International Journal of Rheumatic Diseases

WILEY

International Journal of Rheumatic Diseases

REVIEW

The 2024 APLAR Consensus on the Management of Lupus Nephritis

Chi Chiu Mok[1] | Ho So[2] | Laniyati Hamijoyo[3] | Nuntana Kasitanon[4] | Der Yuan Chen[5] | Sang Cheol Bae[6] | Meng Tao Li[7] | Sandra Navarra[8] | Desmond Yat Hin Yap[9] | Yoshiya Tanaka[10]

[1]Department of Medicine, Tuen Mun Hospital, Hong Kong, SAR, China | [2]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, SAR, China | [3]Rheumatology Division, Department of Internal Medicine, Padjadjaran University, Bandung, Indonesia | [4]Division of Rheumatology, Department of Internal Medicine, Chiang Mai University, Chiang Mai, Thailand | [5]Rheumatology and Immunology Centre, China Medical University Hospital, Taichung, Taiwan | [6]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Hanyang University Institute for Rheumatology Research and Hanyang Institute of Bioscience and Biotechnology, Seoul, South Korea | [7]Chinese Academy of Medical Science, National Clinical Research Centre for Dermatological and Immunological Diseases, Beijing, China | [8]Section of Rheumatology, University of Santo Tomas, Manila, Philippines | [9]Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, SAR, China | [10]The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

Correspondence: Chi Chiu Mok (ccmok2005@yahoo.com)

Received: 4 December 2024 | **Accepted:** 14 December 2024

Keywords: APLAR | consensus | glomerulonephritis | guideline | lupus | nephritis

ABSTRACT

The APLAR has published a set of recommendations on the management of systemic lupus erythematosus (SLE) in 2021. The current consensus paper supplements and updates specifically the treatment of lupus nephritis (LN) according to two rounds of Delphi exercise from members of the APLAR SLE special interest group, invited nephrologists, histopathologists, and lupus nephritis patients. For initial treatment of LN, we recommend a combination of glucocorticoids (GCs) with cyclophosphamide (CYC), mycophenolate mofetil (MMF), or the calcineurin inhibitors (CNIs) as first-line options. An upfront combination of immunosuppressive drugs and the biological agents may be considered in patients at significant risk of disease progression and renal function deterioration. Switching or "add-on" among different immunosuppressive agents, including biological agents, may be considered for refractory disease. Subsequent/maintenance therapy of LN should continue for at least 3 years to reduce the risk of renal flares. Lower dose MMF and azathioprine are options, but MMF maintenance should follow induction by the same drug. Prednisolone or equivalent should be maintained at a dose of 5 mg/day or less. The APLAR consensus for the management of LN includes recommendations for adjunctive therapies, monitoring and treatment of LN-related co-morbidities, and renal replacement therapies. It is hoped that this consensus paper can provide an evidence-based and pragmatic approach to the management of LN, taking into account the evidence level of therapies in Asian patients, cost-effectiveness, and differences in health care resources and reimbursement policies in the Asia-Pacific region.

1 | Introduction

Kidney involvement in patients with systemic lupus erythematosus (SLE) carries significant morbidities and mortality [1–3]. Despite considerable advances in the immunosuppressive and supportive treatment for LN, leading to the reduction of the end-stage renal disease (ESRD) rate in the past few decades, the renal survival rates in developed countries have plateaued in the mid-1990s [4]. ESRD still develops in 5%–30% of patients with LN within 10 years of diagnosis [3, 5]. The standardized mortality ratio (SMR) increases by one-fold in SLE patients with kidney involvement compared to those without [6]. In a large,

multinational Asian cohort of SLE, patients who had kidney disease were demonstrated to accrue more organ damage than those who did not [7]. Impairment of quality of life is frequent and serious in patients with LN [8]. Active renal disease in SLE was associated with poor outcomes in the medication and procreation domains of an SLE-specific health-related quality of life questionnaire (LupusPRO) in a multicentered cross-sectional study, even after adjusting for age, sex, ethnicity, and the country of origin recruitment [9].

The burden of LN shows ethnicity-related disparities [10]. A review of 70 Asian studies showed that Asian SLE patients have more severe disease, higher disease activity, higher susceptibility to renal involvement, more organ damage accrual, and increased morbidity and mortality compared to Caucasians [11]. This is confirmed by another systematic literature review that showed that renal involvement occurred in 21%–65% of patients with SLE at the time of diagnosis and 40%–82% during the disease course, which was much higher than that of the Caucasians (30%) [12]. In a multi-ethnic study in the United States, the rate of ESRD resulting from LN occurred more frequently in Africans, Hispanics, and Asians than the white Caucasians [13].

Genetic factors may play a role in the ethnic differences in susceptibility and prognosis of patients with LN. Genome-wide association studies (GWAS) have identified a number of allelic variants that are associated with susceptibility to both SLE and LN or LN alone [3]. Of particular interest are the APOL1 alleles, which are associated with more severe LN and higher risk of ESKD in the African Americans [14]. Although similar data have not been confirmed in Asian patients, there is increasing evidence that a higher genetic load, as reflected by a higher polygenic risk score (PRS), is associated with earlier development and more severe renal disease in SLE [15–17]. In addition, a number of clinicopathological features and socioeconomic factors, such as health care resources that affect the accessibility to newer medications and early specialist assessment, as well as the adherence to therapies, are major determinants of the prognosis of LN [5, 18, 19].

Poor tolerance to immunosuppressive therapies has been reported in Asian patients with LN. In an RCT that compared mycophenolate mofetil (MMF) with intravenous (IV) pulse cyclophosphamide (CYC) for initial therapy of LN, serious infections and deaths developed in a substantial proportion of Asian patients treated with higher doses of MMF [1, 20]. Similarly, serious infections and mortality were reported in Asian patients with LN in another RCT of ocrelizumab in combination with glucocorticoids (GCs) and MMF, leading to premature termination of the study [21]. Meta-analyses of LN treatment trials showed that the rate of serious infections (4.1%–25.0% vs. 4.4%–8.5%) and infection-related mortality (0.0%–6.7% vs. 0.0%–2.1%) was higher in Asian than non-Asian patients [22]. Moreover, MMF was not associated with a lower infection risk than CYC in the treatment of LN in Asian patients [22]. Although it is uncertain if the difference in tolerability to immunosuppressive agents is related to pharmacogenetic factors, the treatment approach has to be modified in Asian patients with LN.

In view of the disparities in epidemiology, socioeconomic and cultural background, risk of infection, treatment adherence, as well as the response and tolerability to therapeutic regimens in Asian patients with LN, a set of consensus statements is needed for the management of LN in the Asia-Pacific region. The Asia-Pacific League of Associations of Rheumatology (APLAR) has published a set of recommendations on the management of SLE in 2021 to provide a practical guide for specialists, family physicians, specialty nurses, and other health care professionals who take care of SLE patients in the region [23]. Since its publication, two novel agents, namely belimumab and voclosporin, have been approved for the treatment of LN. This consensus paper supplements and updates specifically the treatment of LN according to two rounds of the Delphi exercise from members of the APLAR SLE special interest group (SIG), invited nephrologists, histopathologists, and patients with LN (Table 1). An executive summary of our recommendations will be published in parallel with this full paper.

2 | Delphi Exercise and Consensus Formation

Core members from the APLAR SLE SIG first reviewed the literature by means of a PubMed search using keywords derived from a set of Population Intervention Comparison Outcome (PICO) questions. The following keywords were used: lupus nephritis, lupus glomerulonephritis, lupus renal, glucocorticoid, steroid, corticosteroid, prednisone, methylprednisone, hydroxychloroquine, antimalarial, methotrexate, leflunomide, calcineurin, cyclosporin, tacrolimus, voclosporin, azathioprine, mycophenolate, mycophenolic, cyclophosphamide, rituximab, belimumab, biologic, obinutuzumab, anifrolumab, JAK inhibitors, tofacitinib, baricitinib, deucravacitinib, intravenous immunoglobulin, plasma exchange, and plasmapheresis. Only clinical trials, observational studies, comparative studies, systematic review, and meta-analyses published between 1995 and 2023 and written in the English language were reviewed.

A total of 56 statements were first drafted and selected by the core group based on the search results and clinical practice. The level of evidence (grade A to D) was graded by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [24], and the strength of recommendation (A or B) was suggested for each statement. The agreement score was derived from a Likert scale in which participants were required to vote for the level of agreement to the statements. Invited Delphi members were provided with a reference list, evidence grading, and the suggested strength of recommendations. Anonymous voting and feedback were done through an online platform by 46 doctors (31 rheumatologists, 13 nephrologists, two renal histopathologists) from 21 Asia-Pacific regions who have considerable experience in managing LN patients and two LN patients who are actively involved in self-help group activities. Modification of the statements was subsequently performed after three rounds of teleconferences to discuss the feedback from the Delphi members. Finally, 48 statements were agreed upon, which were categorized into overarching principles, diagnosis and monitoring, initial and subsequent therapies, pure membranous LN, patients at risk of renal progression, adjunctive therapies

TABLE 1 | APLAR consensus statements for the management of lupus nephritis.

Statements	LOE	SOR	% agreement	Score[a]
1. Over-arching principles				
1.1 The optimal management of LN requires a shared decision-making process between patients and physicians, considering the availability of health care resources across APLAR regions	—	A	100	9.59 ± 1.03
1.2 Physicians should monitor SLE patients for renal involvement and refer them promptly to a lupus specialist for proper management	—	A	97.7	9.14 ± 1.66
1.3 The goals of LN treatment include amelioration of symptoms, renal remission, long-term preservation of renal function, prevention of renal and extra-renal flares, minimization of treatment (especially glucocorticoids) related adverse events and comorbidities, and improvement in survival and overall quality of life	—	A	100	9.66 ± 0.95
1.4 Treatment of active LN includes an induction phase with more intense immunosuppression, followed by a prolonged period of maintenance therapy with less intense immunosuppression to control residual disease activity and prevent renal and extra-renal flares	—	A	97.7	9.23 ± 1.82
1.5 Treatment adherence should be ensured and monitored in every patient in order to achieve the best outcomes	—	A	100	9.69 ± 0.83
2. Screening, diagnosis and monitoring of renal disease in SLE				
2.1 Body weight, body mass index, blood pressure, clinical signs, and symptoms of renal and extra-renal disease should be evaluated at every visit	D	A	100	9.18 ± 1.34
2.2 Urine protein (e.g., spot urine protein-creatinine ratio [uP/Cr] or 24 h urine protein) should be performed at every visit, along with periodic assessment of serum creatinine and albumin, calculated estimated glomerular filtration rate (eGFR), anti-dsDNA, and complement levels. Urine microscopy for active urinary sediments should be performed when renal activity/flare is suspected	D	A	84.1	7.52 ± 3.22
2.3 Patients with active LN should be followed frequently (e.g., every 1–4 weeks) initially, with subsequent frequency of visits adjusted according to clinical response and complications. Stable LN patients may be followed at intervals of 3–6 months	D	A	97.7	8.39 ± 1.77
2.4 A renal biopsy should be performed (unless there are contraindications) when there is suspicion or evidence of kidney involvement, as indicated by the following: • Persistent proteinuria ≥ 1.0 g/24 h (or uP/Cr ≥ 1.0 mg/mg) • Persistent proteinuria ≥ 0.5 g/24 h (or uP/Cr ≥ 0.5 mg/mg) in the presence of active urinary sediments (hematuria/pyuria/casts) • Persistent unexplained deterioration in renal function or eGFR	D	A	93.2	7.80 ± 2.42
2.5 The International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification should be used to assess renal histology in LN	D	A	97.7	8.82 ± 1.93
2.6 Activity (0–24) and chronicity (0–12) indices according to the National Institutes of Health (NIH) criteria should be assessed	D	A	97.7	8.75 ± 1.94
2.7 The presence of additional inflammatory, thrombotic, and vascular lesions should be evaluated, e.g., podocytopathy, tubulointerstitial inflammation, and thrombotic microangiopathy	D	A	85.4	8.66 ± 2.33
3. Initial (Induction) therapies for LN				
3.1 Immunosuppressive therapy is indicated for ISN/RPS active class III or IV (±V) LN	C	A	97.8	9.16 ± 1.85
3.2 Immunosuppressive therapy is indicated for ISN/RPS pure class V with significant proteinuria (uP/Cr ≥ 2.0 mg/mg with hypoalbuminemia)	D	A	88.3	7.70 ± 3.01
3.3 Immunosuppressive therapy should be considered for ISN/RPS class I/II disease with significant podocytopathy or nephrotic range of proteinuria	D	A	92.0	8.39 ± 1.73

(Continues)

TABLE 1 | (Continued)

Statements	LOE	SOR	% agreement	Score[a]
3.4 For patients in whom renal biopsy is unavailable, induction therapy should be individualized based on the judgment of clinical parameters (e.g., eGFR, urinary findings, SLE serology and previous response to therapy)	D	B	97.7	8.61 ± 1.96
4. Options for induction therapy of LN (ISN/RPS class III/IV ± V)				
4.1 A combination of moderate doses of glucocorticoids (GC) and a non-GC immunosuppressive agent is recommended	B	A	87.0	8.09 ± 1.80
4.2 First-line therapies: GC plus mycophenolic acid analogues [MPAA] (e.g., mycophenolate mofetil [MMF] or mycophenolate sodium [MPS]) OR standard-dose intravenous cyclophosphamide [CYC] pulses (0.5–1.0 g/m^2 monthly for six doses) OR the calcineurin inhibitors (CNIs)	A	A	88.6	7.61 ± 2.59
4.3 Alternative induction therapy: GC plus low-dose CYC pulse (intravenous 500 mg 2-weekly for six doses)	A	B	94.0	8.03 ± 1.36
4.4 The target of therapy is improvement of uP/Cr by 25% by 3 months, 50% by 6 months and < 0.75 mg/mg by 12 months	C	A	88.7	7.50 ± 3.03
5. Treatment of pure membranous lupus nephropathy (pure class V)				
5.1 Anti-proteinuric therapy (angiotensin-converting enzyme inhibitors [ACEIs], angiotensin receptor blockers [ARBs]) should be optimized.	B	A	93.2	8.41 ± 2.52
5.2 First-line options: GC plus mycophenolic acid analogues (e.g., MMF or MPA) OR the CNIs	B	A	90.9	7.57 ± 2.66
5.3 Alternative therapies: GC plus azathioprine OR standard-dose intravenous CYC pulses for six doses OR low-dose MMF plus tacrolimus	B	B	87.0	7.55 ± 1.31
6. Subsequent (maintenance) therapies of LN				
6.1 Maintenance therapy should be instituted when the target of initial treatment is achieved	B	A	95.5	8.80 ± 2.31
6.2 Maintenance therapy of LN should continue for at least 3 years before tapering. A longer period of maintenance should be considered in high-risk patients	B	B	90.0	8.28 ± 1.63
6.3 First-line options: lower doses of MMF, MPAA, or azathioprine [AZA]	A	A	93.2	8.07 ± 2.48
6.4 Patients who received MMF as induction therapy should be maintained with the same drug instead of switching to AZA	A	A	89.6	7.98 ± 3.15
6.5 AZA or CNIs are preferred in patients who plan for pregnancy	C	A	95.4	8.64 ± 2.18
6.6 Low-dose GC (prednisone ≤ 5 mg/day or equivalent) may be continued for maintenance therapy. The decision to discontinue and the tempo for tapering off GCs should be individualized	B	B	90.9	7.80 ± 2.85
6.7 Patients who receive initial biological therapy may continue treatment depending on the response and residual renal activity	B	B	98.0	8.28 ± 1.27
7. Lupus nephritis at risk of progression and poorer outcome				
7.1 Patients are at risk of progression and poorer renal outcomes when the following features are present: • Impaired or deteriorating eGFR • Nephrotic range of proteinuria • Histologic high-risk features: crescents, fibrinoid necrosis, thrombotic microangiopathy (TMA), severe tubulointerstitial inflammation • Refractory to initial induction therapies • Frequent relapsing disease	C	A	95.4	8.60 ± 2.19

