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Original Article

Mycophenolate Mofetil versus Azathioprine for Maintenance Treatment of Lupus Nephritis

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ABSTRACT. To compare the efficacy of mycophenolate mofetil (MMF) with that of azathioprine (AZA) drugs in the maintenance therapy of lupus nephritis (LN) patients, we studied 81 Sudanese patients with LN (32 in Class III, 34 in Class IV, and 15 in combined Class V + IV of the ISN/RPS 2003 Classification). All patients received induction therapy consisting of monthly intravenous pulse doses of cyclophosphamide (CYC) (500 mg/m^2 of body-surface area) for six months, plus three consecutive pulses of intravenous methylprednisolone 15 mg/kg/day of body weight (maximum 500 mg). Subsequently, 41 (50.6%) patients were randomized into a group that received oral MMF (22 mg/kg/day), and 40 (49.4%) patients randomized to a group that received oral AZA (2 mg/kg/day). All patients initially received oral prednisone (1 mg/kg of body weight daily) for four weeks. The baseline characteristics of the two groups were similar. Total remission rate was 75.3% (80.5% in MMF and 70% in AZA), complete remission rate of 54.3% (56.1% with MMF and 52.5% with AZA), and a partial remission rate of 21% (24.4% with MMF and 17.5% with AZA) over 29 months. During maintenance therapy, six patients died (four in the AZA group and two in the MMF group), and end-stage renal disease (ESRD) developed in five patients (three in the AZA group and two in the MMF group). During the 36-months of the study, both groups had comparable event-free survival rate for the composite end point of death or ESRD and rate of relapse-free survival. Furthermore, both groups had no significant differences in terms of frequency of hospitalization, amenorrhea, infection, nausea, and vomiting. We conclude that our study showed that short-term therapy with intravenous CYC followed by maintenance therapy with oral MMF or AZA had similar efficacy and safety for the treatment of patients with moderate to severe LN.

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Introduction

Lupus nephritis (LN) is one of the most serious complications of systemic lupus erythematosus (SLE), and it can be associated with high morbidity and progression to end-stage renal disease (ESRD).[1] The incidence of LN is more variable and ranges from 25–75% depending on the population studied and the diagnostic criteria used to identify it.[2,3] There is a general consensus that 60% of lupus patients will develop LN sometime in the course of their illness.[4] Evidence of LN usually arises within the first three years after SLE diagnosis; however, at that time, decline of renal function is quite uncommon.[5] About 5–20% of LN patients progress despite treatment to ESRD.[2,6] Kidney biopsy is the mainstay for diagnosis of LN. Tissue obtained by renal biopsy is evaluated by light microscopy, immunofluorescence, and electron microscopy.[4]

Optimal management of LN remains a challenge because of the heterogeneity of the disease at presentation and its unpredictable course.

Owing to the relatively limited studies on LN in our population, we aimed in our study to compare two drugs [mycophenolate mofetil (MMF) and azathioprine (AZA)] in the management of LN in patients from mixed tribes of blacks in Africa (Sudanese).

Materials and Methods

This randomized clinical trial was conducted in the Renal Units at Omdurman Military Hospital (Karary University) and The National Ribat University Hospital, Khartoum, Sudan, in the period from March 2008 to August 2011. The patients enrolled in the study aged from 12 to 75 years and have been diagnosed with SLE according to the American College of Rheumatology (ACR) revised criteria. The criteria for the diagnosis of LN included persistent proteinuria >0.5 g/day and presence of active urine sediment. Renal biopsies were performed at presentation, and all specimens were examined by light and immunofluorescence microscopy and the histopathological observations were categorized according to the ISN/RPS 2003 reclassification of LN by a renal pathologist who was unaware of the patients' treatment assignment. Only patients who had a histological diagnosis of severe proliferative LN (ISN/RPS 2003) Classification; Class III and IV and/or membranous Class V were enrolled in the study.

Patients with ESRD, malignancy, severe cardiovascular or liver disease, and severe infection were excluded from the study.

All patients were subjected to the following baseline investigations: complete blood count (CBC), erythrocyte sedimentation rate (ESR), serum electrolytes, blood urea, serum creatinine and uric acid, urinalysis, and 24 h urine for protein. Anti-nuclear antibodies and anti-dsDNA antibody levels were measured with (ELISA, orgentec diagnostika GmbH, Mainz, Germany) according to the manufacturer's instructions.

