LUNELORD: A descriptive, prospective study to assess demographic, pharmacologic, biomarker, clinical features and QoL of patients with LUpus Nephritis and Long-term Organ Damage

STATISTICAL ANALYSIS PLAN (SAP)

UNIQUE IDENTIFIER	oneCDP: 216989
TITLE	LUNELORD: A descriptive, prospective study to assess demographic, pharmacologic, biomarker, clinical features and QoL of patients with LUpus NEphritis and Long-term ORgan Damage
STUDY ACCOUNTABLE PERSON	PPD
CONTRIBUTING AUTHORS	Main author: Dr. PPD (Phoenix CR) Reviewer: PPD (Phoenix CR)
VERSION	1.0
DATE	06 August 2021
BASED ON	Study Protocol Version 4.0 of 28 June 2021

REVISION HISTORY

Date	Version	Change(s) since last version
06 August 2021	Original (version 1.0) based on Study Protocol Version 4.0 of 28 June 2021	N/A

Contents

1. BACKGROUND AND RATIONALE

1.1. Background

Systemic lupus erythematosus (SLE or lupus) is a complex and severe rheumatic disease with exceedingly diverse clinical manifestations, including renal manifestations. Renal involvement is a frequent aspect of SLE, as 40–75% of SLE patients develop lupus nephritis (LN), most often within five years of the disease onset (1), although some patients do develop this complication later (2).

The risk of developing LN is higher among men, young people, and people of non-European ancestry (3). This risk varies significantly between different regions of the world and different races and ethnicities. For example, black and Hispanic SLE patients develop LN earlier, and have worse outcomes than white patients with SLE, including death and end-stage renal disease (ESRD) (4). As for Arab SLE patients, LN seems to be common and occurring in 37–69% of SLE patients in the Arab dominated groups, particularly among those from Saudi Arabia, and in 50% of the exclusively Arab group (1). Also, LN is more common in patients with anti-dsDNA and it is less frequent in those with positivity for rheumatoid factor and discoid manifestations (2).

LN is recognised as a major cause of morbidity, mortality, health expenditure, and impaired quality of life (QoL) in patients with SLE (1). However, an early diagnosis and treatment are associated with a better prognosis (2). In many patients, LN ends in chronic kidney disease or ESRD despite potent anti-inflammatory and immunosuppressive therapies (4). Also, patients with LN have a higher standardised mortality ratio (6–6.8 versus 2.4) and die earlier than SLE patients without LN (4). Importantly, 10-year survival improves from 46% to 95% if disease remission can be achieved (4). Despite the improvements in care, LN patients often suffer long-term morbidity that can adversely affect their QoL and ability to work (5), resulting in substantial direct and indirect costs. Patients with flares incur higher direct and indirect costs as compared to those without flares. Flares in major organs such as kidneys increase disease costs much more than other organ flares. The high costs associated with LN flare may be reduced by treatments that effectively control disease activity and prevent major organ flares (6,7). Thus, due to both direct and indirect costs, LN leads to a very high burden of disease. Improvement in disease activity and physical health, and prevention of organ damage, may reduce direct and indirect costs in SLE and LN (6-11). LN can be asymptomatic or “silent” (detected by routine renal biopsy), or presenting with trace

proteinuria or active urinary sediments (microscopic haematuria, pyuria or cellular casts), or with serious proteinuria (nephrotic syndrome) and acute nephritic syndrome with rapid progression to acute renal failure (5). LN evaluation consists of assessing serum creatinine level, urine dipstick testing, and urine sediment examination (3). Many patients will have findings suggestive of LN at the initial diagnosis of SLE, and patients with SLE should undergo screening for LN at diagnosis, at least yearly thereafter, and any time there is concern for a lupus flare (3). Furthermore, renal biopsy is the gold standard diagnosis and histological classification of LN (3,5). A complete staining pattern for LN consists of finding positive staining for immunoglobulin (Ig) G, A, and M with C1q, C3, and C4 (5). Moreover, patients with LN that is refractory to treatment should be evaluated for other possible causes for the persistence of proteinuria or deterioration in renal function. These include the nephrotoxic side effects of medications (such as the calcineurin inhibitors and nonsteroidal anti-inflammatory drugs [NSAIDs]), renal vein thrombosis, infections, over diuresis, and poorly controlled hypertension. Treatment compliance should be checked. To help guide further treatment decisions, a repeat renal biopsy should be considered in patients with persistently active serological markers (5,12). Indeed, a second biopsy provides information on: 1) the histological transformation of LN classes; 2) the degree of residual activity in the kidneys; and 3) the extent of chronic irreversible changes and their progression since the initiation of immunosuppressive treatment (5).