(Continues)

TABLE 1 | (Continued)

Statements	LOE	SOR	% agreement	Score[a]
7.2 A repeat renal biopsy may be considered in patients with suspected residual or worsening renal activity despite immunosuppressive therapies, renal flare, and/or deterioration in renal function, and to guide switching or tapering of immunosuppressive therapies	B	B	90.0	8.44 ± 1.66
7.3 More aggressive therapy may be considered in patients at risk of progression and poorer renal outcomes	D	B	93.2	8.09 ± 2.62
7.4 Initial treatment options for high-risk patients include GC combined with the following: (a) standard dose intravenous pulse CYC (0.5–1.0 g/m^2 monthly for six doses); (b) low-dose combination of MMF and CNI; (c) MMF/Euro-Lupus CYC with belimumab	A	B	96.0	8.24 ± 1.36
7.5 Switching among the first-line regimens (MMF, CNIs, and CYC) may be considered for patients who do not respond optimally to initial therapies	B	B	96.0	8.59 ± 1.61
7.6 Alternative options for LN with suboptimal response to initial therapies: (a) addition of CNI to MMF or vice versa; (b) addition of rituximab (1 g intravenously 2-weekly for two doses) to existing regimen; (c) addition of belimumab to MMF or Euro-lupus CYC	B	B	96.0	8.23 ± 1.53
8. Adjunctive therapies and management of disease or treatment-related comorbidities				
8.1 Hydroxychloroquine is recommended to all SLE patients, including lupus nephritis	B	A	97.8	9.16 ± 1.85
8.2 Life-style modification, such as cessation of smoking, healthy diet, and exercise, to achieve an optimal body mass index is recommended	D	A	97.7	9.02 ± 1.89
8.3 Renin-angiotensin system (RAS) blockade with ACEIs or ARBs is recommended for all LN patients with/without hypertension, and the dosage should be optimized as per patient tolerance	A	A	93.2	8.34 ± 2.51
8.4 Anticoagulation is indicated in patients with histologic evidence of aPL nephropathy (e.g., acute/chronic renal vascular or glomerular lesions, e.g., TMA or renal artery thrombosis); anticoagulation may be considered in those with persistent nephrotic syndrome in the presence of aPL antibodies	C	A	93.2	7.75 ± 2.54
8.5 Blood pressure should be controlled to retard the progression to CKD. A level of 130/80 mmHg should be targeted	C	A	97.7	8.61 ± 1.96
8.6 Lipid levels should be controlled by non-pharmacological means with or without statins to minimize the long-term cardiovascular risk. An LDL-cholesterol level of < 2.6 mmol/L (100 mg/dL) should be attempted. Lower levels of LDL-cholesterol (e.g., < 1.8 mmol/L [70 mg/dL]) should be targeted in patients with past major adverse cardiovascular events (MACEs) or multiple atherosclerotic risk factors	D	B	90.0	8.02 ± 1.69
8.7 Calcium and vitamin D should be routinely given unless contraindicated. Anti-resorptive or anabolic therapy and regular assessment of BMD (by DEXA scan) should follow the relevant national glucocorticoid-induced osteoporosis recommendations	C	A	88.7	7.55 ± 2.93
8.8 Monitoring of drug-related toxicities should be performed (e.g., glucose level in users of GC and CNIs; blood counts and liver function in AZA/MMF/CYC users)	D	A	90.9	8.31 ± 2.81
8.9 Prevention of infective complications during immunosuppressive therapies	—	—	93.1	8.60 ± 2.67
9. Renal replacement therapies in LN				
9.1 All modalities of renal replacement therapies are suitable and effective in LN patients	B	A	88.6	7.64 ± 3.08
9.2 Immunosuppressive therapies in LN patients undergoing maintenance dialysis may be tapered with caution unless extra-renal activity is present	C	B	94.0	8.13 ± 1.40
9.3 Renal transplantation should be considered when extra-renal lupus activity is quiescent	C	B	81.0	7.55 ± 2.07

Abbreviations: BMD, bone mineral density; CKD, chronic kidney disease; DEXA, dual energy X-ray absorptiometry; LN, lupus nephritis; LOE, level of evidence; SLE, systemic lupus erythematosus; SOR, strength of recommendation.
[a]Mean score (0–10 points on a Likert scale; higher score indicates greater agreement).

and management of comorbidities, and renal replacement therapy for LN. The consensus level of ≥80% for all the statements and a mean agreement score of ≥7.5 (out of 10 points) was achieved.

3 | Overarching Principles (Statements 1.1–1.5)

Treatment of LN should be a shared decision between physicians and patients, taking into account the availability of health care resources. Delphi members universally agreed that the goals of LN therapy are to induce remission, minimize flares, preserve renal function, and reduce treatment-related morbidities and mortality without compromising quality of life. Non-adherence to medications is fairly common in patients with SLE, which may lead to a suboptimal clinical response and disease flares [25, 26], and is particularly a problem in the Asia-Pacific region because of the accessibility to health care and expensive drugs, as well as cultural belief and the use of complementary medicine [27, 28]. Monitoring for treatment adherence is underscored in our consensus. Patient education and early identification of non-adherence and its reasons by better communication, assisted by drug level monitoring if appropriate, will help improve the adherence rate [29].

4 | Screening, Diagnosis, and Monitoring of LN (Statements 2.1–2.7)

Clinical symptoms and signs of renal involvement should be evaluated in all SLE patients. Urine protein should be assessed at every visit and periodic assessment of serum albumin and creatinine, estimated glomerular filtration rate (eGFR), anti-dsDNA, and complement levels should be performed depending on the clinical status of patients. Urine for active urinary sediments should be obtained when renal activity is suspected. There are no studies that investigate the optimal follow-up intervals for LN patients, and these depend on the phase of treatment, intensity of therapies, clinical response, and the presence of comorbidities and treatment-related complications. We recommend frequent follow-up (e.g., every 1–4 weeks) initially for patients with active LN, with adjustment of the intervals according to clinical response and complications. Stable LN patients may be followed at intervals of 3–6 months.

As there are no studies that investigate the indications of renal biopsy in SLE, these are mainly based on expert opinions [30]. We recommend a renal biopsy to be performed unless contraindicated when there is suspicion of kidney involvement by SLE, as indicated by the presence of persistent proteinuria ≥1.0 g/24 h (uP/Cr ≥1.0 mg/mg); or ≥0.5 g/24 h (uP/Cr ≥0.5 mg/mg) in the presence of active urinary sediments; or persistent/unexplained deterioration in renal function. The ISN/RPS classifications and NIH activity/chronicity scoring system should be used to assess for the histologic class, activity, and chronicity [31, 32]. Additional features such as podocytopathy, microangiopathy, and interstitial inflammation should also be reported because these are important determinants of renal prognosis in addition to glomerular pathologies and affect the choice of initial therapies [31–33].

5 | Initial (Induction) Therapy for Lupus Nephritis (Statement 3.1–5.4)

Delphi members strongly agreed that immunosuppressive therapies should be administered to biopsy-confirmed active class III/IV ± V, pure class V (with uP/Cr ≥2.0 mg/mg and hypoalbuminemia) or class I/II (with significant podocytopathy or nephrotic range of proteinuria) LN patients. Cohort studies and systematic reviews have shown that the prognosis of class III/IV disease was worse than other histological types of LN [34–39]. However, owing to the paucity of evidence, the proteinuria threshold for immunosuppressive therapies for pure class V and class I/II LN is largely based on expert opinions [40, 41] (statements 3.1–3.3).

When kidney biopsy is not feasible or there are contraindications or reluctance to this procedure, the choice of therapies should be individualized based on the best judgment from clinical parameters (statement 3.4).

The first-line option for Asian patients with active class III/IV ± V LN is a combination of moderate doses of glucocorticoids (GCs) with one of the following: (1) mycophenolic acid analogues (MPAA) (mycophenolate mofetil [MMF] or mycophenolic acid [MPA]); (2) standard-dose intravenous (IV) cyclophosphamide (CYC); or (3) calcineurin inhibitor (CNI) (statements 4.1–4.2). The GC regimens used in the treatment of LN vary tremendously in previous clinical trials and real-world experience. More recent RCTs in LN have used lower doses of oral prednisolone for initial therapy [42, 43] and intravenous pulses of methylprednisolone followed by lower doses of oral prednisone with rapid tapering is the protocol of newer LN trials [44, 45]. Lower doses of GCs are likely to be efficacious when used early with other non-GC immunosuppressive drugs. In view of this, we recommend moderate doses of GCs as part of the treatment regimens of LN (statement 4.1).

Pivotal RCTs that showed non-inferiority of MMF to standard-dose IV CYC pulses [20, 46–49]. Moreover, MMF has been shown to have similar efficacy to daily oral CYC in a small RCT [50], and multiple observational or retrospective studies showed comparative efficacy of MMF with IV pulse CYC in LN [51–54]. A meta-analysis of 45 clinical trials confirmed similar efficacy between MMF and IV CYC in LN [55]. The enteric-coated MPA preparation has the advantage of delivery into the small intestine without being released in the stomach, thus causing less gastric irritation [56]. Enteric-coated MPA has been shown to be well tolerated and efficacious in LN in several single-arm longitudinal studies [57–60].

Different from the 2021 recommendations [23], the GC/CNI combination is now one of the first-line options for the initial treatment of LN. Although cyclosporin A was shown to have similar efficacy to IV pulse CYC in an RCT [61, 62], it is not a preferred CNI in the treatment of LN because of the cosmetic side effects and the higher rate of hyperlipidemia and elevated blood pressure [63, 64]. Several major RCTs of LN have shown non-inferiority of tacrolimus to MMF or standard-dose IV CYC in terms of efficacy at 6 months [42, 43, 65, 66]. Systematic reviews and meta-analyses performed at different

periods of time confirmed the non-inferiority or even superiority of tacrolimus to CYC in LN [67–69]. Moreover, in the same meta-analyses [67, 69], tacrolimus was shown to be equally effective as MMF. Considerable real-world experience of CNI, in particular tacrolimus, in LN has been reported in the Asia-Pacific regions [70–77]. Tacrolimus may be difficult to titrate in patients with impaired renal function, but the risk of CNI-related toxicities could be minimized when the trough tacrolimus level was maintained between 4 and 6 ng/mL [42, 43, 78, 79] (Figure 1).

Low-dose CYC (IV 500 mg 2-weekly for six doses) followed by azathioprine (AZA) has been studied in a European RCT in comparison with the standard-dose IV CYC pulses [80, 81]. Results showed that low-dose CYC was similar in efficacy to the standard-dose regimen at 10 years in terms of the rates of doubling of serum creatinine, end-stage renal failure, and death. Although this RCT was not powered to detect a difference between the two CYC treatment arms, adverse effects such as serious infection were reduced in the low-dose CYC regimen [82]. Moreover, serum anti-Müllerian hormone level, which is a surrogate for ovarian reserve, was not affected by the low-dose CYC as compared to the standard-dose CYC regimens [83]. However, in view of the paucity of data on the low-dose CYC regimen in Asian patients [84], it is reserved as a second-line option in special situations such as in patients at risk of infective complications but without poor prognostic factors (statement 4.3).

Cohort studies of LN in Europe have shown that failure to achieve a uP/Cr of less than 0.7–0.8 mg/mg at month 12 of treatment was associated with poorer renal prognosis at 10 years [85, 86]. This is confirmed by a longitudinal study of Asian LN patients, which showed that improvement of uP/Cr to less than 0.75 mg/mg at month 18 best predicted a better renal outcome at year 10 of immunosuppressive therapy [42]. Thus, we recommend the target of LN therapy is improvement of uP/Cr by 25% by 3 months, 50% by 6 months, and <0.75 mg/mg by 12 months (statement 4.4).