Eighty-one patients with LN [32 in Class III, 34 in Class IV, and 15 in combined membranous (Class V + IV)] received induction therapy consisting of intravenous pulse of cyclophosphamide (CYC) (500 mg/m^2 of body-surface area with a maximum dose ≤500 mg) monthly for six months, plus three consecutive pulses of intravenous methylprednisolone 15 mg/kg/day (maximum 500 mg). Subsequently, the patients were assigned by stratified block randomization (stratification factors were gender, age, and weight) to one of two maintenance therapies: either open-label oral AZA (2 mg/kg per day) or oral MMF (CellCept) (22 mg/kg/day, range 1000–3000 mg/day). The dosages of MMF and AZA remained unchanged within the 1st year, and then they were reduced by 25% in stable patients after the 1st year and continued for at least another year before further tapering. All patients initially received oral prednisone (1 mg/kg of body weight daily) for four weeks. Then, the daily dose of prednisolone was reduced by 5 mg per day every two weeks until the dose was 20 mg per day after which it was reduced by 2.5 mg per day every two weeks until a maintenance dose of 10 mg per day was reached, at approxi-

mately six months. The dose of prednisolone was reduced further to 7.5 mg/day after 12 months from baseline and to 5 mg/day at 15 months, and then maintained at the same dose thereafter. In patients with mild leukopenia [total white blood cell (TWBC) 2.0–4.0 × 10^9 L], thrombocytopenia (platelet count 50–100 × 10^9/L), amenorrhea, or gastrointestinal discomfort, the dosage of MMF or AZA was halved and then reincreased slowly to the original level. Maintenance immunosuppressive therapy was stopped in the event of persistent leukopenia (TWBC below 2.0 × 10^9/L), thrombocytopenia, pregnancy, persistent amenorrhea, and severe gastrointestinal upset despite reduction of drug dosage, severe sepsis, or the patient's refusal to continue. Patients with relapsed disease received intravenous CYC (500 mg/m^2 of body-surface area, the maximum dose did not exceed 500 mg) and intravenous methylprednisolone (500 mg/day) for three days, and then they were continued on the original regimen.

The following parameters were measured monthly during the induction and maintenance therapy: serum creatinine, blood urea, CBC, urinalysis, and 24 h urine protein. The patients were evaluated monthly during the maintenance therapy. Clinical and bio-chemical parameters including blood pressure and adverse effects were recorded at follow-up.

The primary endpoints of the study were patient survival and renal survival (ESRD with estimated glomerular filtration rate (eGFR) <15 mL/min or need for long-term maintenance dialysis or renal transplantation). Treatment failure was defined as a <50% reduction in proteinuria, persistence of proteinuria exceeding 2 g/day or any increase in the proteinuria. A complete remission was defined as reduction in proteinuria to ≤0.2 g/day with normal serum creatinine. A partial remission was defined as a reduction of proteinuria from nephrotic range to a range between 0.2 and 2.0 g/day or reduction of proteinuria more than 50% with normal serum creatinine.

The secondary end points of the study were renal relapse. For patients who were in complete or partial remission, disease relapse was defined by an increase in serum creatinine levels 50% or more over the last value besides a nephritic urinary sediment and generally increased proteinuria (nephritic flare) or by an increase in proteinuria without modification of serum creatinine (proteinuric flare). Proteinuria had to increase by at least 2 g per day if the basal proteinuria was <3.0 g per day, or double if the patient had already nephrotic range proteinuria. The efficacy of the two studied drugs was compared with changes in serum creatinine and eGFR and 24 h urine protein excretion rate.

Data collection was accomplished by direct interviews of the patients using a self-constructed questionnaire that consisted of six parts of study variables and by observation and follow-up (medical examination and investigations).

The purpose of this study was clarified and discussed with the patients, their permission and support were requested, and informed consents were obtained from the patients before the beginning of any intervention or data collection. Furthermore, ethical approval of the concerned institutions was obtained.

Statistical Analysis

We used the Statistical Package for the Social Sciences version 17.0 (SPSS, Inc., Chicago, IL, USA) for the analysis of data. The relationship between the categorical variables in small samples was tested by Chi-square test. The relationship between continuous variables in two independent groups was performed using the Student's *t*-test. The patient survival, event-free survival, and relapse-free survival were calculated according to the Kaplan–Meier method. P <0.05 was considered statistically significant.