To help physicians in diagnosis and care management, new guidelines and recommendations for the management of LN have been proposed by the European League Against Rheumatism (EULAR) and European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) in 2020 (12). Beside the EULAR recommendations, other parameters may be considered such as: patient education, coexisting morbidities, fibromyalgia, stress reduction, and many organ specific complications and aspects of SLE (e.g. autoimmune haemolytic anaemia, and screening for pulmonary hypertension) (13). Patients are usually followed up by rheumatologists and nephrologists in hospital-based physicians in specialised SLE centres (14).

As for the treatment of LN, it depends on disease severity and risk for progressive kidney damage (3). A conservative treatment is used for the non-proliferative forms of LN (class II and V with sub-nephrotic range proteinuria and normal glomerular filtration rate), with treatment focused on blood pressure control with renin-angiotensin system blockade and immunomodulation with antimalarials (e.g. hydroxychloroquine) (3). As for immunosuppressive agents, these are used as

needed to treat extrarenal manifestations only. In addition to antimalarials and renin-angiotensin system blockade, proliferative forms of LN (class III, IV, or III/IV+V) and class V with nephrotic syndrome are treated with systemic immunosuppression combined with high-dose corticosteroids to suppress inflammation and control autoimmunity (3). This induction phase of treatment generally lasts 3–6 months and is followed by a prolonged, but less intense maintenance phase, often lasting years. It is not clear when maintenance therapy can be withdrawn. A repeat kidney biopsy showing histologic remission during maintenance in LN patients who have achieved complete clinical remission, or who have stable but persistent proteinuria, may help in making a decision to taper off therapy (4). During the maintenance phase, immunosuppressive/cytotoxic agents are continued but de-escalated slowly over time to limit risk for LN flares. Biological drugs developed more recently show interesting beneficial effects in LN (4). They decrease the level of B lymphocytes which contributes to the decrease in autoantibodies known to play the central role in disease activity and consequently decrease the global inflammation level (15).

There is a paucity of data in the Gulf countries on LN care management (treatment strategies, healthcare pathways, healthcare resource utilisation [HCRU] and costs), especially in moderate and severe cases. In this context, GSK has decided to carry out an observational study mainly to characterise LN patients in 5 Gulf countries who may benefit from early intervention. Also, in order to have an accurate estimation of the costs of LN care management. This study aims at evaluating disease costs according to patients' profile.

1.2. Rationale

SLE is a potentially serious, chronic, autoimmune disease, which can affect multiple organs of the body, including the kidneys (LN). The high variability and its unpredictable course (flaring/remission), combined with a lack of indicated and integrated treatments, induce a high unmet need within the patient population. Reliable data on SLE- and LN-related care patterns and resource utilisation in the Gulf region are currently unavailable. The expected key outcomes of this study will be:

- Description of clinical characteristics, demographics, treatment, and health-related quality of life (HRQoL) of LN patients.

- Description of "real-world" standard of care and HCRU associated with LN in the Gulf region.

The information collected may be used for scientific interactions with HCP's and payers and for developing a scientific communication plan for Gulf. It can also be used for clinical research, for health planners, for clinical management and education/information for patients/ healthcare professionals/ payers, etc. The study protocol is designed to obtain an accurate, "real-life" picture of LN patients in the Gulf countries.

2. STUDY OBJECTIVES

2.1. Primary Objective

To describe patient profile, demographic features, clinical manifestations, comorbidities, severity, treatments and HRQoL of LN patients over one-year period across 5 Gulf countries (UAE, Qatar, Bahrain, Kuwait and Oman).