Pure membranous LN comprises only one-fifth of all cases of LN, and major therapeutic trials are lacking [87]. For the treatment of this histological type of LN, we suggest the early use of renin-angiotensin system (RAS) blocking agents before considering immunosuppression, which is indicated in patients with significant proteinuria (uP/Cr ≥ 2.0 mg/mg) with hypoalbuminemia (statement 5.1). As there is no direct evidence of RAS blockade in LN, its benefits are extrapolated from studies in non-diabetic nephropathy and idiopathic membranous nephropathy [88–90]. The first-line immunosuppressive treatment options are GCs combined with either MPAA or CNI, based on the non-inferiority of MMF to CYC or tacrolimus in subgroup analyses of major RCTs [42, 43, 91] and evidence from observational studies [92–95] (statement 5.2). Moreover, an RCT [96] and two meta-analyses have shown that the combination of GC and another non-GC immunosuppressive agent such as MMF or CNI is more effective than GC alone in the treatment of pure class V LN [97, 98]. Older observational studies have shown efficacy and safety of GC combined with oral or standard-dose IV CYC [99, 100] or azathioprine [100–102] in pure membranous LN. A subgroup analysis of an RCT showed superiority of a low-dose combination of MMF and tacrolimus to standard-dose IV

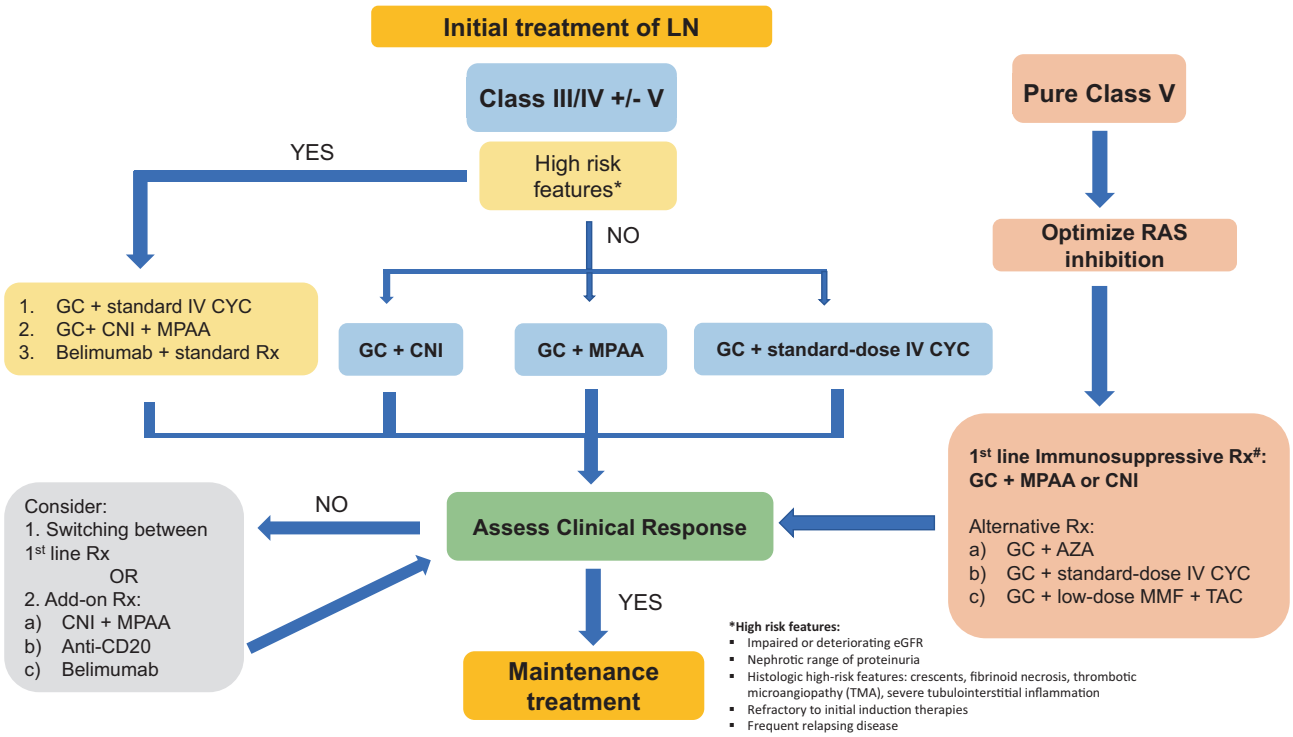

FIGURE 1 | Algorithm for initial treatment of lupus nephritis. LN, lupus nephritis; GC, glucocorticoid; IV, intravenous; CYC, cyclophosphamide; CNI, calcineurin inhibitor; MPAA, mycophenolic acid analogue; RAS, renin angiotensin system; Rx, treatment; AZA, azathioprine; TAC, tacrolimus.

CYC in pure class V LN [79]. Therefore, we recommend azathioprine (AZA), CYC, or a low-dose combination of MMF and tacrolimus as alternative treatment options for this histological subtype of LN (statement 5.3).

6 | Subsequent/Maintenance Therapy for LN (Statements 6.1–6.7)

Longitudinal cohort studies have reported a high rate of flare of LN upon discontinuation of immunosuppression [103, 104]. As a result, maintenance immunosuppressive therapies are recommended for LN (statement 6.1). In a recent RCT testing for the discontinuation of immunosuppressive agents while continuing low-dose GC and hydroxychloroquine in patients with remitted severe LN for 2–3 years, a significant increase in renal flares was observed at month 24 in the immunosuppression discontinuation group [105]. Another multi-center RCT in the US also demonstrated a trend of more renal flares upon discontinuation of MMF as compared to continuation of the drug in patients with quiescent SLE (76% with LN) for at least 1–2 years, 70% of whom had LN, at week 60 [106]. Finally, in a multicenter RCT conducted in France, continuation of low-dose prednisone (< 5 mg/day) was associated with a significantly lower risk of SLE flares at 1 year compared to discontinuation in patients with stable SLE for ≥ 1 year, 38% of whom had LN [107]. The increase in renal and non-renal flares of SLE in these studies upon discontinuation of low-dose GCs or non-GC immunosuppressive agents could be partially related to the relatively short duration of disease quiescence at enrollment (≥ 1–2 years). As prevention of renal flares is one of the treatment goals of LN, we recommend maintenance immunosuppressive therapy should continue for at least 3 years for LN (statement 6.2), and the duration of maintenance treatment may be prolonged in patients at risk of relapse or renal progression. This is supported by a long-term study of the efficacy of MMF or tacrolimus treatment of LN in Asian patients that reported a duration of maintenance therapy of < 62.5 months best predicted the first renal flare by receiver operating characteristic (ROC) analysis [42] and is in line with the 2023 updated EULAR recommendations [108]. A daily dose of prednisolone of ≤ 5 mg should be used for maintenance to minimize adverse effects. The decision to discontinue GCs and the tempo for tapering should be individualized (statement 6.6).

The ALMS maintenance phase RCT demonstrated superiority of MMF (2 g/day) over azathioprine (AZA) (2 mg/kg/day) in the reduction of a composite outcome of treatment failure over 3 years, defined as death, ESRD, doubling of the serum creatinine, renal flare, or rescue therapy, in those who responded to induction therapy with either IV CYC or MMF [109]. However, another European multicenter RCT did not show superiority of MMF over AZA, although patients were switched to MMF/AZA regardless of the initial response to low-dose CYC induction therapy of LN [110, 111]. Two RCTs also showed similar efficacy of MMF with AZA as maintenance therapy of LN after initial CYC induction [112, 113], and meta-analyses of RCTs did not reveal significant differences between MMF and AZA as maintenance therapy of LN [114–116]. However, leukopenia was more common with MMF than AZA. Taking into account the drug cost and accessibility in the Asia-Pacific region, we recommend lower doses of MPAA (MMF or MPA) or AZA to be considered as first-line options for maintenance therapy of LN (statement 6.3). Patients who were treated with MPAA initially should follow with a lower dose of the same drug instead of switching to AZA because the latter approach was associated with the highest risk of flare as demonstrated in the ALMS study [109] (statement 6.4). The CNIs are alternatives for maintenance therapy for contraindication or intolerance to MMF or AZA, and the CNIs or AZA are preferred in patients who have a conception plan (statement 6.5) because multiple observational studies have reported the safety of the CNIs and AZA during lupus pregnancies [117–120]. Leflunomide has been used as maintenance therapy of LN after initial treatment with IV pulse CYC, and similar efficacy was reported with AZA in terms of renal and non-renal flares [121]. However, there is a general lack of experience of using this drug for LN maintenance in the Delphi panel. Finally, patients who receive initial biological therapy may continue treatment depending on clinical response and residual renal activity (statement 6.7). Extended observation from the BLISS-LN study [122] and several long-term observational studies of rituximab in LN demonstrated efficacy and safety [123–126] (Figure 2).

7 | Treatment of LN at Risk of Renal Function Deterioration (Statements 7.1–7.6)

There were discussions about the indications for upfront combination of GCs, MPAA, or CYC with the CNI or the biological agents, which are recommended by the recently updated KDIGO and EULAR guidelines [40, 108]. Evidence from two more recent RCTs on belimumab (BLISS-LN) and voclosporin (AURORA-1), a newer generation CNI, when combined with standard therapies as initial therapies, showed augmented renal response rates after 104 and 52 weeks, respectively, without an increased risk of serious adverse events [44, 127], although the effect size of treatment compared to placebo is not particularly impressive [128]. Belimumab has also been shown to be equally effective in the Asian subgroup of the BLISS-LN study [129]. Owing to the issues of cost-effectiveness and increased risk of infection in susceptible patients, we recommend upfront triple immunosuppression (i.e., GCs plus MMF or low-dose CYC with belimumab; GCs plus MMF and CNIs) in patients at risk of progression and kidney function deterioration (statements 7.3 and 7.4). This is different from the 2021 APLAR SLE management guideline in which triple immunosuppression was only recommended for refractory LN [23].

Clinical features that indicate poor LN prognosis are listed in statement 7.1, and they have been associated with more aggressive renal disease and worse prognosis in LN in observational studies [34, 39, 130–138]. The standard dose IV CYC is also an option for aggressive renal disease at first presentation or during relapses, based on its long track record in the treatment of severe LN [104, 139–142] (statement 7.4). A subgroup analysis of patients with an initial eGFR of < 30 mL/min in the ALMS study showed similar efficacy of MMF with CYC [143]. Pooled data from several studies showed that CYC tended to be more effective than MMF in the long-term preservation of renal function in more severe LN [144]. However, treatment decisions should be individualized after judging the overall clinical status,

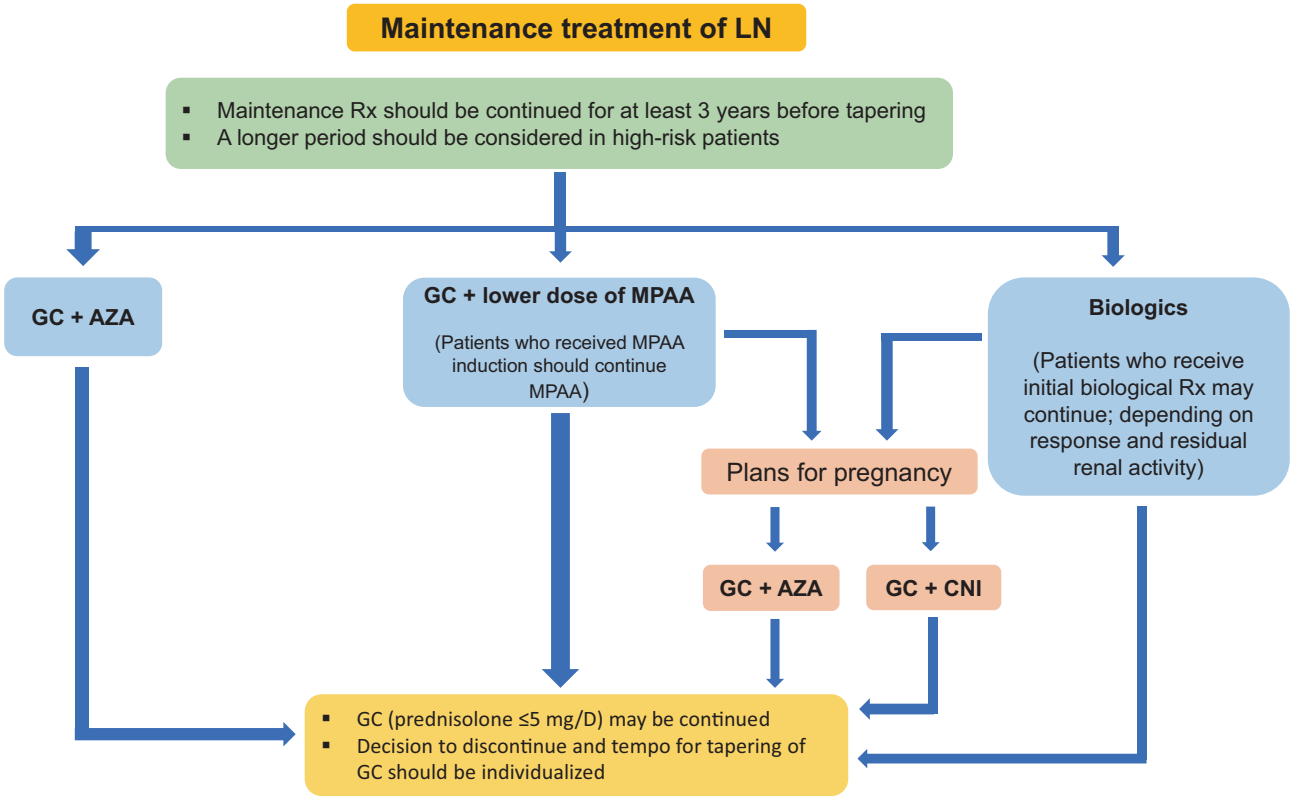

FIGURE 2 | Algorithm for maintenance treatment of lupus nephritis. LN, lupus nephritis; Rx, treatment; GC, glucocorticoid; AZA, azathioprine; MPAA, mycophenolic acid analogue; CNI, calcineurin inhibitor.

contraindications to certain regimens, as well as the preferences of patients.

We recommend a repeat renal biopsy in patients with suspected residual or worsening renal activity despite immunosuppressive therapies, renal flare, and/or deterioration in renal function, and to guide switching or tapering of immunosuppressive therapies (statement 7.2). This is based on the observation that clinical parameters such as proteinuria correlate poorly with renal histologic activity [145–149]. In the absence of validated biomarkers for monitoring of LN, histological examination is still the gold standard to evaluate for residual renal activity and the degree of scarring. Prospective studies have also shown that routine post-treatment repeat renal biopsy at month 12 could guide switching or tapering of immunosuppressive agents [148–153].

Retrospective data indicated that MMF was non-inferior or even superior to CYC in more serious proliferative LN [154, 155]. However, interpretation of these retrospective case series should be taken with caution as there might be selection and publication bias. The CNIs have also been shown to have similar efficacy with either MMF or CYC in RCTs and observational studies [42, 43, 61, 62, 65, 66]. Therefore, switching among different regimens (MMF/CNI/CYC) could be considered in patients who respond sub-optimally to initial therapies for LN (statement 7.5).