Results

Forty-one (50.6%) out of the 81 study patients were randomized into the MMF group, and 40 (49.4%) patients were randomized into the AZA group; 92.7% were females and 92.5% were females in MMF group and in

Table 1. Comparison of the demographic data between two groups.

Manifestation	Number of patients (%)	
	MMF	AZA
Age at presentation/year (mean±SD)	27.1±9.8	29.4±11.6
Gender		
Male	3 (7.3%)	3 (7.5%)
Female	38 (92.7%)	37 (92.5%)
Marital status		
Married	19 (46.3%)	19 (47.5%)
Single	22 (53.7%)	21 (52.5%)
Weight/kg (mean±SD)	53.5±15.6	57.3±13.6
Duration of disease/month (mean±SD)	58.6±50.6	54.7±44.7
Total number	41 (100)	40 (100)

SD: Standard deviation, MMF: Mycophenolate mofetil, AZA: Azathioprine.

AZA groups, respectively. Table 1 shows the comparison of demographics data between the two groups. The ACR revised criteria for classification of SLE (1982) were similar between the two groups (Table 2).

The mean of serum creatinine was 1.5 ± 1.1 mg/dL in the MMF group and 1.9 ± 1.5 mg/dL in AZA group (P = 0.12). The mean of proteinuria was 3.2 ± 2.1 mg/dL in the MMF group, and 3.2 ± 4 mg/dL in the AZA group (P = 0.97). Table 3 shows the comparison of the main laboratory data between the two study groups.

The serum creatinine levels decreased insignificantly from 1.5 ± 1.1 mg/dL to 1.2 ± 1.2 mg/dL in the MMF group (P = 0.3319), and decreased insignificantly from 1.9 ± 1.5 mg/dL to 1.7 ± 1.7 mg/dL in the AZA group (P = 0.49).

Serum creatinine levels improved in 11 patients in the MMF group and ten patients in the AZA group, remained stable (within normal range) in 24 and 22 patients, and became

Table 2. Comparison of the American Rheumatology Association criteria between the lupus nephritis patients treated with mycophenolate mofetil and azathioprine.

Manifestations of disease	Number of patients (%)	
	MMF	AZA
Malar rash	21 (51.2)	24 (60)
Discoid lupus	4 (9.8)	9 (22.5)
Photosensitivity	7 (17.1)	11 (27.5)
Oral ulcer	8 (19.5)	15 (37.5)
Articular	35 (85.4)	33 (82.5)
Serositis	15 (36.6)	16 (40)
Neuropsychiatric	6 (14.3)	1 (2.5)
Hematological	18 (43.9)	19 (47.5)
Hemolytic anemia	11 (26.3)	9 (22.5)
Leukopenia	12 (29.3)	12 (30)
Thrombocytopenia	3 (7.3)	1 (2.5)
Lymphopenia	6 (14.6)	4 (10)
Renal	41 (100)	40 (100)
Positive ANA	41 (100)	38 (95)
Positive Anti-ds DNA	28 (68.3)	30 (75)
False positive VDRL	0	0
Number of ARA criteria	6 (4–8)	6 (4–10)
Total number of patients	41	40

MMF: Mycophenolate mofetil, AZA: Azathioprine, ARA: American Rheumatology Association, ANA: Anti-nuclear antibodies, VDRL: Venereal Disease Research Laboratory.

Table 3. Comparison of the main laboratory data between the lupus nephritis patients treated with mycophenolate mofetil and azathioprine.

Data	MMF	AZA
Hb mg/dL (mean±SD)	9.3±1.6	9.7±2.4
WBCC cell/mm^3 (mean±SD)	6.6±3.9	6.1±2.8
Platelets cell/mm^3 (mean±SD)	272±108.1	339.3 (±187.1)
ESR mm/h (mean±SD)	100.6±27.9	92.2±35.1
Urine sugar	1 (2.4%)	4 (10%)
Urine RBC cell	28 (68.3%)	27 (67.5%)
Urine pus cell	32 (78%)	34 (85%)
Urine casts	26	24
Granular	24	23
Hyaline	2	2
RBC	2	0
Cellular	0	1
Wax	1	0
Blood urea mg/dL (mean±SD)	34	37
Serum creatinine mg/dL (mean±SD)	1.5±1.1	1.9±1.5
Creatinine clearance (mean±SD)	63.3±26.1	59.3±36.5
24 h urine protein (g/day)		
>3	17	17
>2–3	15	6
>0.2–2	9	17
Total number of patients	41	40

