LP-127 TACROLIMUS IS EFFECTIVE TREATMENT IN PATIENTS WITH REFRACTORY LUPUS NEPHRITIS

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Background The standard treatment of lupus nephritis is based on immunosuppressive therapy using mycophenolate mofetil or cyclophosphamide and with glucocorticoids, however, these treatments are not consistently effective. Tacrolimus (TAC), a novel calcineurin inhibitor with immunosuppressive effects, has recently become increasingly interested in its role as a potential therapeutic agent in SLE. We aimed to evaluate the efficacy of TAC as a treatment for LN.

Methods A total 170 patients with biopsy proven LN were enrolled by reviewing the medical records of patients with LN in Ajou Lupus cohort. The clinical response of TAC treatment was evaluated by proteinuria, estimated glomerular filtration rate (eGFR), anti-double-stranded DNA (anti-dsDNA) antibody, complement 3 (C3), complement 4 (C4), and renal SLE disease activity index (SLEDAI). Complete renal response was defined as urine protein to creatinine ratio <0.5, normal serum creatinine or, if normal at baseline, not increased by ≥15%, and partial renal response was defined as a normal or near-normal GFR with a ≥50% reduction in proteinuria to sub-nephrotic levels. The definition of poor outcomes was determined by end stage renal disease or death.

Results The baseline clinical manifestations between 92 TAC group and 87 non-TAC group showed no significant differences. Most of TAC group received multi-target therapy with other immunosuppressants, while the non-TAC group usually used monotherapy. After 5 years, there were no statistically significant differences in proteinuria, eGFR levels, anti-dsDNA, serum C3/C4, and renal SLEDAI. The overall (complete and partial) renal response rate was not significantly different (TAC group versus non-TAC group=72.9% versus 85.5%; p=0.1). The poor outcomes were similar in both groups (log-rank p=0.837).

Conclusions TAC is an effective maintenance therapy for LN, and may be a reasonable option for patients with refractive LN or LN who have not reached remission. In conclusion, TAC can help patients with LN achieve a renal response and slow progression.

LP-128 RELATIVE EFFICACY AND SAFETY OF TACROLIMUS, MYCOPHENOLATE MOFETIL, AND AZATHIOPRINE AS MAINTENANCE THERAPIES FOR LUPUS NEPHRITIS: A NETWORK META-ANALYSIS

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Background Tacrolimus, mycophenolate mofetil (MMF), and azathioprine (AZA) have all shown considerable effectiveness as maintenance therapy for lupus nephritis in randomized controlled trials (RCTs), but their relative efficacy and safety in patients with lupus nephritis are still unknown. The objective of this research was to compare the relative effectiveness and safety of tacrolimus, MMF, and AZA as maintenance therapies for lupus nephritis.

Methods RCTs examining the efficacy and safety of tacrolimus, MMF, and AZA as maintenance therapies in patients with lupus nephritis were included. We performed a Bayesian random-effects network meta-analysis to combine the direct and indirect evidence from RCTs.

Results Nine RCTs comprising 815 patients were included in the study. Although the difference was not statistically significant, MMF showed a trend toward a lower relapse rate compared with AZA (OR 0.73, 95% CrI 0.44 – 1.30). Similarly, tacrolimus showed a trend toward a lower relapse rate compared with AZA (OR 0.92, 95% CrI 0.24 – 2.84). Ranking probability based on the surface under the cumulative ranking curve indicated that MMF had the highest probability of being the best treatment based on the relapse rate, followed by tacrolimus and AZA. The incidence of leukopenia in the tacrolimus and MMF groups was significantly lower than that in the AZA group (OR 0.11, 95% CrI 0.02 – 0.56; OR 0.12, 95% CrI 0.03 – 0.32). Fewer patients with infections were observed in the MMF group than in the AZA group, although the difference was not statistically significant. The analysis of withdrawal due to adverse events showed a similar pattern.