Triple immunosuppression, such as the combination of GC and MMF with CNI, and the addition of belimumab or rituximab to standard therapies are also therapeutic options for refractory LN (statement 7.6). The addition of tacrolimus to MMF has been shown to be effective in LN patients who responded sub-optimally to MMF in multiple single-arm studies [78, 156–160]. In fact, several RCTs have reported better efficacy of combining CNIs (such as tacrolimus or voclosporin) with GC and MMF in terms of renal response for the initial treatment of severe LN [44, 79, 161]. Despite the negative result from a RCT (LUNAR) [162], rituximab has long been used off-label to treat refractory LN [163]. Retrospective open-label single-arm observational studies have reported efficacy of rituximab in 50%–80% of Asian and non-Asian LN patients with unfavorable responses to initial therapy [164–176].

As aforementioned, recent data suggest the addition of belimumab to MMF or low-dose CYC enhances the response rate of LN at 2 years (BLISS-LN) [127]. A 28-week open-label extension of the BLISS-LN study showed an increase in primary renal response rate in both the placebo-to-belimumab and belimumab-to-belimumab groups of patients [122]. Therefore, the addition of belimumab to an MMF- or CYC-based regimen is one of the options for refractory LN. A pharmacokinetic study demonstrated that the steady-state belimumab concentrations were comparable between weekly subcutaneous (SC) and monthly IV dosing of belimumab [177]. Therefore, SC belimumab can also be used for the treatment of LN. However, it should be noted that belimumab may not be as efficacious in the subgroup of patients with uP/Cr ≥ 3.0 mg/mg in the BLISS-LN study [178].

8 | Adjunctive Therapies and Management of Comorbidities (Statements 8.1–8.9)

Hydroxychloroquine (HCQ) is an anti-malarial drug that has been shown to have benefits in reducing SLE activity, preventing

flares, and enhancing the response rate of LN, and hence reducing renal damage and mortality [179, 180]. In addition to its immunomodulatory effects, HCQ also improves lipid profile and glucose level in patients with SLE, and cohort studies have also shown a beneficial effect of HCQ on reducing the risk of thrombosis [29]. There is excellent agreement among Delphi members on the use of HCQ in all SLE patients, including those with LN (statement 8.1). Despite the absence of RCTs comparing HCQ and placebo, multiple cohort and observational studies have reported benefits of HCQ in increasing the renal response rate and reducing the risk of renal function deterioration in LN, including pure membranous LN [181, 182].

Lifestyle modification, renin-angiotensin (RAS) blockade, control of cardiovascular risk factors such as blood pressure and lipid level, and prevention of osteoporosis and drug-related toxicities, including infective complications, are important in the management of LN (statements 8.2, 8.3, 8.5, 8.6, 8.8, and 8.9). The reno-protective effects of RAS blockade are extrapolated from other non-LN glomerular diseases and chronic kidney disease (CKD) [183]. Two studies in SLE also demonstrated RAS blockade was associated with a delay in the onset of nephritis, proteinuria reduction, renal function stabilization, and reduced renal flares [184, 185].

Hypertension is a risk factor for progression of CKD. The European Society of Hypertension (ESH) recommends a blood pressure (BP) target of less than 130/80 mmHg in patients with proteinuric non-diabetic CKD [186]. Despite the lack of specific RCTs of BP control in LN, a small single-arm study reported benefits of a tight BP control protocol, along with adherence to dietary restriction and treatment and cessation of smoking, in reducing proteinuria [187]. Another retrospective study of membranous LN reported that better BP control was associated with a lower risk of doubling of serum creatinine, ESRD, or death [188]. Therefore, Delphi members agreed that blood pressure control in LN patients should be targeted to less than 130/80 mmHg (statement 8.5).

Hyperlipidemia is one of the traditional cardiovascular risk factors that are more prevalent in SLE/LN patients than the general population [189–192]. While there is inadequate evidence to show the efficacy of lipid-lowering in halting CKD progression [193], controlling hyperlipidemia is beneficial in reducing cardiovascular risk in patients with LN [194]. We recommended achievement of an LDL-cholesterol level of less than 2.6 mmol/L (100 mg/dL) in patients with LN. A tighter control of level to less than 1.8 mmol/L (70 mg/dL) should be targeted in patients with a past history of major adverse cardiovascular events or multiple cardiovascular risk factors (statement 8.6). The proprotein convertase subtilisin kexin9 (PCSK9) inhibitors are novel agents that lower LDL-cholesterol and cardiovascular risk effectively [195]. While there are no specific studies of the PCSK9 inhibitors in SLE, they are recommended for patients with excessively high cardiovascular risk who cannot achieve the cholesterol target with the statins and other lipid-lowering therapies, including those who are intolerant to the latter drugs.

The sodium-glucose transport protein 2 (SGLT2) inhibitors have been shown to halt CKD progression in patients with diabetic and non-diabetic kidney disease [196–198]. Although the autoimmune glomerulonephropathies, including LN, are underrepresented in these pivotal studies, the use of SGLTs inhibitors may be considered in LN patients with CKD and persistent proteinuria [199]. Other non-pharmacological measures that may help retard CKD progression, such as a lower sodium and protein diet, avoidance of nephrotoxic drugs, maintaining an optimal body mass index, lowering of uric acid level, and cessation of smoking, should also be undertaken [200].

Calcium and vitamin D should be routinely used in LN patients unless contraindicated (statement 8.7). Screening and regular assessment of bone mineral density (BMD) (by dual-energy X-ray absorptiometry [DEXA] scan) and treatment with antiresorptive or anabolic agents should follow the relevant national glucocorticoid-induced osteoporosis recommendations.

Anticoagulation is indicated in patients with histologic evidence of antiphospholipid (aPL) nephropathy (e.g., acute/chronic renal vascular or glomerular lesions such as thrombotic microangiopathy [TMA] or renal artery thrombosis) (statement 8.4). In a multicenter retrospective study of LN patients with histologic TMA lesions and antiphospholipid antibodies, the use of anticoagulation was associated with higher complete renal response than non-users [201]. Patients with persistent nephrotic syndrome and antiphospholipid antibodies are at significant risk of thromboembolic events [202, 203]. Anticoagulation may be considered in these patients.

Adverse effects to immunosuppressive drugs should be regularly monitored (statement 8.8). For instance, glucose level should be monitored in users of GCs and the CNIs. Blood counts and liver function should be assessed regularly in those treated with CYC, AZA, and MPAA. The genotypes of thiopurine S-methyltransferase (TMPT) enzyme, if available, should be obtained before initiation of AZA to reduce the risk of profound leukopenia. For the prevention of infective complications during immunosuppressive therapies of SLE, please refer to our 2021 recommendations (statement 8.9) [23].

9 | Renal Replacement Therapies in LN (Statements 9.1–9.3)

Multiple retrospective studies and large registry data have reported respectable patients' survival in LN patients receiving different modalities of renal replacement therapies [204–220]. Some of these studies also reported comparable outcomes of kidney transplantation in LN and non-LN CKD patients. As in ESRD in non-SLE disease, post-renal transplanted LN patients had a better survival rate than those who were on dialysis while waiting for transplantation. Thus, all modalities of renal replacement therapies are suitable and effective in LN patients (statement 9.1) and the choice should take into consideration concomitant comorbidities, availability of kidney donors, health care resources, and local health policies, as well as the preference of patients.

Studies have suggested that clinical and serological activity of SLE would become more quiescent after reaching ESRD that was commenced on dialysis treatment [221, 222]. However, there is recent literature to indicate an increase in extra-renal flares of SLE in patients maintained on dialysis when immunosuppression was stopped, especially during the first year of dialysis [223, 224].

Tapering of immunosuppression in LN patients undergoing dialysis should be done with caution when extra-renal SLE activity is quiescent, taking into consideration prior history of SLE flares and adverse effects to treatment (statement 9.2).

Finally, we recommend kidney transplantation in LN patients to be considered when extra-renal SLE activity is quiescent (statement 9.3). In fact, few studies have investigated the optimal timing for kidney transplantation in LN patients. Historically, kidney transplantation is only considered when extra-renal SLE activity is quiescent for 3–12 months [225]. More recent evidence suggests that longer waiting time to transplant may be associated with equivalent or even worse outcomes among LN patients with ESRD [226]. Thus, patients with ESRD due to LN without clinically active SLE could be recommended for transplantation without a waiting time even when lupus serology is active [227].

10 | Conclusions

The APLAR recommendations for the management of LN are an update of the 2021 version [23] with a focus on LN. Our consensus provides an evidence-based but yet pragmatic approach to the management of LN, taking into account the level of evidence of therapies in the Asian subgroups of patients, cost-effectiveness, disparity in health care resources and reimbursement policies, as well as the accessibility to newer drugs in the Asia-Pacific region. We will continue to update the consensus statements upon the emergence of newer therapies that are available in the near future. Specific recommendations on the reproductive and pregnancy issues in LN and the associated antiphospholipid antibody syndrome are in progress.

Acknowledgments

We would like to thank the following members who had participated in the Delphi exercise: Drs. Alberta Hoi, Shamim Ahmed, Md. Nahiduzzaman Shazzad, Rowsan Ara, Zhuoli Zhang, Natalia Chu Oi Ciang, Shirley Chiu Wai Chan, Seyedeh Tahereh Faezi, Asal Adnan, Kimito Kawahata, Seung Cheol Shim, Benjamin Cheah Tien Eang, Danzan Nandin-Erdene, Buddhi Paudyal, Shahida Perveen, Maryanu Aamer, Evan Vista, Leonid Zamora, Samar A.Al Razaq Mohd. S. Alemadi, Howe Hwee Siew, Poh Yih Jia, GunenDrika Kasthuriratne, Chang-Youh Tsai, Nguyen Dinh Khoa, Jisoo Lee, Cho Mar Lwin, Anushka Ediriweera, Qian Wang, Kathryn Connelly, Kenji Oku, Nighat Mir Ahmad, Bilal Azeem Butt, Muhammad Rafaqat Hameed, Mitsuhiro Kawano, Jun Ishizaki, Elizabeth Lapid-Roasa, Maximus Yeung, Haitao Zhang, Jianfang Cai, Afiatin, Yingyos Avihingsanon, Bancha Satirapoj, Kajohnsak Noppakun, Adrian Liew, Alexander Tang, Su Mein Goh, Richard Kitching, Joanna Kent, Juan Javier Lichauco, Niansheng Yang, Cesarius Singgih Wahono, Sumariyono, Punchong Hanvivadhanakul, Yew-Kuang Cheng, Kristine Ng, Nicola Tugnet, Mandy Wong, Ms. Robelle Mae Tanangunan, Chee Ding Yin.

Author Contributions

All authors contribute equally to the core group discussion and establishment of the consensus statements.

Conflicts of Interest

Chi Chiu Mok: none. Ho So: none. Laniyati Hamijoyo: none. Nuntana Kasitanon: none. Der Yuan Chen: none. Sang Cheol Bae: none. Meng Tao Li: none. Sandra Navarra: consultation fee and speaker honorarium from Astra Zeneca and Boehringer Ingelheim; safety monitoring board for Biogen. Desmond Yat Hin Yap: financial support from Fresenius Kabi for conference attendance. Yoshiya Tanaka: grants from Behringer-Ingelheim, Taisho, Chugai; speaker honoraria from Abbvie, Eisai, Chugai, Eli-Lilly, Behringer-Ingelheim, GlaxoSmithKline, Taisho, AstraZeneca, Daiichi-Sankyo, Gilead, Pfizer, UCB, Asahikasei, Astellas.

Data Availability Statement

The authors have nothing to report.

References

1. C. C. Mok, R. W. S. Wong, and K. N. Lai, "Treatment of Severe Proliferative Lupus Nephritis: The Current State," *Annals of the Rheumatic Diseases* 62 (2003): 799–804.

2. C. C. Mok, "Systemic Lupus Erythematosus: Withdrawing Standard of Care Therapies in SLE Trials?," *Nature Reviews Rheumatology* 13 (2017): 328–330.

3. C. C. Mok, Y. K. O. Teng, R. Saxena, and Y. Tanaka, "Treatment of Lupus Nephritis: Consensus, Evidence and Perspectives," *Nature Reviews Rheumatology* 19 (2023): 227–238.

4. M. G. Tektonidou, A. Dasgupta, and M. M. Ward, "Risk of End-Stage Renal Disease in Patients With Lupus Nephritis, 1971-2015: A Systematic Review and Bayesian Meta-Analysis," *Arthritis and Rheumatology* 68 (2016): 1432–1441.

5. C. C. Mok, "Towards New Avenues in the Management of Lupus Glomerulonephritis," *Nature Reviews Rheumatology* 12 (2016): 221–234.

6. C. C. Mok, R. C. L. Kwok, and P. S. F. Yip, "Effect of Renal Disease on the Standardized Mortality Ratio and Life Expectancy of Patients With Systemic Lupus Erythematosus," *Arthritis and Rheumatism* 65 (2013): 2154–2160.

7. R. Kandane-Rathnayake, J. R. Kent, W. Louthrenoo, et al., "Longitudinal Associations of Active Renal Disease With Irreversible Organ Damage Accrual in Systemic Lupus Erythematosus," *Lupus* 28 (2019): 1669–1677.

8. S. Kharawala, G. Kaur, H. Shukla, et al., "Health-Related Quality of Life, Fatigue and Health Utilities in Lupus Nephritis: A Systematic Literature Review," *Lupus* 31 (2022): 1029–1044.

9. M. Jolly, S. Toloza, B. Goker, et al., "Disease-Specific Quality of Life in Patients With Lupus Nephritis," *Lupus* 27 (2018): 257–264.

10. C. C. Mok, "Racial Difference in the Prognosis of Lupus Nephritis," *Nephrology* 15 (2010): 480–481.

11. Y. Tanaka, S. O'Neill, M. Li, I. C. Tsai, and Y. W. Yang, "Systemic Lupus Erythematosus: Targeted Literature Review of the Epidemiology, Current Treatment, and Disease Burden in the Asia Pacific Region," *Arthritis Care and Research* 74 (2022): 187–198.

12. R. W. Jakes, S. C. Bae, W. Louthrenoo, C. C. Mok, S. V. Navarra, and N. Kwon, "Systematic Review of the Epidemiology of Systemic Lupus Erythematosus in the Asia-Pacific Region: Prevalence, Incidence, Clinical Features, and Mortality," *Arthritis Care and Research* 64 (2012): 159–168.

13. K. H. Costenbader, A. Desai, G. S. Alarcón, et al., "Trends in the Incidence, Demographics, and Outcomes of End-Stage Renal Disease Due to Lupus Nephritis in the US From 1995 to 2006," *Arthritis and Rheumatism* 63 (2011): 1681–1688.