SD: Standard deviation, MMF: Mycophenolate mofetil, AZA: Azathioprine, ESR: Erythrocyte sedimentation rate, WBCC: White blood cell count, RBC: Red blood cell.

worse in six and eight patients, respectively. Seven patients showed doubling of baseline serum creatinine levels (2 in the MMF and 5 in the AZA groups). In both groups, the proteinuria decreased significantly from 3.2 ± 2.1 g/day to 1.2 ± 1.8 g/day (P = 0.0001) after MMF treatment and from 3.2 ± 4 g/day to 1.6 ± 2.4 g/day in AZA group, (P = 0.03).

In the MMF group, blood pressure was controlled with the use of angiotensin-converting enzyme inhibitors (ACEi) drugs in 22 patients, with lifestyle modification and diet in 12 patients, and with three drugs in seven patients. In the AZA group, blood pressure was controlled with the use of ACEi drugs in 23 patients, with lifestyle modification in ten patients, and with three drugs in seven patients.

The total remission rate in the MMF and the AZA groups was 80.5% and 70%, respectively; 23 patients in the MMF group and 21 in the AZA had complete remission and 10 and seven patients achieved partial remission, respectively (P = 0.81). The incidence of complete remission was unrelated to baseline values of proteinuria, creatinine, or anti-dsDNA antibodies.

Disease relapsed in four patients in the MMF group and four patients in the AZA group after achieving remission, at 13.5 ± 5.8 and 11.8 ±

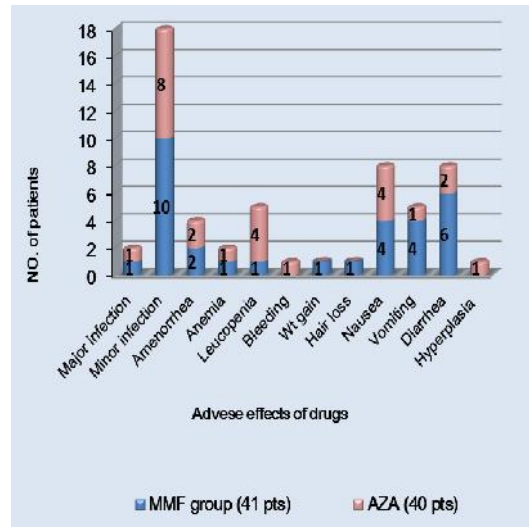

Figure 1. Adverse events in the lupus nephritis patients treated with mycophenolate mofetil and azathioprine.

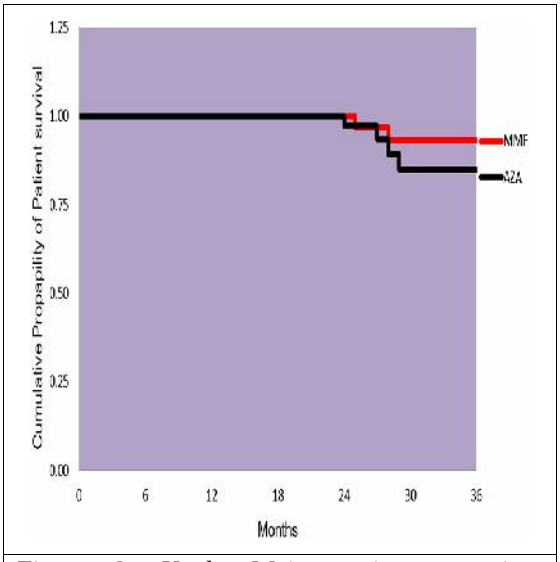

Figure 2. Kaplan–Meier estimates patient survival of the lupus nephritis patients treated with mycophenolate mofetil and azathioprine.

4.8 months from baseline, respectively (P = 0.63).

Four patients in the MMF group and five patients in the AZA group showed progressive renal impairment during follow-up. Two of the four patients in MMF group and three of the five patients in the AZA group reached ESRD, (P = 0.29).