2.2. Secondary Objectives

2.2.1. Secondary objective 1

To describe refractory LN cases, involving rituximab, and to assess changes in serological markers of disease activity (including anti-nuclear antibody, anti-dsDNA antibody and complement levels) over the treatment period.

2.2.2. Secondary objective 2

To assess the association between clinical factors, biomarkers, treatment, and renal remission.

2.2.3. Secondary objective 3

To assess impact of LN on HRQoL over a one-year period after diagnosis or enrolment.

2.2.4. Secondary objective 4

To describe LN HCRU and direct medical cost, associated with LN management across 5 Gulf countries over a one-year period.

2.2.5. Secondary objective 5

CCI [redacted]

3. STUDY DESIGN

The LUNELORD study is a multicentre prospective study compromising of a patient-completed survey and retrospective chart review. This study will enrol approximately 200 patients with clinician diagnosed LN cases from 5 different countries in the Gulf (UAE, Bahrain, Qatar, Kuwait and Oman). The recruitment will not be competitive among participating sites for optimal representation of the study population. Since rheumatologists usually play a leading role in the disease management in multidisciplinary setting, clinical sites will predominantly be selected from this clinical specialty. Centres from the private and public sectors will be chosen based on their ability to fulfil the objectives of the study and the ability to enter data onto the electronic case report form (eCRF). Given the ethnic diversity of the region study investigators will ensure to include all ethnicities.

GSK study team will choose sites, representing major lupus treatment centres in respective countries, based on availability of sufficient potentially eligible patient population, their competency and experience to conduct research, their ability to fulfil the objectives of the study, ability to enter the data onto the eCRF. Prior to selection feasibility all clinical sites and pilot eCRF will be tested and trainings will be conducted.

3.1. Patient Eligibility

3.1.1. Inclusion criteria

- ≥age of 18 years
- Clinician diagnosed LN patient
- At least one visit to the investigational centre during 12 months prior to the baseline visit, recorded in medical documentation
- Written informed consent by the patient

3.1.2. Exclusion criteria

- Incomplete medical records to be able to assess the disease severity or absence of any of the following renal laboratory results from the medical record within the last (12) twelve months:
    a. UPCR or 24-hour proteinuria or urine sediment (activity)
    b. Serum creatinine or eGFR; or measured GFR, if eGFR is not available
- Current or medical history of:
    a. Congenital or acquired immunodeficiency
    b. Malignancy in active treatment phase
    c. Acute viral infection, such as HIV infection, requiring hospitalisation

3.2. Sample Size

As other similar research recruited a sample size ranging between 200 and 300 patients (16,17) the decision was made to proceed with 200 sample size in this research. This sample size would provide a significant power to interpret the results of the study. In addition, due to overall budget constraints the maximum number of participants allocated for the study has been determined as 200.

Based on the sample size determination using Slovin's formula and assuming the total SLE population in Gulf countries is 5,600 patients, while 40% of SLE patients manifest with LN, the entire LN population size was estimated as 2,240 patients disease onset (16).

The margin of error (significance level), denoting the allowed probability of committing an error in selecting a small representative of the population, is 0.067 for the 93% of confidence that the data are going to be reflective of the entire LN population, given the assumptions of 200 LN patients, required to achieve this significance level (18).

Significance of the adverse factors, impacting the data accuracy and completeness, will be assessed during the data acquisition and may result in respective adjustments to the sample size.

In addition, taking into account our secondary hypothesis on the association between clinical factors, biomarkers, treatment and renal remission, a sample size of 200 observations (of which 65% are in not in renal remission=0 and 35% are in renal remission=1) achieves 80% power at a 0.050 significance level to detect a change in Prob(Y=1) from the baseline value of 0.200 to 0.385. This change corresponds to an odds ratio of 2.508.

4. STATISTICAL ANALYSIS

4.1. General Considerations

For each patient in the database eligibility and proof of signing consent will be checked. Those who do not satisfy eligibility or for whom there is no proof of consent signature will not be included in the analysis.