14. B. I. Freedman, C. D. Langefeld, K. K. Andringa, et al., "End-Stage Renal Disease in African Americans With Lupus Nephritis Is Associated With APOL1," *Arthritis and Rheumatism* 66 (2014): 390–396.

15. C. C. Mok, "Polygenic Risk Score: The Potential Role in the Management of Systemic Lupus Erythematosus," *RMD Open* 10 (2024): e004156.

16. Y. C. Kwon, E. Ha, H. H. Kwon, et al., "Higher Genetic Risk Loads Confer More Diverse Manifestations and Higher Risk of Lupus Nephritis in Systemic Lupus Erythematosus," *Arthritis and Rheumatism* 75 (2023): 1566–1572.

17. Y. J. Chen, T. H. Hsiao, Y. C. Lin, et al., "Polygenic Risk Score Predicts Earlier-Onset Adult Systemic Lupus Erythematosus and First-Year Renal Diseases in a Taiwanese Cohort," *RMD Open* 10 (2024): e003293.

18. C. C. Mok, "Prognostic Stratification of Lupus Nephritis: The Importance of Renal Histology," *Journal of Rheumatology* 50 (2023): 1095–1096.

19. C. C. Mok, "Prognostic Factors in Lupus Nephritis," *Lupus* 14 (2005): 39–44.

20. G. B. Appel, G. Contreras, M. A. Dooley, et al., "Mycophenolate Mofetil Versus Cyclophosphamide for Induction Treatment of Lupus Nephritis," *Journal of the American Society of Nephrology* 20 (2009): 1103–1112.

21. E. F. Mysler, A. J. Spindler, R. Guzman, et al., "Efficacy and Safety of Ocrelizumab in Active Proliferative Lupus Nephritis: Results From a Randomized, Double-Blind, Phase III Study," *Arthritis and Rheumatism* 65 (2013): 2368–2379.

22. K. M. Thong and T. M. Chan, "Infectious Complications in Lupus Nephritis Treatment: A Systematic Review and Meta-Analysis," *Lupus* 28 (2019): 334–346.

23. C. C. Mok, L. Hamijoyo, N. Kasitanon, et al., "The Asia-Pacific League of Associations for Rheumatology Consensus Statements on the Management of Systemic Lupus Erythematosus," *Lancet Rheumatology* 3 (2021): e517–e531.

24. D. Atkins, D. Best, P. A. Briss, et al., "Grading Quality of Evidence and Strength of Recommendations," *BMJ* 328 (2004): 1490.

25. Y. Nguyen, B. Blanchet, M. B. Urowitz, et al., "Association Between Severe Nonadherence to Hydroxychloroquine and Systemic Lupus Erythematosus Flares, Damage, and Mortality in 660 Patients From the SLICC Inception Cohort," *Arthritis and Rheumatism* 75 (2023): 2195–2206.

26. N. Costedoat-Chalumeau, J. Pouchot, G. Guettrot-Imbert, et al., "Adherence to Treatment in Systemic Lupus Erythematosus Patients," *Best Practice & Research. Clinical Rheumatology* 27 (2013): 329–340.

27. P. S. Helliwell and G. Ibrahim, "Ethnic Differences in Responses to Disease Modifying Drugs," *Rheumatology* 42 (2003): 1197–1201.

28. K. Kumar, C. Gordon, V. Toescu, et al., "Beliefs About Medicines in Patients With Rheumatoid Arthritis and Systemic Lupus Erythematosus: A Comparison Between Patients of South Asian and White British Origin," *Rheumatology* 47 (2008): 690–697.

29. C. C. Mok, "Non-Adherence to Hydroxychloroquine in Systemic Lupus Erythematosus: The Elephant in the Clinic Room," *International Journal of Rheumatic Diseases* 27 (2024): e15188.

30. B. H. Hahn, M. A. McMahon, A. Wilkinson, et al., "American College of Rheumatology Guidelines for Screening, Treatment, and Management of Lupus Nephritis," *Arthritis Care and Research* 64 (2012): 797–808.

31. J. J. Weening, V. D. D'Agati, M. M. Schwartz, et al., "The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited," *Kidney International* 65 (2004): 521–530.

32. I. M. Bajema, S. Wilhelmus, C. E. Alpers, et al., "Revision of the International Society of Nephrology/Renal Pathology Society Classification for Lupus Nephritis: Clarification of Definitions, and Modified National Institutes of Health Activity and Chronicity Indices," *Kidney International* 93 (2018): 789–796.

33. L. H. Wu, F. Yu, Y. Tan, et al., "Inclusion of Renal Vascular Lesions in the 2003 ISN/RPS System for Classifying Lupus Nephritis Improves Renal Outcome Predictions," *Kidney International* 83 (2013): 715–723.

34. B. Obrișcă, R. Jurubiță, A. Andronesi, et al., "Histological Predictors of Renal Outcome in Lupus Nephritis: The Importance of Tubulointerstitial Lesions and Scoring of Glomerular Lesions," *Lupus* 27 (2018): 1455–1463.

35. C. C. Mok, R. W. Wong, and C. S. Lau, "Lupus Nephritis in Southern Chinese Patients: Clinicopathologic Findings and Long-Term Outcome," *American Journal of Kidney Diseases* 34 (1999): 315–323.

36. F. Farinha, R. J. Pepper, D. G. Oliveira, T. McDonnell, D. A. Isenberg, and A. Rahman, "Outcomes of Membranous and Proliferative Lupus Nephritis—Analysis of a Single-Centre Cohort With More Than 30 Years of Follow-Up," *Rheumatology* 59 (2020): 3314–3323.

37. A. Mahajan, J. Amelio, K. Gairy, et al., "Systemic Lupus Erythematosus, Lupus Nephritis and End-Stage Renal Disease: A Pragmatic Review Mapping Disease Severity and Progression," *Lupus* 29 (2020): 1011–1020.

38. E. Kapsia, S. Marinaki, I. Michelakis, et al., "New Insights Into an Overlooked Entity: Long-Term Outcomes of Membranous Lupus Nephritis From a Single Institution Inception Cohort," *Frontiers in Medicine* 9 (2022): 809533.

39. J. Rodelo, L. Aguirre, K. Ortegón, et al., "Predicting Kidney Outcomes Among Latin American Patients With Lupus Nephritis: The Prognostic Value of Interstitial Fibrosis and Tubular Atrophy and Tubulointerstitial Inflammation," *Lupus* 32 (2023): 411–423.

40. B. H. Rovin, I. M. Ayoub, T. M. Chan, et al., "Executive Summary of the KDIGO 2024 Clinical Practice Guideline for the Management of Lupus Nephritis," *Kidney International* 105 (2024): 31–34.

41. A. Fanouriakis, M. Kostopoulou, K. Cheema, et al., "2019 Update of the Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) Recommendations for the Management of Lupus Nephritis," *Annals of the Rheumatic Diseases* 79 (2020): 713–723.

42. C. C. Mok, L. Y. Ho, S. K. Y. Ying, M. C. Leung, C. H. To, and W. L. Ng, "Long-Term Outcome of a Randomised Controlled Trial Comparing Tacrolimus With Mycophenolate Mofetil as Induction Therapy for Active Lupus Nephritis," *Annals of the Rheumatic Diseases* 79 (2020): 1070–1076.

43. C. C. Mok, K. Y. Ying, C. W. Yim, et al., "Tacrolimus Versus Mycophenolate Mofetil for Induction Therapy of Lupus Nephritis: A Randomised Controlled Trial and Long-Term Follow-Up," *Annals of the Rheumatic Diseases* 75 (2016): 30–36.

44. B. H. Rovin, Y. K. O. Teng, E. M. Ginzler, et al., "Efficacy and Safety of Voclosporin Versus Placebo for Lupus Nephritis (AURORA 1): A Double-Blind, Randomised, Multicentre, Placebo-Controlled, Phase 3 Trial," *Lancet* 397 (2021): 2070–2080.

45. R. A. Furie, G. Aroca, M. D. Cascino, et al., "B-Cell Depletion With Obinutuzumab for the Treatment of Proliferative Lupus Nephritis: A Randomised, Double-Blind, Placebo-Controlled Trial," *Annals of the Rheumatic Diseases* 81 (2022): 100–107.

46. E. M. Ginzler, M. A. Dooley, C. Aranow, et al., "Mycophenolate Mofetil or Intravenous Cyclophosphamide for Lupus Nephritis," *New England Journal of Medicine* 353 (2005): 2219–2228.

47. L. M. Ong, L. S. Hooi, T. O. Lim, et al., "Randomized Controlled Trial of Pulse Intravenous Cyclophosphamide Versus Mycophenolate Mofetil in the Induction Therapy of Proliferative Lupus Nephritis," *Nephrology* 10 (2005): 504–510.

48. S. Mendonca, D. Gupta, S. Ali, and P. Gupta, "Mycophenolate Mofetil or Cyclophosphamide in Indian Patients With Lupus Nephritis: Which Is Better? A Single-Center Experience," *Saudi Journal of Kidney Diseases and Transplantation* 28 (2017): 1069–1077.

49. A. Sedhain, R. Hada, R. K. Agrawal, G. R. Bhattarai, and A. Baral, "Low Dose Mycophenolate Mofetil Versus Cyclophosphamide in the

Induction Therapy of Lupus Nephritis in Nepalese Population: A Randomized Control Trial," *BMC Nephrology* 19 (2018): 175.

50. T. M. Chan, F. K. Li, C. S. Tang, et al., "Efficacy of Mycophenolate Mofetil in Patients With Diffuse Proliferative Lupus Nephritis. Hong Kong-Guangzhou Nephrology Study Group," *New England Journal of Medicine* 343 (2000): 1156–1162.

51. Y. B. Joo, Y. M. Kang, H. A. Kim, et al., "Outcome and Predictors of Renal Survival in Patients With Lupus Nephritis: Comparison Between Cyclophosphamide and Mycophenolate Mofetil," *International Journal of Rheumatic Diseases* 21 (2018): 1031–1039.

52. N. Prasad, J. Kurian, V. Agarwal, et al., "Long-Term Outcomes of Lupus Nephritis Treated With Regimens Based on Cyclophosphamide and Mycophenolate Mofetil," *Lupus* 29 (2020): 845–853.

53. N. Ohkubo, S. Iwata, K. Nakano, et al., "Efficacy and Safety of High-Dose of Mycophenolate Mofetil Compared With Cyclophosphamide Pulse Therapy as Induction Therapy in Japanese Patients With Proliferative Lupus Nephritis," *Modern Rheumatology* 32 (2022): 1077–1085.

54. W. Pichaiwong, S. Lawanaskol, P. Phinyo, and T. Kitumnuaypong, "The Efficacy of Induction Treatment in Thai Patients With Lupus Nephritis: Observational Cohort Analysis," *Lupus* 32 (2023): 444–452.

55. L. K. Henderson, P. Masson, J. C. Craig, et al., "Induction and Maintenance Treatment of Proliferative Lupus Nephritis: A Meta-Analysis of Randomized Controlled Trials," *American Journal of Kidney Diseases* 61 (2013): 74–87.

56. D. Ranganathan, M. H. Abdul-Aziz, G. T. John, et al., "Pharmacokinetics of Enteric-Coated Mycophenolate Sodium in Lupus Nephritis (POEMSLUN)," *Therapeutic Drug Monitoring* 41 (2019): 703–713.

57. C. Kitiyakara, V. Ophascharoensuk, S. Changsirikulchai, et al., "Treatment of Lupus Nephritis and Primary Glomerulonephritis With Enteric-Coated Mycophenolate Sodium," *Clinical Nephrology* 69 (2008): 90–101.

58. M. Zeher, A. Doria, J. Lan, et al., "Efficacy and Safety of Enteric-Coated Mycophenolate Sodium in Combination With Two Glucocorticoid Regimens for the Treatment of Active Lupus Nephritis," *Lupus* 20 (2011): 1484–1493.

59. O. Traitanon, Y. Avihingsanon, V. Kittikovit, et al., "Efficacy of Enteric-Coated Mycophenolate Sodium in Patients With Resistant-Type Lupus Nephritis: A Prospective Study," *Lupus* 17 (2008): 744–751.

60. S. K. Mak, K. Y. Lo, M. W. Lo, et al., "Efficacy of Enteric-Coated Mycophenolate Sodium in Patients With Active Lupus Nephritis," *Nephrology* 13 (2008): 331–336.

61. J. Zavada, S. Pesickova, R. Rysava, et al., "Cyclosporine A or Intravenous Cyclophosphamide for Lupus Nephritis: The Cyclofa-Lune Study," *Lupus* 19 (2010): 1281–1289.

62. J. Závada, S. Sinikka Pesicková, R. Rysavá, et al., "Extended Follow-Up of the CYCLOFA-LUNE Trial Comparing Two Sequential Induction and Maintenance Treatment Regimens for Proliferative Lupus Nephritis Based Either on Cyclophosphamide or on Cyclosporine A," *Lupus* 23 (2014): 69–74.

63. C. C. Mok, "Calcineurin Inhibitors in Systemic Lupus Erythematosus," *Best Practice & Research. Clinical Rheumatology* 31 (2017): 429–438.

64. L. Penninga, E. I. Penninga, C. H. Møller, M. Iversen, D. A. Steinbrüchel, and C. Gluud, "Tacrolimus Versus Cyclosporin as Primary Immunosuppression for Lung Transplant Recipients," *Cochrane Database of Systematic Reviews* 31 (2013): CD008817.

65. Z. Zheng, H. Zhang, X. Peng, et al., "Effect of Tacrolimus vs Intravenous Cyclophosphamide on Complete or Partial Response in Patients With Lupus Nephritis: A Randomized Clinical Trial," *JAMA Network Open* 5 (2022): e224492.

66. N. Kamanamool, A. Ingsathit, S. Rattanasiri, et al., "Comparison of Disease Activity Between Tacrolimus and Mycophenolate Mofetil in Lupus Nephritis: A Randomized Controlled Trial," *Lupus* 27 (2018): 647–656.

67. X. Zhang, L. Ji, L. Yang, X. Tang, and W. Qin, "The Effect of Calcineurin Inhibitors in the Induction and Maintenance Treatment of Lupus Nephritis: A Systematic Review and Meta-Analysis," *International Urology and Nephrology* 48 (2016): 731–743.