Adverse effects (AEs) shown in Figure 1 occurred in 29 (70.7%) patients in the MMF group and in 30 (75%) patients in the AZA group. Major infection developed in one patient of each group (pneumonia), minor infections developed in 24.4% of the MMF group, and in 22.5% of the AZA group (urinary tract infection, upper respiratory tract infection, herpes zoster, cellulitis, and malaria).

The gastrointestinal tract adverse effects occurred in 34.1% of the patients in the MMF and 20% of the patients in the AZA group.

Transient amenorrhea developed in two (7.3%) patients in the MMF group, and in two (12.5%) patients in the AZA group. In both groups, no patients were diagnosed with premature ovarian failure (postmenopausal before 40 years of age, proven with high FSH and LH levels). One patient in the AZA group developed reactive follicular hyperplasia.

There were three withdrawals from the study; one in MMF group as a result of sustained diarrhea and two in the AZA group due to severe leukopenia. Six patients died, two in MMF group (both due to infection), and four in the AZA group (two due to infection and two due to myocardial infarction). One patient in the MMF group was non-compliant and one patient lost to follow-up in the AZA group. In relation to most commonly reported AEs in the

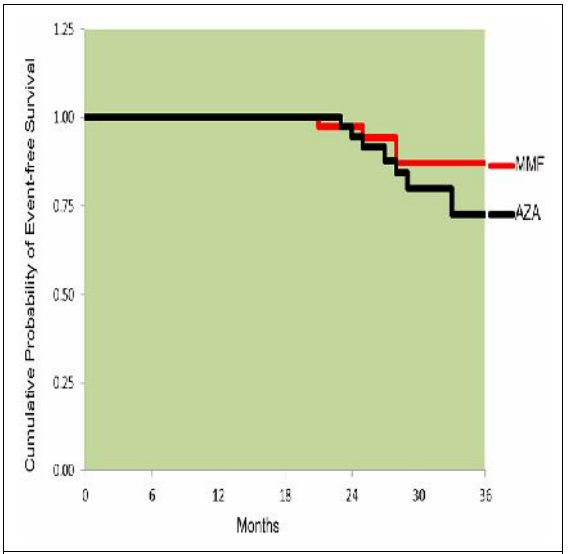

Figure 3. Kaplan–Meier estimates of event-free survival in the lupus nephritis patients treated with mycophenolate mofetil and azathioprine.

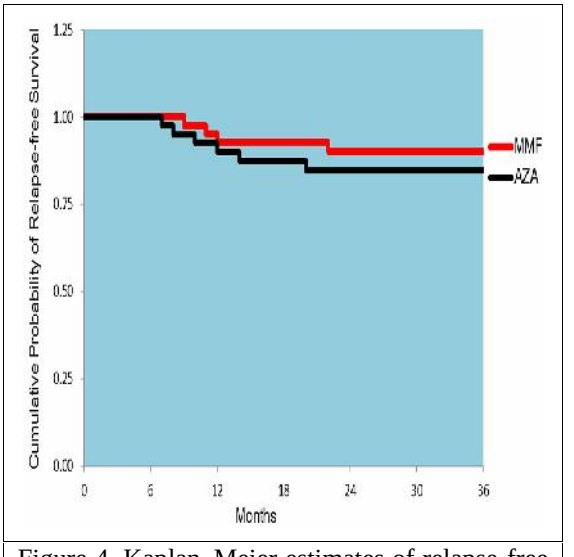

Figure 4. Kaplan–Meier estimates of relapse-free survival of the lupus nephritis patients treated with mycophenolate mofetil and azathioprine.

two groups ($P = 0.65$).

The estimated 36-month-patient survival rate in the MMF group was 95.1% and 90% in the AZA group, ($P = 0.37$, Figure 2). The estimated 36-month-event-free survival rate for the composite end points of death and ESRD was 95.1% in the MMF group and 91.3% in the AZA group ($P = 0.31$, Figure 3). The estimated 36-month-relapse-free survival rate was 90.2% in the MMF group and 85% in the AZA group ($P = 0.45$, Figure 4).