Numeric variables will be summarised using means ± standard deviations, medians, interquartile ranges (Q1-Q3) and, minimum and maximum values. Categorical variables will be described by frequencies and related percentages. The number of patients with missing values will be indicated for each variable.

Normality of continuous variables will be assessed using histograms and Q-Q plots.

In general, comparing numeric values between baseline and 12 months will be done using the paired t-test (or Wilcoxon signed rank test for non-normal data). Also for such variable, repeated

measures analysis will be used to test trends over time. For Dichotomous variables, the McNemar test will be used to compared between baseline and 12 months.

Significance level will be set at the 5% level. All analysis will be done using IBM-SPSS (version 27, Armonk NY).

4.2. Analysis Population

All patients who consented and are eligible will be part of the study population will be included in the final analysis. For those who declined to participate, reasons will be summarised using a frequency distribution.

4.3. Handling Missing Data

Missing data in this study can arise from the retrospective part (information not in the charts), or from the prospective part where patients either refuse to answer a question or are lost to follow up. Missing data will not be imputed. The number of missing entries for each variable will be indicated.

4.4. Interim Analyses

There is no scheduled interim analysis for this study.

4.5. Specific Analyses

4.5.1. Analysis of the primary objective

Patient demographics will be summarised using the methods presented in the general consideration section (see Table 1). Similar analysis will be done for the clinical manifestations, comorbidities, severity, treatments and HRQoL of LN patients over one year (Tables 2-5).

4.5.2. Analysis of secondary objective 1

Summary statistics will be used to describe refractory LN cases and the independent t-test or Wilcoxon signed rank test along with repeated measures analysis will be used to test for changes in serological markers of disease activity at one year and over the treatment period. Changes in categorical variables at one-year period will be tested using the McNemar's test (see Table 6).

4.5.3. Analysis of secondary objective 2

Univariate and multivariate logistic regression with renal remission as the dependent variable and clinical factors and treatment as the independent variables. Odds ratios and 95% confidence intervals (CIs) will be presented. Variables with a p-value of 0.25 or less along with known associated factors with renal remission will be used to build the final multivariate model. The final multivariable model will contain only significant factors or those who have confounding effect on others in the model.(see Table 7).

4.5.4. Analysis of secondary objective 3

Changes in SF-36 total score from baseline to one year will be test for significance using the paired t-test (or Wilcoxon signed rank test for non-normal distribution. The same analysis will be done for all subscales of the SF-36 (see Table 8).

4.5.5. Analysis of secondary objective 4

For each country, the average HCRU and direct medical cost will be estimated along with its 95%CI (see Table 9).

4.5.6. Analysis of secondary objective 5

CCI [redacted]

5. LIST OF TABLES

5.1. Table 1: Patients Demographics

Variable		Summary stat
Age	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Gender	**Female**	n(%)
	Male	n(%)
	Missing	XX
Race	**Arab**	n(%)
	Caucasian/White	n(%)
	Black/African-American	n(%)
	Hispanic/Latino	n(%)
	other	n(%)
	Missing	XX
Ethnicity	**Arab**	n(%)
	Turkish	n(%)
	Persian	n(%)
	Kurds	n(%)
	Other	n(%)
	Missing	XX
Nationality	**Bangladeshi**	n(%)
	Egyptian	n(%)
	Emirati	n(%)
	Indian	n(%)
	Jordanian	n(%)
	Kuwaiti	n(%)
	Lebanese	n(%)
	Omani	n(%)
	Pakistani	n(%)
	Palestinian	n(%)
	Qatari	n(%)
	other	n(%)
	Missing	XX
Health insurance coverage	**Yes**	n(%)
	No	n(%)
	Missing	XX
Employment status	**Full-time employment**	n(%)

	Part-time employment	n(%)
	Self-employment	n(%)
	Housewife	n(%)
	Retired	n(%)
	Not working	n(%)
	Other	n(%)
	Missing	XX
Smoking status	**Current**	n(%)
	Former	n(%)
	Never	n(%)
	Missing/unknown	XX
Alcohol consumption	**Current**	n(%)
	Former	n(%)
	Never	n(%)
	Missing/unknown	XX
BMI (in Kg/m^2)	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX

5.2. Table 2: Baseline Clinical Characteristics of the Patients

Variable		Summary stat
Comorbidities (since the date of first diagnosis of SLE or LN)	**Yes**	n(%)
	No	n(%)
	Missing	XX
Comorbidity	**Antiphospholipid syndrome**	n(%)
	Other autoimmune disorder	XX
	Head and neck disorders	n(%)
	Eyes disorders	n(%)
	Ears, nose and throat disorders	n(%)
	Chest/respiratory disorders	n(%)
	Arterial hypertension	n(%)
	Other heart/cardiovascular disorders	n(%)
	Gastrointestinal/liver disorders	n(%)
	⋮	⋮
	Substance abuse	n(%)
	Missing	XX
SLE		
Age at manifestation	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Age at diagnosis	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Age at last visit in 2020	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Diagnosis period (in months)	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
SLEDAI-2K	**Yes**	n(%)
	No	n(%)
	Missing	XX
SLEDAI2K VALUE	**mean±sd**	XX.X±XX.X

Variable		Summary stat
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
ACR2012 classification		
Clinical Criteria	**Acute cutaneous lupus**	n(%)
	Chronic cutaneous lupus	n(%)
	Oral ulcers	n(%)
	Nonscarring alopecia	n(%)
	Synovitis involving two or more joints	n(%)
	Serositis	n(%)
	Renal	n(%)
	Neurologic	n(%)
	Haemolytic anaemia	n(%)
	Leukopenia	n(%)
	Thrombocytopenia	n(%)
Immunological criteria	**ANA above laboratory reference range**	n(%)
	Anti-dsDNA above laboratory reference range…	n(%)
	Anti-Sm	n(%)
	Antiphospholipid antibody…	n(%)
	Low complement…	n(%)
	Direct Coombs test in the absence of haemolytic anaemia	n(%)
Refractory SLE	**Yes**	n(%)
	No	n(%)
	Missing	XX
Lupus Nephritis		
Age at manifestation	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Age at diagnosis	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Diagnosis period (in months)	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X

Variable		Summary stat
	Missing	XX
Renal biopsy in past year	**Yes**	n(%)
	No	n(%)
	Missing	XX
NIH LN Activity Indices	**Yes**	n(%)
	No	n(%)
	Missing	XX
NIH LN Activity Indices	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
NIH LN Chronicity Indices	**Yes**	n(%)
	No	n(%)
	Missing	XX
NIH LN Chronicity Indices	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Number of glomeruli	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Active clinical manifestation	**Pedal oedema**	n(%)
	Serositis	n(%)
	Hair loss	n(%)
	Decreased urine output	n(%)
	⋮	⋮
	Leukopenia	n(%)
Antibodies assessment	**Anti-C1q**	n(%)
	Anti-dsDNA test	n(%)
	⋮	⋮
	Anti-β2-glycoprotein I antibodies	n(%)
LN pathological type (ISN/RPS 2003 classification)	**Class I**	n(%)
	Class II	n(%)
	Class III	n(%)
	Class IV	n(%)
	Class V	n(%)
	Class VI	n(%)
Tubular atrophy	**Mild**	n(%)

Variable		Summary stat
	Moderate	n(%)
	Severe	n(%)
	not present	n(%)
Interstitial inflammation and fibrosis	**Mild**	n(%)
	Moderate	n(%)
	Severe	n(%)
	not present	n(%)
Arteriosclerosis	**Mild**	n(%)
	Moderate	n(%)
	Severe	n(%)
	not present	n(%)
Other vascular lesions	**Mild**	n(%)
	Moderate	n(%)
	Severe	n(%)
	not present	n(%)
Organ Damage (SLICC/ACR Damage Index (SDI)	**Yes**	n(%)
	No	n(%)
	Missing	XX
Organ Damage Score	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Renal remission	**Yes**	n(%)
	No	n(%)
	Missing	XX
Renal remission duration	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
LN treatment history		
Number of prior treatment failures/relapse	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
ever had an end-stage renal disease (ESRD)?	**Yes**	n(%)
	No	n(%)