68. Y. H. Lee, H. S. Lee, S. J. Choi, J. Dai Ji, and G. G. Song, "Efficacy and Safety of Tacrolimus Therapy for Lupus Nephritis: A Systematic Review of Clinical Trials," *Lupus* 20 (2011): 636–640.

69. J. Hannah, A. Casian, and D. D'Cruz, "Tacrolimus Use in Lupus Nephritis: A Systematic Review and Meta-Analysis," *Autoimmunity Reviews* 15 (2016): 93–101.

70. H. Tanaka, S. Watanabe, T. Aizawa-Yashiro, et al., "Long-Term Tacrolimus-Based Immunosuppressive Treatment for Young Patients With Lupus Nephritis: A Prospective Study in Daily Clinical Practice," *Nephron. Clinical Practice* 121 (2012): c165–c173.

71. T. Takeuchi, N. Wakasugi, T. Hashida, S. Uno, and H. Makino, "Long-Term Safety and Effectiveness of Tacrolimus in Patients With Lupus Nephritis in Japan: 10-Year Analysis of the Real-World TRUST Study," *Journal of Rheumatology* 51 (2024): 613–621.

72. C. C. Mok, K. H. Tong, C. H. To, Y. P. Siu, and T. C. Au, "Tacrolimus for Induction Therapy of Diffuse Proliferative Lupus Nephritis: An Open-Labeled Pilot Study," *Kidney International* 68 (2005): 813–817.

73. N. Miyasaka, S. Kawai, and H. Hashimoto, "Efficacy and Safety of Tacrolimus for Lupus Nephritis: A Placebo-Controlled Double-Blind Multicenter Study," *Modern Rheumatology* 19 (2009): 606–615.

74. Y. Asamiya, K. Uchida, S. Otsubo, T. Takei, and K. Nitta, "Clinical Assessment of Tacrolimus Therapy in Lupus Nephritis: One-Year Follow-Up Study in a Single Center," *Nephron. Clinical Practice* 113 (2009): c330–c336.

75. H. Ogawa, H. Kameda, H. Nagasawa, et al., "Prospective Study of Low-Dose Cyclosporine A in Patients With Refractory Lupus Nephritis," *Modern Rheumatology* 17 (2007): 92–97.

76. L. S. Tam, E. K. Li, C. B. Leung, et al., "Long-Term Treatment of Lupus Nephritis With Cyclosporin A," *QJM* 91 (1998): 573–580.

77. L. W. Fu, L. Y. Yang, W. P. Chen, and C. Y. Lin, "Clinical Efficacy of Cyclosporin a Neoral in the Treatment of Paediatric Lupus Nephritis With Heavy Proteinuria," *British Journal of Rheumatology* 37 (1998): 217–221.

78. D. Y. H. Yap, P. H. Li, C. Tang, et al., "Long-Term Results of Triple Immunosuppression With Tacrolimus Added to Mycophenolate and Corticosteroids in the Treatment of Lupus Nephritis," *Kidney International Reports* 7 (2022): 516–525.

79. Z. Liu, H. Zhang, Z. Liu, et al., "Multitarget Therapy for Induction Treatment of Lupus Nephritis: A Randomized Trial," *Annals of Internal Medicine* 162 (2015): 18–26.

80. F. A. Houssiau, C. Vasconcelos, D. D'Cruz, et al., "Immunosuppressive Therapy in Lupus Nephritis: The Euro-Lupus Nephritis Trial, a Randomized Trial of Low-Dose Versus High-Dose Intravenous Cyclophosphamide," *Arthritis and Rheumatism* 46 (2002): 2121–2131.

81. F. A. Houssiau, C. Vasconcelos, D. D'Cruz, et al., "The 10-Year Follow-Up Data of the Euro-Lupus Nephritis Trial Comparing Low-Dose and High-Dose Intravenous Cyclophosphamide," *Annals of the Rheumatic Diseases* 69 (2010): 61–64.

82. C. C. Mok, "Cyclophosphamide for Severe Lupus Nephritis: Where Are We Now?," *Arthritis and Rheumatism* 50 (2004): 3748–3750.

83. F. Tamirou, S. N. Husson, D. Gruson, F. Debiève, B. R. Lauwerys, and F. A. Houssiau, "Brief Report: The Euro-Lupus Low-Dose Intravenous Cyclophosphamide Regimen Does Not Impact the Ovarian Reserve, as Measured by Serum Levels of Anti-Müllerian Hormone," *Arthritis and Rheumatism* 69 (2017): 1267–1271.

84. M. Rathi, A. Goyal, A. Jaryal, et al., "Comparison of Low-Dose Intravenous Cyclophosphamide With Oral Mycophenolate Mofetil in the Treatment of Lupus Nephritis," *Kidney International* 89 (2016): 235–242.

85. F. Tamirou, B. R. Lauwerys, M. Dall'Era, et al., "A Proteinuria Cut-Off Level of 0.7 g/Day After 12 Months of Treatment Best Predicts Long-Term Renal Outcome in Lupus Nephritis: Data From the MAINTAIN Nephritis Trial," *Lupus Science & Medicine* 2 (2015): e000123.

86. M. Dall'Era, M. G. Cisternas, D. E. Smilek, et al., "Predictors of Long-Term Renal Outcome in Lupus Nephritis Trials: Lessons Learned From the Euro-Lupus Nephritis Cohort," *Arthritis and Rheumatism* 67 (2015): 1305–1313.

87. C. C. Mok, "Membranous Nephropathy in Systemic Lupus Erythematosus: A Therapeutic Enigma," *Nature Reviews. Nephrology* 5 (2009): 212–220.

88. "Randomised Placebo-Controlled Trial of Effect of Ramipril on Decline in Glomerular Filtration Rate and Risk of Terminal Renal Failure in Proteinuric, Non-diabetic Nephropathy. The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia)," *Lancet* 349 (1997): 1857–1863.

89. P. Ruggenenti, L. Mosconi, G. Vendramin, et al., "ACE Inhibition Improves Glomerular Size Selectivity in Patients With Idiopathic Membranous Nephropathy and Persistent Nephrotic Syndrome," *American Journal of Kidney Diseases* 35 (2000): 381–391.

90. G. Kosmadakis, V. Filiopoulos, C. Georgoulias, N. Tentolouris, and S. Michail, "Comparison of the Influence of Angiotensin-Converting Enzyme Inhibitor Lisinopril and Angiotensin II Receptor Antagonist Losartan in Patients With Idiopathic Membranous Nephropathy and Nephrotic Syndrome," *Scandinavian Journal of Urology and Nephrology* 44 (2010): 251–256.

91. J. Radhakrishnan, D. A. Moutzouris, E. M. Ginzler, N. Solomons, I. I. Siempos, and G. B. Appel, "Mycophenolate Mofetil and Intravenous Cyclophosphamide Are Similar as Induction Therapy for Class V Lupus Nephritis," *Kidney International* 77 (2010): 152–160.

92. N. Kasitanon, M. Petri, M. Haas, L. S. Magder, and D. M. Fine, "Mycophenolate Mofetil as the Primary Treatment of Membranous Lupus Nephritis With and Without Concurrent Proliferative Disease: A Retrospective Study of 29 Cases," *Lupus* 17 (2008): 40–45.

93. D. N. Spetie, Y. Tang, B. H. Rovin, et al., "Mycophenolate Therapy of SLE Membranous Nephropathy," *Kidney International* 66 (2004): 2411–2415.

94. D. Y. H. Yap, X. Yu, X. M. Chen, et al., "Pilot 24 Month Study to Compare Mycophenolate Mofetil and Tacrolimus in the Treatment of Membranous Lupus Nephritis With Nephrotic Syndrome," *Nephrology* 17 (2012): 352–357.

95. C. C. Szeto, B. C. H. Kwan, F. M. M. Lai, et al., "Tacrolimus for the Treatment of Systemic Lupus Erythematosus With Pure Class V Nephritis," *Rheumatology* 47 (2008): 1678–1681.

96. H. A. Austin, G. G. Illei, M. J. Braun, and J. E. Balow, "Randomized, Controlled Trial of Prednisone, Cyclophosphamide, and Cyclosporine in Lupus Membranous Nephropathy," *Journal of the American Society of Nephrology* 20 (2009): 901–911.

97. K. T. Tang, C. H. Tseng, T. Y. Hsieh, and D. Y. Chen, "Induction Therapy for Membranous Lupus Nephritis: A Systematic Review and Network Meta-Analysis," *International Journal of Rheumatic Diseases* 21 (2018): 1163–1172.

98. J. T. Swan, D. M. Riche, K. D. Riche, and V. Majithia, "Systematic Review and Meta-Analysis of Immunosuppressant Therapy Clinical Trials in Membranous Lupus Nephritis," *Journal of Investigative Medicine* 59 (2011): 246–258.

99. T. M. Chan, F. K. Li, W. K. Hao, et al., "Treatment of Membranous Lupus Nephritis With Nephrotic Syndrome by Sequential Immunosuppression," *Lupus* 8 (1999): 545–551.

100. J. M. Mejía-Vilet, B. M. Córdova-Sánchez, N. O. Uribe-Uribe, and R. Correa-Rotter, "Immunosuppressive Treatment for Pure Membranous Lupus Nephropathy in a Hispanic Population," *Clinical Rheumatology* 35 (2016): 2219–2227.

101. C. C. Mok, K. Y. Ying, C. S. Lau, et al., "Treatment of Pure Membranous Lupus Nephropathy With Prednisone and Azathioprine: An Open-Label Trial," *American Journal of Kidney Diseases* 43 (2004): 269–276.

102. C. C. Mok, K. Y. Ying, C. W. Yim, W. L. Ng, and W. S. Wong, "Very Long-Term Outcome of Pure Lupus Membranous Nephropathy Treated With Glucocorticoid and Azathioprine," *Lupus* 18 (2009): 1091–1095.

103. G. G. Illei, K. Takada, D. Parkin, et al., "Renal Flares Are Common in Patients With Severe Proliferative Lupus Nephritis Treated With Pulse Immunosuppressive Therapy: Long-Term Followup of a Cohort of 145 Patients Participating in Randomized Controlled Studies," *Arthritis and Rheumatism* 46 (2002): 995–1002.

104. C. C. Mok, C. T. K. Ho, K. W. Chan, C. S. Lau, and R. W. S. Wong, "Outcome and Prognostic Indicators of Diffuse Proliferative Lupus Glomerulonephritis Treated With Sequential Oral Cyclophosphamide and Azathioprine," *Arthritis and Rheumatism* 46 (2002): 1003–1013.

105. N. Jourde-Chiche, N. Costedoat-Chalumeau, K. Baumstarck, et al., "Weaning of Maintenance Immunosuppressive Therapy in Lupus Nephritis (WIN-Lupus): Results of a Multicentre Randomised Controlled Trial," *Annals of the Rheumatic Diseases* 81 (2022): 1420–1427.

106. E. F. Chakravarty, T. Utset, D. L. Kamen, et al., "Mycophenolate Mofetil Withdrawal in Patients With Systemic Lupus Erythematosus: A Multicentre, Open-Label, Randomised Controlled Trial," *Lancet Rheumatology* 6 (2024): e168–e177.

107. A. Mathian, M. Pha, J. Haroche, et al., "Withdrawal of Low-Dose Prednisone in SLE Patients With a Clinically Quiescent Disease for More Than 1 Year: A Randomised Clinical Trial," *Annals of the Rheumatic Diseases* 79 (2020): 339–346.

108. A. Fanouriakis, M. Kostopoulou, J. Andersen, et al., "EULAR Recommendations for the Management of Systemic Lupus Erythematosus: 2023 Update," *Annals of the Rheumatic Diseases* 83 (2023): 15–29.

109. M. A. Dooley, D. Jayne, E. M. Ginzler, et al., "Mycophenolate Versus Azathioprine as Maintenance Therapy for Lupus Nephritis," *New England Journal of Medicine* 365 (2011): 1886–1895.

110. F. A. Houssiau, D. D'Cruz, S. Sangle, et al., "Azathioprine Versus Mycophenolate Mofetil for Long-Term Immunosuppression in Lupus Nephritis: Results From the MAINTAIN Nephritis Trial," *Annals of the Rheumatic Diseases* 69 (2010): 2083–2089.

111. F. Tamirou, D. D'Cruz, S. Sangle, et al., "Long-Term Follow-Up of the MAINTAIN Nephritis Trial, Comparing Azathioprine and Mycophenolate Mofetil as Maintenance Therapy of Lupus Nephritis," *Annals of the Rheumatic Diseases* 75 (2016): 526–531.

112. B. G. Kaballo, A. E. Ahmed, M. M. Nur, I. O. Khalid, and H. Abu-Aisha, "Mycophenolate Mofetil Versus Azathioprine for Maintenance Treatment of Lupus Nephritis," *Saudi Journal of Kidney Diseases and Transplantation* 27 (2016): 717–725.

113. G. Contreras, V. Pardo, B. Leclercq, et al., "Sequential Therapies for Proliferative Lupus Nephritis," *New England Journal of Medicine* 350 (2004): 971–980.

114. J. Deng, H. Xie, L. Zhu, L. Luo, and H. Xie, "Maintenance Therapy for Lupus Nephritis With Mycophenolate Mofetil or Azathioprine. A Meta-Analysis," *Clinical Nephrology* 91 (2019): 172–179.

115. L. Feng, J. Deng, D. M. Huo, Q. Y. Wu, and Y. H. Liao, "Mycophenolate Mofetil Versus Azathioprine as Maintenance Therapy for Lupus Nephritis: A Meta-Analysis," *Nephrology* 18 (2013): 104–110.

116. J. R. Maneiro, N. Lopez-Canoa, E. Salgado, and J. J. Gomez-Reino, "Maintenance Therapy of Lupus Nephritis With Mycophenolate or Azathioprine: Systematic Review and Meta-Analysis," *Rheumatology* 53 (2014): 834–838.

117. P. Webster, A. Wardle, K. Bramham, L. Webster, C. Nelson-Piercy, and L. Lightstone, "Tacrolimus Is an Effective Treatment for Lupus Nephritis in Pregnancy," *Lupus* 23 (2014): 1192–1196.

118. M. Á. Saavedra, A. Sánchez, S. Morales, U. Ángeles, and L. J. Jara, "Azathioprine During Pregnancy in Systemic Lupus Erythematosus Patients Is Not Associated With Poor Fetal Outcome," *Clinical Rheumatology* 34 (2015): 1211–1216.