Conclusions Lower relapse rates combined with a more favorable safety profile suggest that tacrolimus and MMF are superior to AZA as maintenance treatments in lupus nephritis patients.

LP-129 LUPUS LOW DISEASE ACTIVITY STATE AS AN ATTAINABLE AND COMPLEMENTARY TARGET FOR LUPUS NEPHRITIS

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Background Lupus nephritis (LN) affects up to 60% of patients with systemic lupus erythematosus. Complete renal response (CRR) at 12 months is recommended as a treatment target. Remission or low disease activity in extra-renal domains also contributes to one of the important treatment goals. This study evaluated the usefulness of Lupus Low Disease Activity State (LLDAS) as a treatment target in LN.

Methods Patients with a biopsy-proven active LN during the period of 2010–2020 were included. CRR was defined as proteinuria ≤0.5g/day (or equivalent) and normal estimate glomerular filtration rate (eGFR); partial renal response (PRR) was defined as a reduction of proteinuria by ≥50% with near-normal eGFR. The attainment of CRR, PRR, and LLDAS was evaluated at 12 months post-treatment. LN relapse was defined as worsening of proteinuria/serum creatinine and confirmed activity in repeat renal biopsy. The frequency of relapse was evaluated in patients who have achieved ≥50% proteinuria reduction to sub-nephrotic range post-treatment.

Results 143 LN patients were included with a median follow-up duration of 10.4 years. Most patients (74%) had class III/IV (±V) histological subtypes (table 1). At 12 months, 57 (40%), 14(10%) and 69(48%) patients achieved CRR, PRR and LLDAS, respectively. Among 136 patients who achieved ≥50% proteinuria reduction to sub-nephrotic range, 30(22%) patients developed LN relapse after a median 2.98 years. CRR/PRR and LLDAS at 12 months were independent negative predictors of LN relapse. The risk of LN relapse was

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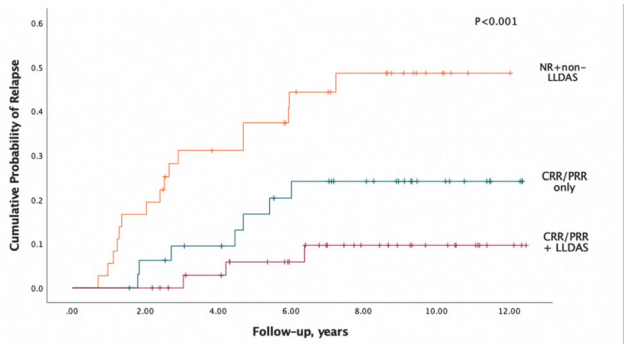

Abstract LP-129 Figure 1 CRR=complete renal remission; LLDAS=lupus low disease activity state; NR=no response; PRR=partial renal response

Abstract LP-129 Table 1 C3=complement 3; C4=complement 4; CKD=chronic kidney disease; dsDNA=double stranded DNA; eGFR=estimated glomerular filtration rate; RNP=ribonucleoprotein; Sm=smith; UPCR=urinary protein-creatinine ratio; 24huP= 24-hour urine protein. eGFR calculated by MDRD formula

Characteristics	Number (%) or median (IQR)
Sex (female)	131/143 (92%)
Age of SLE at diagnosis	27 (15)
Follow up duration	10.44 (4.38)
24huP(g) or UPCR (mg/mg)	1.6 (1.2)
Serum albumin (g/L)	32 (7)
Serum creatinine (μmol/L)	64 (35)
eGFR (mL/min/1.73m^2)	98 (56)
History of Lupus Nephritis	55/143 (38%)
WHO classes	
Class III (+/- V)	38/143 (27%)
Class IV (+/- V)	68/143 (48%)
Pure Class V	24/143 (17%)
CKD categories	
CKD1	83/143 (56%)
CKD2	35/143 (24%)
CKD3	19/143 (13%)
CKD4	3/143 (2%)
CKD5	3/143 (2%)
Presence of antibodies	
Anti-dsDNA	119/143 (83%)
Anti-Sm	23/129 (18%)
Anti-Ro	63/129 (49%)
Anti-La	13/129 (10%)
Anti-RNP	41/129 (32%)
Titre of immunological factors	
C3 (mg/dL)	51 (29)
C4 (mg/dL)	10 (9)
Anti-dsDNA (IU/mL)	190 (256)
Induction medication	
Mycophenolate Mofetil	105/143 (73%)
Azathioprine	13/143 (9%)
Calcineurin inhibitors	6/143 (4%)
Cyclophosphamide	2/143 (1%)
Hydroxychloroquine	78/143 (55%)