Variable		Summary stat
	Missing	XX
Age at ESRD diagnosis	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Duration from date of LN diagnosis to ESRD diagnosis	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX
Dialysis		
Haemodialysis	**No**	n(%)
	yes in the past	n(%)
	Yes current	n(%)
Peritoneal dialysis	**No**	n(%)
	yes in the past	n(%)
	Yes current	n(%)
CRRT	**No**	n(%)
	yes in the past	n(%)
	Yes current	n(%)
Listed for transplant	**Yes**	n(%)
	No	n(%)
	Missing	XX
Prior transplant	**Yes**	n(%)
	No	n(%)
	Missing	XX
Duration from LN to transplant	**mean±sd**	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X
	Missing	XX

5.3. Table 3: Treatments and Concomitant Medication

Variable		Summary stat
NSAID	**Yes**	n(%)
	No	n(%)
	Ongoing	n(%)
Prednisone	**Yes**	n(%)
	No	n(%)
	Ongoing	n(%)
Other corticosteroid	**Yes**	n(%)
	No	n(%)
	Ongoing	n(%)
⋮	⋮	⋮
other	**Yes**	n(%)
	No	n(%)
	Ongoing	n(%)
Concomitant medication	**Yes**	n(%)
	No	n(%)
Concomitant medication 1		n(%)
Concomitant medication 1		n(%)
Concomitant medication 1		n(%)

5.4. Table 4: Changes in Disease Activity and Chronicity Over Time

		Prior 12 months	At baseline	At 3 months	At 6 months	At 9 months	At 12 months	Total change baseline to 12 months	p-value comparing baseline to 12 months
Change in insurance coverage	**Yes** **No** **Missing**		n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	
SLE									
Change in disease activity	**Yes** **No** **Missing**		n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	
SLEDAI2K value	**mean ±sd** **median (Q1-Q3)** **Min-Max** **Missing**	XX.X±XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X±XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	X.XXX
Refractory SLE	**Yes** **No** **Missing**	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	
LN									
Organ Damage (SLICC/ACR Damage Index (SDI)	**Yes**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	

	No **Missing**	n(%) XX	n(%) XX	n(%) XX	n(%) XX	n(%) XX	n(%) XX	n(%) XX	
Organ Damage Score	**mean ±sd** **median (Q1-Q3)** **Min-Max** **Missing**	XX.X±X.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X±XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	X.XXX
Renal remission	**Yes** **No** **Missing**	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	n(%) n(%) XX	
Renal remission duration	**mean ±sd** **median (Q1-Q3)** **Min-Max** **Missing**	XX.X±X.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X± XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	XX.X±XX.X XX.X (XX.X - XX.X) XX.X - XX.X XX	X.XXX
Renal biopsy requested	**Yes** **No**	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	
NIH LN activity	**Yes** **No**	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	n(%) n(%)	

	mean ±sd	XX.X±X.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X±XX.X	X.XXX
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	
	Missing	XX	XX	XX	XX	XX	XX	XX	
NIH chronicity	**Yes**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	
	No	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	
	mean ±sd	XX.X±X.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X±XX.X	X.XXX
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	
	Missing	XX	XX	XX	XX	XX	XX	XX	
Number of glomeruli	**mean ±sd**	XX.X±X.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X± XX.X	XX.X±XX.X	X.XXX
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	
	Missing	XX	XX	XX	XX	XX	XX	XX	
changes in clinical manifestation									

Pedal oedema	**No changes**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Worsening	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Improvement	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Serositis	**No changes**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Worsening	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Improvement	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮

5.5. Table 5: Medication Over Time

Variable		At baseline	At 3 months	At 6 months	At 9 months	At 12 months	Overall change
NSAID	**No change**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Adjustment of the dose by >=20%	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Changes happening for longer than 1 month	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Change or addition in the type or groups of medication	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Prednisone	**No change**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Adjustment of the dose by >=20%	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Changes happening for longer than 1 month	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Change or addition in the type or groups of medication	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Other corticosteroid	**No change**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Adjustment of the dose by >=20%	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Changes happening for longer than 1 month	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Change or addition in the type or groups of medication	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮
LN/SLE medication							
Rituximab	**No change**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Adjustment of the dose by >=20%	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Changes happening for longer than 1 month	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
	Change or addition in the type or groups of medication	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮

5.6. Table 6: Lab Tests and Changes Over Time

Variable		Prior 12 months	At baseline	At 3 months	At 6 months	At 9 months	At 12 months	Change over 12 months	p-value	p-value (Repeated measures)
Haematology										
WBCC	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
Haemoglobin	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		

	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
Platelet	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮		
Plasma albumin	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		

	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
Lipid profile										
Total cholesterol		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Tested									
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
LDL-cholesterol	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		

	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮		
Liver function										
SGPT	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
SGOT	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		

	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮		
Renal function										
Serum creatinine	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
Estimated 24-hour urinary protein	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		

	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮		
Serological tests										
C3	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
C4	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Normal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		

	Abnormal	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	X.XXX	X.XXX
	Median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)		
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X		
	Missing	XX	XX	XX	XX	XX	XX	XX		
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮		
APL antibody tests										
LAC	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Negative	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Positive	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
ACL	**Tested**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Not tested	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
ACL-IgA	**Negative**	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
	Positive	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)		
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮		

5.7. Table 7: Logistic Regression for Associated Factors with Renal Remission

	AOR	95% CI	p-value
Age	X.XXX	X.XXX - X.XXX	X.XXX
Gender (Female vs Male)	X.XXX	X.XXX - X.XXX	X.XXX
Treatment 1	ref		
Treatment 2	X.XXX	X.XXX - X.XXX	X.XXX
⋮	⋮	⋮	⋮
SLEDAI2K VALUE	X.XXX	X.XXX - X.XXX	X.XXX

5.8. Table 8: Changes in Quality of Life

Variable		Baseline visit	12 months	Change	p-value
SF36	**Yes**	n(%)	n(%)		
	No	n(%)	n(%)		
	mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	
Physical functioning	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
Role limitation due to physical health	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
Role limitation due to emotional health	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
Energy/fatigue	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
Social functioning	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
Pain	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
General health	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX
Emotional well-being	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	0.XXX

5.9. Table 9: Health Care Utility and Cost

Variable		Baseline visit 1	At 3 months	At 6 months	At 9 months	At 12 months	Overall
Number of office visits	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X
	Missing	XX	XX	XX	XX	XX	XX
Number of visits to other specialties for LN-related reasons	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X
	Missing	XX	XX	XX	XX	XX	XX
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮
Cost (per patient)	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X
	95% CI	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X
	Missing	XX	XX	XX	XX	XX	XX
Bahrain cost (per patient)	**mean±sd**	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X
	95% CI	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)	(XX.X - XX.X)
	median (Q1-Q3)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)	XX.X (XX.X - XX.X)
	Min-Max	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X	XX.X - XX.X
	Missing	XX	XX	XX	XX	XX	XX
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮
	mean±sd	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X	XX.X±XX.X

UAE cost (per patient)	**95% CI** **median (Q1-Q3)** **Min-Max** **Missing**	(XX.X - XX.X) XX.X (XX.X - XX.X) XX.X - XX.X XX	(XX.X - XX.X) XX.X (XX.X - XX.X) XX.X - XX.X XX	(XX.X - XX.X) XX.X (XX.X - XX.X) XX.X - XX.X XX	(XX.X - XX.X) XX.X (XX.X - XX.X) XX.X - XX.X XX	(XX.X - XX.X) XX.X (XX.X - XX.X) XX.X - XX.X XX	(XX.X - XX.X) XX.X (XX.X - XX.X) XX.X - XX.X XX