Discussion

The regional variation in the presentation of SLE is related to different genetic and environmental influences.[7] Renal involvement is common in SLE and often determines the course of the disease.[8] The prevalence of LN in the Sudan was previously reported as 14.7% of all glomerulonephritidis.[9] In this study, female to male ratio was found to be 15.7:1. This ratio is similar to what was seen in the United Arab Emirates (UAE)[10] and South Africa.[11] However, the ratio is higher compared to other studies from Senegal,[12] Tunisia,[13] Saudi Arabia,[14] Lebanon,[15] Kuwait,[16] USA,[17] and Europe,[18] and lowers than studies from Nigeria,[19] Zimbabwe,[20] and Sudan.[21] The mean age at presentation was 27.9 ± 10.2 years; this is similar to the pattern seen in Senegal,[12] Zimbabwe,[20] UAE,[10] Saudi Arabia,[14] Lebanon,[15] and Europe.[18] However, it differs from previous studies from Sudan,[21] Nigeria,[19] Tunisia,[13] South Africa,[11] Kuwait,[16] and the USA.[17] In this study, we achieved a total remission rate 75.3% (80.5% with MMF and 70% with AZA), complete remission rate of 54.3% (56.1% with MMF and 52.5% with AZA), and a partial remission rate of 21% (24.4% with MMF and 17.5% with AZA) over 29 ± 5.1 months. The survival rate, the event-free survival rate, and relapse-free survival were insignificantly higher in the patients in the MMF group than those in the AZA group.

Regarding side effects of drug therapy, gastrointestinal complications were more frequent within the MMF group than the AZA group. However, leukopenia was more common in the patients treated with AZA than those treated with MMF. Hospitalization, amenorrhea, infections, bleeding, hair loss, and gain weight frequencies were similar with MMF and AZA. Most events were mild and reversible with dose reduction. A recent retrospective study in Turkey reported by Sahin et al[22] evaluated the efficacy of maintenance regimens using either MMF or AZA in LN. The study population included 32 patients (17 in MMF and 15 in AZA), all patients were Caucasian. The total remission occurred in 84% of patients (82% with MMF and 87% with AZA), complete remission rate of 59.3% (58% with MMF and 60% with AZA), and a partial remission rate of 25% (22% with MMF and 27% with AZA) over 41.5 ± 7 months. The adverse events experienced during this study were mostly unremarkable and were not severe enough to lead to the interruption of therapy.

Moreover, Contreras et al[23] found that fewer patients treated with AZA and MMF reached the primary end points of death and CRF compared to the CYC group. Relapse-free survival was higher with MMF (78%) and AZA (58%) compared to IV CYC (43%). Mortality was increased with IV CYC compared to both oral agents. They concluded that maintenance therapy with either MMF or AZA was superior to IV CYC.

Recently, Houssiau FA, et al[24] compared AZA versus MMF for long-term immunosuppression in lupus nephritis; the results were from the MAINTAIN Nephritis Trial, which was limited to European patients. They concluded that fewer renal flares were observed in patients receiving MMF, but the difference did not reach statistical significance.

Another trial comparing MMF against AZA as remission-maintaining treatment for PLN following induction with a short course of intravenous CYC of the Aspreva Lupus Management Study.[25] It did not show any difference in the incidence of renal flares between the two maintenance therapies regarding the adverse events in our study, gastrointestinal complications were more common in the

MMF group than the AZA group. Leukopenia was more frequent with AZA than MMF, and hospitalization, ame-norrhea, and infections frequencies were similar in patients in the MMF group and the AZA group.

There were some limitations of our study. Our study was not powered to detect small differences between the two groups. In addition, our results cannot be generalized to patients with mild forms of LN since such patients were excluded from the trial.

Conclusion

We conclude that short-term therapy with intravenous CYC followed by maintenance therapy with oral MMF or AZA has similar efficacy and safety for the treatment of patients with moderate to severe LN. Oral MMF and AZA have similar effects in reducing the risk of relapse or ESRD and maintaining remission of LN. There is no significant difference between the two groups. Although our study supports the use of oral MMF or AZA as the first-line maintenance agent for LN, large controlled trials with long-term follow-up to confirm these findings are still needed.

Conflict of Interests

Each of the authors declares no financial or other conflict of interests in relationship with a company/organization or commercial identities.