119. K. Ichinose, S. Sato, Y. Kitajima, et al., "The Efficacy of Adjunct Tacrolimus Treatment in Pregnancy Outcomes in Patients With Systemic Lupus Erythematosus," *Lupus* 27 (2018): 1312–1320.

120. A. Kitada, T. Nakai, S. Fukui, et al., "Safety of Tacrolimus Use During Pregnancy and Related Pregnancy Outcomes in Patients With Systemic Lupus Erythematosus: A Retrospective Single-Center Analysis in Japan," *Lupus* 32 (2023): 352–362.

121. Q. Fu, C. Wu, M. Dai, et al., "Leflunomide Versus Azathioprine for Maintenance Therapy of Lupus Nephritis: A Prospective, Multicentre, Randomised Trial and Long-Term Follow-Up," *Annals of the Rheumatic Diseases* 81 (2022): 1549–1555.

122. R. Furie, B. H. Rovin, F. Houssiau, et al., "Safety and Efficacy of Belimumab in Patients With Lupus Nephritis: Open-Label Extension of BLISS-LN Study," *Clinical Journal of the American Society of Nephrology* 17 (2022): 1620–1630.

123. J. N. Boletis, S. Marinaki, C. Skalioti, S. S. Lionaki, A. Iniotaki, and P. P. Sfikakis, "Rituximab and Mycophenolate Mofetil for Relapsing Proliferative Lupus Nephritis: A Long-Term Prospective Study," *Nephrology, Dialysis, Transplantation* 24 (2009): 2157–2160.

124. D. Roccatello, S. Sciascia, S. Baldovino, et al., "A 4-Year Observation in Lupus Nephritis Patients Treated With an Intensified B-Lymphocyte Depletion Without Immunosuppressive Maintenance Treatment-Clinical Response Compared to Literature and Immunological Re-Assessment," *Autoimmunity Reviews* 14 (2015): 1123–1130.

125. X. Chen, X. Shi, H. Xue, et al., "Rituximab as Maintenance Therapy Following Remission Induction in Relapsing or Refractory Systemic Lupus Erythematosus," *Rheumatology* 62 (2023): 1145–1152.

126. T. Jónsdóttir, A. Zickert, B. Sundelin, E. W. Henriksson, R. F. van Vollenhoven, and I. Gunnarsson, "Long-Term Follow-Up in Lupus Nephritis Patients Treated With Rituximab—Clinical and Histopathological Response," *Rheumatology* 52 (2013): 847–855.

127. R. Furie, B. H. Rovin, F. Houssiau, et al., "Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis," *New England Journal of Medicine* 383 (2020): 1117–1128.

128. C. C. Mok, "Combination Strategies for Lupus Nephritis: Facts and Controversies," *Expert Review of Clinical Immunology* 19 (2023): 527–536.

129. X. Yu, N. Chen, J. Xue, et al., "Efficacy and Safety of Belimumab in Patients With Lupus Nephritis: Subgroup Analyses of a Phase 3 Randomized Trial in the East Asian Population," *American Journal of Kidney Diseases* 81 (2023): 294–306.e1.

130. W. X. Hu, Z. Z. Liu, H. P. Chen, H. T. Zhang, L. S. Li, and Z. H. Liu, "Clinical Characteristics and Prognosis of Diffuse Proliferative Lupus Nephritis With Thrombotic Microangiopathy," *Lupus* 19 (2010): 1591–1598.

131. S. Chen, Z. Tang, H. Zhang, W. Hu, and Z. Liu, "Prediction of Renal Outcomes in Patients With Crescentic Lupus Nephritis," *American Journal of the Medical Sciences* 349 (2015): 298–305.

132. W. Chen, S. Liang, K. Zuo, L. Yang, C. Zeng, and W. Hu, "Clinicopathological Features and Outcomes of SLE Patients With Renal Injury Characterised by Thrombotic Microangiopathy," *Clinical Rheumatology* 40 (2021): 2735–2743.

133. G. Hernandez-Molina, L. P. García-Trejo, N. Uribe, and A. R. Cabral, "Thrombotic Microangiopathy and Poor Renal Outcome in Lupus Patients With or Without Antiphospholipid Syndrome," *Clinical and Experimental Rheumatology* 33 (2015): 503–508.

134. N. Pattanashetti, H. Anakutti, R. Ramachandran, et al., "Effect of Thrombotic Microangiopathy on Clinical Outcomes in Indian Patients With Lupus Nephritis," *Kidney International Reports* 2 (2017): 844–849.

135. C. Li, D. Y. H. Yap, G. Chan, et al., "Clinical Outcomes and Clinico-Pathological Correlations in Lupus Nephritis With Kidney Biopsy Showing Thrombotic Microangiopathy," *Journal of Rheumatology* 46 (2019): 1478–1484.

136. J. Tao, H. Wang, S. X. Wang, F. Yu, and M. H. Zhao, "The Predictive Value of Crescents in the Disease Progression of Lupus Nephritis Based on the 2018 International Society of Nephrology/Renal Pathology Society Revision System: A Large Cohort Study From China," *Renal Failure* 42 (2020): 166–172.

137. M. F. Gomes, C. Mardones, M. Xipell, et al., "The Extent of Tubulointerstitial Inflammation Is an Independent Predictor of Renal Survival in Lupus Nephritis," *Journal of Nephrology* 34 (2021): 1897–1905.

138. S. Lin, J. Zhang, B. Chen, et al., "Role of Crescents for Lupus Nephritis in Clinical, Pathological and Prognosis: A Single-Center Retrospective Cohort Study," *European Journal of Medical Research* 28 (2023): 60.

139. H. A. Austin, J. H. Klippel, J. E. Balow, et al., "Therapy of Lupus Nephritis. Controlled Trial of Prednisone and Cytotoxic Drugs," *New England Journal of Medicine* 314 (1986): 614–619.

140. C. C. Mok, "Con: Cyclophosphamide for the Treatment of Lupus Nephritis," *Nephrology, Dialysis, Transplantation* 31 (2016): 1053–1057.

141. J. V. Donadio, K. E. Holley, R. H. Ferguson, and D. M. Ilstrup, "Treatment of Diffuse Proliferative Lupus Nephritis With Prednisone and Combined Prednisone and Cyclophosphamide," *New England Journal of Medicine* 299 (1978): 1151–1155.

142. D. T. Boumpas, H. A. Austin, E. M. Vaughn, et al., "Controlled Trial of Pulse Methylprednisolone Versus Two Regimens of Pulse Cyclophosphamide in Severe Lupus Nephritis," *Lancet* 340 (1992): 741–745.

143. M. Walsh, N. Solomons, L. Lisk, and D. R. W. Jayne, "Mycophenolate Mofetil or Intravenous Cyclophosphamide for Lupus Nephritis With Poor Kidney Function: A Subgroup Analysis of the Aspreva Lupus Management Study," *American Journal of Kidney Diseases* 61 (2013): 710–715.

144. B. H. Rovin, S. V. Parikh, L. A. Hebert, et al., "Lupus Nephritis: Induction Therapy in Severe Lupus Nephritis—Should MMF Be Considered the Drug of Choice?," *Clinical Journal of the American Society of Nephrology* 8 (2013): 147–153.

145. A. Chedid, G. M. Rossi, F. Peyronel, et al., "Low-Level Proteinuria in Systemic Lupus Erythematosus," *Kidney International Reports* 5 (2020): 2333–2340.

146. M. E. Zabaleta-Lanz, L. E. Muñoz, F. J. Tapanes, et al., "Further Description of Early Clinically Silent Lupus Nephritis," *Lupus* 15 (2006): 845–851.

147. D. Wakasugi, T. Gono, Y. Kawaguchi, et al., "Frequency of Class III and IV Nephritis in Systemic Lupus Erythematosus Without Clinical Renal Involvement: An Analysis of Predictive Measures," *Journal of Rheumatology* 39 (2012): 79–85.

148. A. Malvar, P. Pirruccio, V. Alberton, et al., "Histologic Versus Clinical Remission in Proliferative Lupus Nephritis," *Nephrology, Dialysis, Transplantation* 32 (2017): 1338–1344.

149. A. S. Alvarado, A. Malvar, B. Lococo, et al., "The Value of Repeat Kidney Biopsy in Quiescent Argentinian Lupus Nephritis Patients," *Lupus* 23 (2014): 840–847.

150. A. Pakozdi, D. Pyne, M. Sheaff, and R. Rajakariar, "Utility of a Repeat Renal Biopsy in Lupus Nephritis: A Single Centre Experience," *Nephrology, Dialysis, Transplantation* 33 (2018): 507–513.

151. A. Malvar, V. Alberton, B. Lococo, et al., "Kidney Biopsy-Based Management of Maintenance Immunosuppression Is Safe and May Ameliorate Flare Rate in Lupus Nephritis," *Kidney International* 97 (2020): 156–162.

152. M. De Rosa, F. Azzato, J. E. Toblli, et al., "A Prospective Observational Cohort Study Highlights Kidney Biopsy Findings of Lupus Nephritis Patients in Remission Who Flare Following Withdrawal of Maintenance Therapy," *Kidney International* 94 (2018): 788–794.

153. U. Das, R. Patel, S. Guditi, and G. Taduri, "Correlation Between the Clinical Remission and Histological Remission in Repeat Biopsy Findings of Quiescent Proliferative Lupus Nephritis," *Lupus* 30 (2021): 876–883.

154. Z. Tang, G. Yang, C. Yu, et al., "Effects of Mycophenolate Mofetil for Patients With Crescentic Lupus Nephritis," *Nephrology* 13 (2008): 702–707.

155. J. Wang, W. Hu, H. Xie, et al., "Induction Therapies for Class IV Lupus Nephritis With Non-Inflammatory Necrotizing Vasculopathy: Mycophenolate Mofetil or Intravenous Cyclophosphamide," *Lupus* 16 (2007): 707–712.

156. C. M. Lanata, T. Mahmood, D. M. Fine, and M. Petri, "Combination Therapy of Mycophenolate Mofetil and Tacrolimus in Lupus Nephritis," *Lupus* 19 (2010): 935–940.

157. C. C. Mok, C. H. To, K. L. Yu, and L. Y. Ho, "Combined Low-Dose Mycophenolate Mofetil and Tacrolimus for Lupus Nephritis With Suboptimal Response to Standard Therapy: A 12-Month Prospective Study," *Lupus* 22 (2013): 1135–1141.

158. J. Cortés-Hernández, M. T. Torres-Salido, A. S. Medrano, M. V. Tarrés, and J. Ordi-Ros, "Long-Term Outcomes—Mycophenolate Mofetil Treatment for Lupus Nephritis With Addition of Tacrolimus for Resistant Cases," *Nephrology, Dialysis, Transplantation* 25 (2010): 3939–3948.

159. C. B. Choi, S. Won, and S. C. Bae, "Outcomes of Multitarget Therapy Using Mycophenolate Mofetil and Tacrolimus for Refractory or Relapsing Lupus Nephritis," *Lupus* 27 (2018): 1007–1011.

160. D. Y. H. Yap, M. K. M. Ma, M. M. Y. Mok, L. P. Y. Kwan, G. C. W. Chan, and T. M. Chan, "Long-Term Data on Tacrolimus Treatment in Lupus Nephritis," *Rheumatology* 53 (2014): 2232–2237.

161. H. Bao, Z. H. Liu, H. L. Xie, W. X. Hu, H. T. Zhang, and L. S. Li, "Successful Treatment of Class V+IV Lupus Nephritis With Multitarget Therapy," *Journal of the American Society of Nephrology* 19 (2008): 2001–2010.

162. B. H. Rovin, R. Furie, K. Latinis, et al., "Efficacy and Safety of Rituximab in Patients With Active Proliferative Lupus Nephritis: The Lupus Nephritis Assessment With Rituximab Study," *Arthritis and Rheumatism* 64 (2012): 1215–1226.

163. S. Teng, Y. Tian, N. Luo, Q. Zheng, M. Shao, and L. Li, "Efficacy and Safety of an Anti-CD20 Monoclonal Antibody, Rituximab, for Lupus Nephritis: A Meta-Analysis," *International Journal of Rheumatic Diseases* 25 (2022): 101–109.

164. M. Vigna-Perez, B. Hernández-Castro, O. Paredes-Saharopulos, et al., "Clinical and Immunological Effects of Rituximab in Patients With Lupus Nephritis Refractory to Conventional Therapy: A Pilot Study," *Arthritis Research & Therapy* 8 (2006): R83.

165. I. Gunnarsson, B. Sundelin, T. Jónsdóttir, S. H. Jacobson, E. W. Henriksson, and R. F. van Vollenhoven, "Histopathologic and Clinical Outcome of Rituximab Treatment in Patients With Cyclophosphamide-Resistant Proliferative Lupus Nephritis," *Arthritis and Rheumatism* 56 (2007): 1263–1272.

166. C. Melander, M. Sallée, P. Trolliet, et al., "Rituximab in Severe Lupus Nephritis: Early B-Cell Depletion Affects Long-Term Renal Outcome," *Clinical Journal of the American Society of Nephrology* 4 (2009): 579–587.

167. M. Garcia-Carrasco, C. Mendoza-Pinto, M. Sandoval-Cruz, et al., "Anti-CD20 Therapy in Patients With Refractory Systemic Lupus Erythematosus: A Longitudinal Analysis of 52 Hispanic Patients," *Lupus* 19 (2010): 213–219.

168. C. Díaz-Lagares, S. Croca, S. Sangle, et al., "Efficacy of Rituximab in 164 Patients With Biopsy-Proven Lupus Nephritis: Pooled Data From European Cohorts," *Autoimmunity Reviews* 11 (2012): 357–364.

169. S. Y. Bang, C. K. Lee, Y. M. Kang, et al., "Multicenter Retrospective Analysis of the Effectiveness and Safety of Rituximab in Korean Patients With Refractory Systemic Lupus Erythematosus," *Autoimmune Diseases* 2012 (2012): 565039.

170. M. Weidenbusch, C. Römmele, A. Schröttle, and H. J. Anders, "Beyond the LUNAR Trial. Efficacy of Rituximab in Refractory Lupus Nephritis," *Nephrology, Dialysis, Transplantation* 28 (2013): 106–111.

171. L. Iaccarino, E. Bartoloni, L. Carli, et al., "Efficacy and Safety of Off-Label Use of Rituximab in Refractory Lupus: Data From the Italian Multicentre Registry," *Clinical and Experimental Rheumatology* 33 (2015): 449–456.