6. REFERENCES

1. Al Attia HM. Lupus nephritis among arabs - differences with other races; emphasis on clinicopathological and serological perspectives. Saudi J Kidney Dis Transpl. 2000;11(3):370–80. PMID: 18209329
2. Delfino J, Dos Santos TAFG, Skare TL. Comparison of lupus patients with early and late onset nephritis: a study in 71 patients from a single referral center. Adv Rheumatol. 2020;60(1):5. doi: 10.1186/s42358-019-0105-5
3. Parikh SV, Almaani S, Brodsky S, Rovin BH. Update on lupus nephritis: core curriculum 2020. Am J Kidney Dis. 2020;76(2):265–81. Published online March 24, 2020. doi: 10.1053/ j.ajkd.2019.10.017
4. Almaani S, Meara A, Rovin BH. Update on lupus nephritis. Clin J Am Soc Nephrol. 2017;12(5):82–35. doi: 10.2215/CJN.05780616
5. Mok CC. Understanding lupus nephritis: diagnosis, management, and treatment options. Int J Womens Health. 2012;4:213–22. doi: 10.2147/IJWH.S28034
6. Zhu TY, Tam LS, Lee VW, Lee KK, Li EK. The impact of flare on disease costs of patients with systemic lupus erythematosus. Arthritis Rheum. 2009;61(9):1159–67. doi: 10.1002/art.24725
7. Carls G, Li T, Panopalis P, et al. Direct and indirect costs to employers of patients with systemic lupus erythematosus with and without nephritis. J Occup Environ Med. 2009;51(1):66–79. doi: 10.1097/JOM.0b013e31818a405a
8. Sutcliffe N, Clarke AE, Taylor R, Frost C, Isenberg DA. Total costs and predictors of costs in patients with systemic lupus erythematosus. Rheumatology (Oxford). 2001;40(1):37–47. doi: 10.1093/rheumatology/40.1.37
9. Huscher D, Merkesdal S, Thiele K, et al. Cost of illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus erythematosus in Germany. Ann Rheum Dis. 2006;65(9):1175–83. doi: 10.1136/ard.2005.046367

10. Wilson EC, Jayne DR, Dellow E, Fordham RJ. The cost-effectiveness of mycophenolate mofetil as firstline therapy in active lupus nephritis. Rheumatology. 2007;46(7):1096–101. doi: 10.1093/rheumatology/kem054

11. Clarke AE, Panopalis P, Petri M, et al. SLE patients with renal damage incur higher health care costs. Rheumatology (Oxford). 2008;47(3):329–33. doi: 10.1093/rheumatology/kem373

12. Fanouriakis A, Kostopoulou M, Cheema K, 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 [published online March 27, 2020]. Ann Rheum Dis. doi: 10.1136/annrheumdis-2020-216924

13. Wallace DJ. New European Recommendations (European League against Rheumatism 2008) for the management of Lupus Erythematosus: American perspective. Pol Arch Med Wewn. 2008;118 (7-8):402–3. PMID: 18714734

14. Mok CC. Who should treat lupus nephritis: rheumatologists or nephrologists?. Nat Rev Nephrol0 2008;4:E1. doi: 10.1038/ncpneph0654

15. Panopalis P, Clarke AE. Systemic lupus erythematosus: clinical manifestations, treatment and economics. Expert Rev Pharmacoeconomics Outcomes Res. 2006;6(5):563–75. doi: 10.1586/14737167.6.5.563

16. Davidson JE, Fu Q, Ji B, Rao S, Roth D, Magder LS, Petri M. Renal remission status and longterm renal survival in patients with lupus nephritis: a retrospective cohort analysis. J Rheumatol. 2018;45(5):671–7. doi: 10.3899/jrheum.161554. Epub 2018 Mar 1. PMID: 29496892; PMCID: PMC5932209.

17. Moroni G, Quaglini S, Radice A, et al. The value of a panel of autoantibodies for predicting the activity of lupus nephritis at time of renal biopsy. J Immunol Res. 2015;2015:106904. doi:10.1155/2015/106904

18. Kim M, Merrill JT, Wang C, et al. SLE clinical trials: impact of missing data on estimating treatment effects. Lupus Sci Med. 2019;6(1):e000348. doi: 10.1136/lupus-2019-000348