References

1. Cervera R, Khamashta MA, Font J, et al. Systemic lupus erythematosus: Clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. The European Working Party on Systemic Lupus Erythematosus. Medicine (Baltimore) 1993;72:113-24.
2. Cameron JS. Lupus nephritis. J Am Soc Nephrol 1999;10:413-24.
3. Wallace DJ, Podell TE, Weiner JM, et al. Lupus nephritis. Experience with 230 patients in a private practice from 1950 to 1980. Am J Med 1982;72:209-20.
4. Singh S, Saxena R. Lupus nephritis. Am J Med Sci 2009;337:451-60.
5. Nossent HC, Henzen-Logmans SC, Vroom TM, Berden JH, Swaak TJ. Contribution of renal biopsy data in predicting outcome in lupus nephritis. Analysis of 116 patients. Arthritis Rheum 1990;33:970-7.
6. Huong DL, Papo T, Beaufils H, et al. Renal involvement in systemic lupus erythematosus. A study of 180 patients from a single center. Medicine (Baltimore) 1999;78:148-66.
7. Nossent HC. Systemic lupus erythematosus in the Arctic region of Norway. J Rheumatol 2001;28:539-46.
8. Mok CC, Wong RW, Lau CS. Lupus neph-ritis in Southern Chinese patients: clinico-pathologic findings and long-term outcome. Am J Kidney Dis 1999;34:315-23.
9. Khalifa EH, Kaballo BG, Suleiman SM, Khalil EA, El-Hassan AM. Pattern of glomerulo-nephritis in Sudan: histopathological and immunofluorescence study. Saudi J Kidney Dis Transpl 2004;15:176-9.
10. al-Attia HM. Clinicolaboratory profile of 33 Arabs with systemic lupus erythematosus. Postgrad Med J 1996;72:677-9.
11. Wadee S, Muhammed T. Lupus nephritis and its impact in a South African population. J Am Soc Nephrol 2004;15:791.
12. Ka MM, Diallo S, Kane A, et al. Systemic lupus erythematosus and lupus syndromes in Senegal. A retrospective study of 30 patients seen over 10 years. Rev Rhum Engl Ed 1998; 65:471-6.
13. Houman MH, Smiti-Khanfir M, Ben Ghorbell I, Miled M. Systemic lupus erythematosus in Tunisia: demographic and clinical analysis of 100 patients. Lupus 2004;13:204-11.
14. Alballa SR. Systemic lupus erythematosus in Saudi patients. Clin Rheumatol 1995;14:342-6.
15. Uthman IW, Muffarij AA, Mudawar WA, Nasr FW, Masri AF. Lupus nephritis in Lebanon. Lupus 2001;10:378-81.
16. Al-Jarallah K, Al-Awadi A, Siddiqui H, et al. Systemic lupus erythematosus in Kuwait – hospital based study. Lupus 1998;7:434-8.
17. Cooper GS, Parks CG, Treadwell EL, et al. Differences by race, sex and age in the clinical and immunologic features of recently diagnosed systemic lupus erythematosus patients in the southeastern United States. Lupus 2002; 11:161-7.
18. Cervera R, European Working Party on Systemic Lupus Erythematosus. Lessons from the Euro-Lupus Cohort. Ann Med Interne 2002;

153:530-6.
19. Adelowo OO, Oguntona SA. Pattern of systemic lupus erythematosus among Nigerians. Clin Rheumatol 2009;28:699-703.
20. Taylor HG, Stein CM. Systemic lupus erythematosus in Zimbabwe. Ann Rheum Dis 1986; 45:645-8.
21. Kaballo BG, Abubakr A, Nur MM, et al. Ethnic distribution and clinical features of systemic lupus erythematosus in the Sudan. Sudan Med J 2009;45:45-57.
22. Sahin GM, Sahin S, Kiziltas S, Masatlioglu S, Oguz F, Ergin H. Mycophenolate mofetil versus azathioprine in the maintenance therapy of lupus nephritis. Ren Fail 2008;30: 865-9.
23. Contreras G, Pardo V, Leclercq B, et al. Sequential therapies for proliferative lupus nephritis. N Engl J Med 2004;350:971-80.
24. Houssiau FA, D'Cruz D, Sangle S, et al. Azathioprine versus mycophenolate mofetil for long-term immunosuppression in lupus nephritis: results from the MAINTAIN Nephritis Trial. Ann Rheum Dis 2010;69: 2083-9.
25. Sundel R, Solomons N, Lisk L; Aspreva Lupus Management Study (ALMS) Group. Efficacy of mycophenolate mofetil in adolescent patients with lupus nephritis: evidence from a two-phase, prospective randomized trial. Lupus 2012;21:1433-43.