London, UK. In his centre, the multidisciplinary team (MDT) includes clinicians working across various clinics, a clinical nurse specialist (CNS) and various allied health professionals who provide psychology, physiotherapy and dietetic support (**Figure 4**). The CNS conducts annual reviews, cardiovascular risk assessment, administers vaccinations, provides a telephone and email hotline and runs focus groups for patients and their families. A regional MDT meeting (which also includes a histopathologist) is held to discuss complex cases and gain approval for the use of biologics and other high-cost drugs.

Dr Rajakariar then went on to discuss LN treatments. The unlicensed use of tacrolimus and cyclosporin is widespread as part of multi-target therapy. While both drugs are associated with reductions in proteinuria, data from clinical trials with long-term follow up are limited. Therapeutic drug monitoring is also required and target plasma concentrations vary in clinical practice.[11,16,17] Nine patients are currently receiving treatment with voclosporin (duration 40–285 days) at Barts Lupus Centre. To date, there have been no treatment withdrawals and no nephrotoxicity, infections or drug intolerance. In terms of steroid use, three patients are off steroids, three patients are on a daily dose of 2.5–5.0 mg and three patients are on a daily dose of 7.5–10.0 mg. In seven patients, substantial decreases in proteinuria have been observed with voclosporin treatment. Clinical practice has evolved at Barts such that patients with biopsy-proven Class III/IV and/or Class V LN who have an eGFR >45 mL/min plus minimal or no chronicity on renal biopsy are now started immediately on voclosporin plus MMF plus a rapid steroid taper. Compared with the BLISS-LN patient population, in Barts, belimumab is used more frequently in Black patients, in patients with ower eGFR (52 v 100 mL/min) and higher Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score (16 vs 12) and as a second- or third-line treatment.

Health literacy is needed to read and interpret health information, follow a management plan and make informed decisions.[18,19] Levels of health literacy may vary according to socioeconomic status, education, culture and ethnicity and language.[18,19] A health literacy survey of patients at Barts found that only 62% of had adequate health literacy, assessed using the Brief Health Literacy Screening Tool (BRIEF), and patients had low levels of SLE-specific knowledge, assessed using the Lupus Knowledge Assessment Test (LKAT). Dr Rajakariar recommended measurement of patient's health literacy with the BRIEF/IKAT within 1 year of lupus diagnosis.

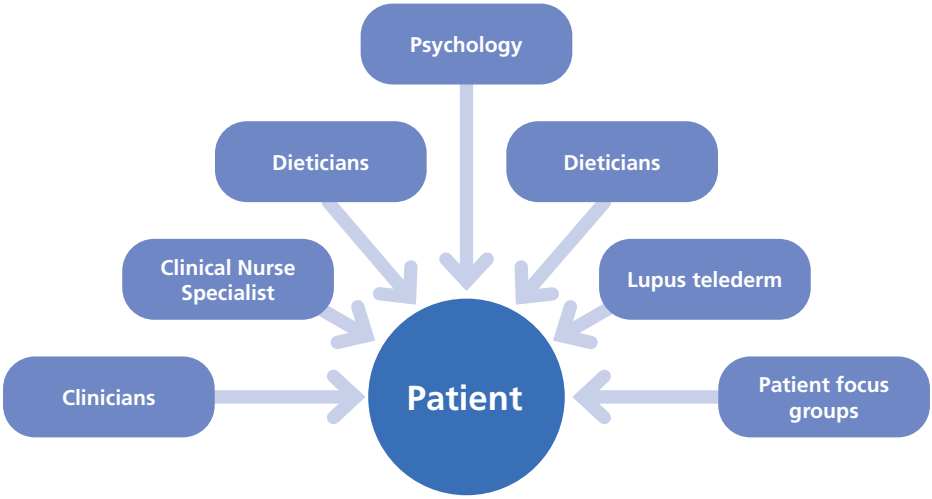


**Figure 4.**

The multidisciplinary team Barts lupus centre, London, UK

Targeted interventions for patients with inadequate health literacy may include the use of translation services, provision of adapted educational materials, more frequent reviews and the use of medication cards. In patients with SLE, rates of non-adherence (either intentional or non-intentional) range from 43% to 75%.[20,21] Causes of non-adherence include forgetfulness, concern about harmful side effects, being easily distracted and scepticism.[21] Getting to know each individual patient is important to be able to personalise a management plan that takes into account their level of health literacy and any potential barriers to adherence.

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