172. A. Contis, H. Vanquaethem, M. E. Truchetet, et al., "Analysis of the Effectiveness and Safety of Rituximab in Patients With Refractory Lupus Nephritis: A Chart Review," *Clinical Rheumatology* 35 (2016): 517–522.

173. Y. Tanaka, T. Takeuchi, N. Miyasaka, et al., "Efficacy and Safety of Rituximab in Japanese Patients With Systemic Lupus Erythematosus and Lupus Nephritis Who Are Refractory to Conventional Therapy," *Modern Rheumatology* 26 (2016): 80–86.

174. S. Iwata, K. Saito, S. Hirata, et al., "Efficacy and Safety of Anti-CD20 Antibody Rituximab for Patients With Refractory Systemic Lupus Erythematosus," *Lupus* 27 (2018): 802–811.

175. Y. Tanaka, S. Nakayamada, K. Yamaoka, K. Ohmura, and S. Yasuda, "Rituximab in the Real-World Treatment of Lupus Nephritis: A Retrospective Cohort Study in Japan," *Modern Rheumatology* 33 (2023): 145–153.

176. R. J. Davies, S. R. Sangle, N. P. Jordan, et al., "Rituximab in the Treatment of Resistant Lupus Nephritis: Therapy Failure in Rapidly Progressive Crescentic Lupus Nephritis," *Lupus* 22 (2013): 574–582.

177. S. W. S. Yapa, D. Roth, D. Gordon, and H. Struemper, "Comparison of Intravenous and Subcutaneous Exposure Supporting Dose Selection of Subcutaneous Belimumab Systemic Lupus Erythematosus Phase 3 Program," *Lupus* 25 (2016): 1448–1455.

178. B. H. Rovin, R. Furie, Y. K. O. Teng, et al., "A Secondary Analysis of the Belimumab International Study in Lupus Nephritis Trial Examined Effects of Belimumab on Kidney Outcomes and Preservation of Kidney Function in Patients With Lupus Nephritis," *Kidney International* 101 (2022): 403–413.

179. A. Dima, C. Jurcut, F. Chasset, R. Felten, and L. Arnaud, "Hydroxychloroquine in Systemic Lupus Erythematosus: Overview of Current Knowledge," *Therapeutic Advances in Musculoskeletal Disease* 14 (2022): 1759720X211073001.

180. I. R. Rao, A. Kolakemar, S. V. Shenoy, et al., "Hydroxychloroquine in Nephrology: Current Status and Future Directions," *Journal of Nephrology* 36 (2023): 2191–2208.

181. N. Kasitanon, D. M. Fine, M. Haas, L. S. Magder, and M. Petri, "Hydroxychloroquine Use Predicts Complete Renal Remission Within

12 Months Among Patients Treated With Mycophenolate Mofetil Therapy for Membranous Lupus Nephritis," *Lupus* 15 (2006): 366–370.

182. A. Sisó, M. Ramos-Casals, A. Bové, et al., "Previous Antimalarial Therapy in Patients Diagnosed With Lupus Nephritis: Influence on Outcomes and Survival," *Lupus* 17 (2008): 281–288.

183. K. Kalantar-Zadeh, T. H. Jafar, D. Nitsch, B. L. Neuen, and V. Perkovic, "Chronic Kidney Disease," *Lancet* 398 (2021): 786–802.

184. S. Durán-Barragán, G. McGwin, L. M. Vilá, J. D. Reveille, G. S. Alarcón, and LUMINA (LIX): a multiethnic US cohort, "Angiotensin-Converting Enzyme Inhibitors Delay the Occurrence of Renal Involvement and Are Associated With a Decreased Risk of Disease Activity in Patients With Systemic Lupus Erythematosus—Results From LUMINA (LIX): A Multiethnic US Cohort," *Rheumatology* 47 (2008): 1093–1096.

185. H. Kanda, K. Kubo, S. Tateishi, et al., "Antiproteinuric Effect of ARB in Lupus Nephritis Patients With Persistent Proteinuria Despite Immunosuppressive Therapy," *Lupus* 14 (2005): 288–292.

186. G. Mancia, R. Kreutz, M. Brunström, et al., "2023 ESH Guidelines for the Management of Arterial Hypertension the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA)," *Journal of Hypertension* 41 (2023): 1874–2071.

187. M. Castro, M. Ugolini-Lopes, E. F. Borba, E. Bonfá, and L. P. C. Seguro, "Effectiveness of Renoprotective Approaches for Persistent Proteinuria in Lupus Nephritis: More Than Just Immunosuppression," *Lupus* 27 (2018): 2215–2219.

188. I. G. Okpechi, O. E. Ayodele, E. S. W. Jones, M. Duffield, and C. R. Swanepoel, "Outcome of Patients With Membranous Lupus Nephritis in Cape Town South Africa," *Nephrology, Dialysis, Transplantation* 27 (2012): 3509–3515.

189. C. C. Mok, "Accelerated Atherosclerosis, Arterial Thromboembolism, and Preventive Strategies in Systemic Lupus Erythematosus," *Scandinavian Journal of Rheumatology* 35 (2006): 85–95.

190. A. Hoi, T. Igel, C. C. Mok, and L. Arnaud, "Systemic Lupus Erythematosus," *Lancet* 403 (2024): 2326–2338.

191. C. Y. Wong, B. M. Y. Ma, D. Zhang, W. Cheung, T. M. Chan, and D. Y. H. Yap, "Cardiovascular Risk Factors and Complications in Patients With Systemic Lupus Erythematosus With and Without Nephritis: A Systematic Review and Meta-Analysis," *Lupus Science & Medicine* 11 (2024): e001152.

192. C. C. Mok, L. Y. Ho, and C. H. To, "Annual Incidence and Standardized Incidence Ratio of Cerebrovascular Accidents in Patients With Systemic Lupus Erythematosus," *Scandinavian Journal of Rheumatology* 38 (2009): 362–368.

193. V. M. Campese, "Dyslipidemia and Progression of Kidney Disease: Role of Lipid-Lowering Drugs," *Clinical and Experimental Nephrology* 18 (2014): 291–295.

194. C. C. Mok, C. K. Wong, C. H. To, J. P. S. Lai, and C. S. Lam, "Effects of Rosuvastatin on Vascular Biomarkers and Carotid Atherosclerosis in Lupus: A Randomized, Double-Blind, Placebo-Controlled Trial," *Arthritis Care and Research* 63 (2011): 875–883.

195. J. L. Katzmann and U. Laufs, "PCSK9-Directed Therapies: An Update," *Current Opinion in Lipidology* 35 (2024): 117–125.

196. H. J. L. Heerspink, N. Jongs, G. M. Chertow, et al., "Effect of Dapagliflozin on the Rate of Decline in Kidney Function in Patients With Chronic Kidney Disease With and Without Type 2 Diabetes: A Prespecified Analysis From the DAPA-CKD Trial," *Lancet Diabetes and Endocrinology* 9 (2021): 743–754.

197. The EMPA-KIDNEY Collaborative Group, W. G. Herrington, N. Staplin, et al., "Empagliflozin in Patients With Chronic Kidney Disease," *New England Journal of Medicine* 388 (2023): 117–127.

198. H. J. L. Heerspink, B. V. Stefánsson, R. Correa-Rotter, et al., "Dapagliflozin in Patients With Chronic Kidney Disease," *New England Journal of Medicine* 383 (2020): 1436–1446.

199. B. R. Wagner and P. S. Rao, "Sodium-Glucose Cotransporter 2 Inhibitors: Are They Ready for Prime Time in the Management of Lupus Nephritis?," *Current Opinion in Rheumatology* 36 (2024): 163–168.

200. J. Lichtnekert and H. J. Anders, "Lupus Nephritis-Related Chronic Kidney Disease," *Nature Reviews Rheumatology* 20 (2024): 699–711.

201. S. Sciascia, J. Yazdany, M. Dall'Era, et al., "Anticoagulation in Patients With Concomitant Lupus Nephritis and Thrombotic Microangiopathy: A Multicentre Cohort Study," *Annals of the Rheumatic Diseases* 78 (2019): 1004–1006.

202. R. Singhal and K. S. Brimble, "Thromboembolic Complications in the Nephrotic Syndrome: Pathophysiology and Clinical Management," *Thrombosis Research* 118 (2006): 397–407.

203. G. Ruiz-Irastorza, M. J. Cuadrado, I. Ruiz-Arruza, et al., "Evidence-Based Recommendations for the Prevention and Long-Term Management of Thrombosis in Antiphospholipid Antibody-Positive Patients: Report of a Task Force at the 13th International Congress on Antiphospholipid Antibodies," *Lupus* 20 (2011): 206–218.

204. G. Contreras, A. Mattiazzi, G. Guerra, et al., "Recurrence of Lupus Nephritis After Kidney Transplantation," *Journal of the American Society of Nephrology* 21 (2010): 1200–1207.

205. D. S. Gipson, M. E. Ferris, M. A. Dooley, K. Huang, and S. L. Hogan, "Renal Transplantation in Children With Lupus Nephritis," *American Journal of Kidney Diseases* 41 (2003): 455–463.

206. G. Moroni, F. Tantardini, B. Gallelli, et al., "The Long-Term Prognosis of Renal Transplantation in Patients With Lupus Nephritis," *American Journal of Kidney Diseases* 45 (2005): 903–911.

207. S. Bunnapradist, P. Chung, A. Peng, et al., "Outcomes of Renal Transplantation for Recipients With Lupus Nephritis: Analysis of the Organ Procurement and Transplantation Network Database," *Transplantation* 82 (2006): 612–618.

208. H. Tang, M. Chelamcharla, B. C. Baird, F. S. Shihab, J. K. Koford, and A. S. Goldfarb-Rumyantzev, "Factors Affecting Kidney-Transplant Outcome in Recipients With Lupus Nephritis," *Clinical Transplantation* 22 (2008): 263–272.

209. S. H. Kang, B. H. Chung, S. R. Choi, et al., "Comparison of Clinical Outcomes by Different Renal Replacement Therapy in Patients With End-Stage Renal Disease Secondary to Lupus Nephritis," *Korean Journal of Internal Medicine* 26 (2011): 60–67.

210. C. S. Oliveira, I. Oliveira, A. B. S. Bacchiega, et al., "Renal Transplantation in Lupus Nephritis: A Brazilian Cohort," *Lupus* 21 (2012): 570–574.

211. C. S. Wagner, P. Malafronte, D. P. Demetrio, J. F. de Souza, and Y. A. Sens, "Outcomes in Renal Transplant Recipients With Lupus Nephritis: Experience at a Single Center," *Renal Failure* 36 (2014): 912–915.

212. A. ÇeltİK, S. Şen, A. F. Tamer, et al., "Recurrent Lupus Nephritis After Transplantation: Clinicopathological Evaluation With Protocol Biopsies," *Nephrology* 21 (2016): 601–607.

213. J. Gołębiewska, A. Dębska-Ślizień, B. Bułło-Piontecka, and B. Rutkowski, "Outcomes in Renal Transplant Recipients With Lupus Nephritis-A Single-Center Experience and Review of the Literature," *Transplantation Proceedings* 48 (2016): 1489–1493.

214. L. Zhang, G. Lee, X. Liu, et al., "Long-Term Outcomes of End-Stage Kidney Disease for Patients With Lupus Nephritis," *Kidney International* 89 (2016): 1337–1345.

215. E. S. Park, S. S. Ahn, S. M. Jung, J. J. Song, Y. B. Park, and S. W. Lee, "Renal Outcome After Kidney-Transplantation in Korean Patients With Lupus Nephritis," *Lupus* 27 (2018): 461–467.

216. A. Jorge, Z. S. Wallace, N. Lu, Y. Zhang, and H. K. Choi, "Renal Transplantation and Survival Among Patients With Lupus Nephritis: A Cohort Study," *Annals of Internal Medicine* 170 (2019): 240–247.

217. J. Rodelo, L. A. González, J. Ustáriz, et al., "Kidney Transplantation Outcomes in Lupus Nephritis: A 37-Year Single-Center Experience From Latin America," *Lupus* 30 (2021): 1644–1659.

218. H. Ye, P. Cao, J. Lin, et al., "Long-Term Clinical Outcomes of Lupus Nephritis Patients Undergoing Peritoneal Dialysis: A Matched, Case-Control Study," *Peritoneal Dialysis International* 39 (2019): 570–573.

219. D. Martínez-López, L. Sánchez-Bilbao, M. De Cos-Gómez, et al., "Long-Term Survival of Renal Transplantation in Patients With Lupus Nephritis: Experience From a Single University Centre," *Clinical and Experimental Rheumatology* 40 (2022): 581–588.

220. H. Wasik, V. Chadha, S. Galbiati, B. Warady, and M. Atkinson, "Dialysis Outcomes for Children With Lupus Nephritis Compared to Children With Other Forms of Nephritis: A Retrospective Cohort Study," *American Journal of Kidney Diseases* 79 (2022): 626–634.

221. C. F. Mojcik and J. H. Klippel, "End-Stage Renal Disease and Systemic Lupus Erythematosus," *American Journal of Medicine* 101 (1996): 100–107.

222. Y. S. Goo, H. C. Park, H. Y. Choi, et al., "The Evolution of Lupus Activity Among Patients With End-Stage Renal Disease Secondary to Lupus Nephritis," *Yonsei Medical Journal* 45 (2004): 199–206.

223. F. Gaillard, D. Bachelet, C. Couchoud, et al., "Lupus Activity and Outcomes in Lupus Patients Undergoing Maintenance Dialysis," *Rheumatology* 63 (2024): 780–786.

224. Y. E. Kim, S. J. Choi, D. H. Lim, et al., "Disease Flare of Systemic Lupus Erythematosus in Patients With Endstage Renal Disease on Dialysis," *Journal of Rheumatology* 49 (2022): 1131–1137.

225. J. S. Cheigh and K. H. Stenzel, "End-Stage Renal Disease in Systemic Lupus Erythematosus," *American Journal of Kidney Diseases* 21 (1993): 2–8.

226. L. C. Plantinga, R. E. Patzer, C. Drenkard, et al., "Association of Time to Kidney Transplantation With Graft Failure Among U.S. Patients With End-Stage Renal Disease due to Lupus Nephritis," *Arthritis Care and Research* 67 (2015): 571–581.

227. T. Wong and S. Goral, "Lupus Nephritis and Kidney Transplantation: Where Are we Today?," *Advances in Chronic Kidney Disease* 26 (2019): 313–322.