lowest among patients who achieved both LLDAS and CRR/PRR at 12 months (figure 1).

Conclusions LLDAS is an attainable target in LN and is associated with a lower risk of relapse. This study advocates the potential role of LLDAS as a complementary target to renal response in LN patients.

LP-131 SERUM URIC ACID AND THE RISK OF RENAL INVOLVEMENT IN PREMENOPAUSAL FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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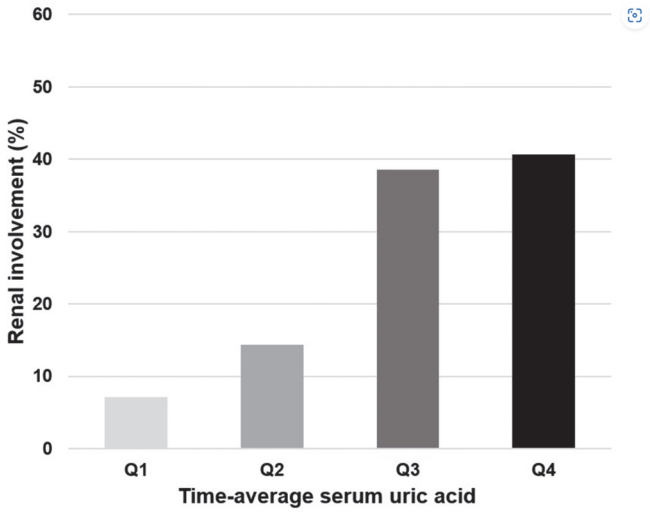
Background Serum uric acid (SUA) is a risk factor for the development of renal involvement in systemic lupus erythematosus (SLE), but the effect of SUA on renal involvement in specific genders and ages is not well known. We evaluated the association between SUA and the development of renal involvement in premenopausal female SLE patients.

Methods We retrospectively reviewed 155 premenopausal female patients with newly diagnosed SLE in a tertiary medical center. Baseline characteristics including SUA were compared between those who did (n = 48) or did not (n = 107) develop renal involvement. Patients without baseline renal involvement were followed up to identify factors affecting future renal involvement. Time-averaged SUA was divided into four categories of increasing levels (Q1, Q2, Q3, and Q4).

Results At baseline, patients with renal involvement showed higher SUA than patients without renal involvement (mean, 6.3 vs. 4.2 mg/dL, p < 0.001). Among 107 patients without baseline renal involvement (median follow-up of 6.6 years), 28 (26.2%) patients developed renal involvement. Although baseline SUA did not differ between both groups, patients with developing renal involvement showed higher time-averaged SUA (median, 4.4 vs. 4.1 mg/dL, p = 0.001) and higher last SUA (median, 4.9 vs. 3.8 mg/dL, p < 0.001) than those without developing renal involvement. The incidence of developing renal involvement in each time-averaged SUA



Abstract LP-131 Figure 1 Incidence of developing renal involvement according to time-averaged serum uric acid level in premenopausal female patients with systemic lupus erythematosus. Q1: < 3.9 mg/dL (n = 28), Q2: 3.9–4.1 mg/dL (n = 21), Q3: 4.2–4.6 mg/dL (n = 26), and Q4: ≥ 4.7 mg/dL (n = 32), respectively.

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