

Supplemental Table S1: Adverse prognostic factors dictating aggressive immunosuppressive therapy in lupus nephritis

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- Nephrotic-range proteinuria
 - Reduced glomerular filtration rate (GFR) or rapidly-progressive glomerulonephritis
 - Uncontrolled hypertension
 - Class IV, or mixed (class V + III/IV) nephritis
 - High-risk histological features
 - High activity [NIH AI] >11; high chronicity [NIH CI] >3
 - Combination of AI > 10 and CI > 2
 - Cellular crescents, fibrinoid necrosis
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SUPPLEMENTAL BOXES

Supplemental Box 1. Global outcome measures and response criteria in SLE

- ***SLE responder index (SRI)***
 - Combines SLEDAI, BILAG and physician global assessment (PGA).
 - SRI 4 denotes a 4-point improvement in SLEDAI; SRI 6, a 6-point improvement; SRI 8, an 8-point improvement.
- ***Remission (on treatment)***
 - *Inactivity or disease remission on treatment* in patients with previous history of active moderate-to-severe disease. *All of the following* three conditions must be fulfilled for at least 6 months:
 - (a) clinical (i.e. excluding serology) SLEDAI-2K ≤ 2 and;
 - (b) low-dose glucocorticoids (≤ 7.5 mg/day) and/or stable, well-tolerated dose of maintenance immunosuppressive or biological drugs.
 - (c) A Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI physician global assessment (PGA, scale 0–3) ≤ 0.5 ;
- ***Lupus low disease activity state (LLDAS)***
 - (a) SLEDAI-2K ≤ 4 , with no activity in major organ systems (renal, central nervous system (CNS), cardiopulmonary, vasculitis, fever) and no haemolytic anaemia or gastrointestinal activity;
 - (b) no new lupus disease activity compared to the previous assessment;
 - (c) A SELENA-SLEDAI PGA (scale 0–3) ≤ 1 ;
 - (d) a current prednisolone (or equivalent) dose ≤ 7.5 mg daily; and
 - (e) well tolerated standard maintenance doses of immunosuppressive and approved biological agents.

Supplemental Box 2. Key points in Lupus Nephritis

- Identify patients at higher risk to develop nephritis (cSLE, young patients, high disease activity- clinically and/or serologically) and monitor for renal disease by regular urinalysis and measurement of serum creatinine
- Do not underestimate isolated glomerular haematuria-especially in the presence of active serology and extrarenal lupus or low-grade proteinuria (below 0.5 gm/day). Be aware of evolution of lupus nephritis into more severe forms
- The individual predictive value of clinical features and laboratory tests (haematuria, proteinuria, serology) for lupus nephritis at particular time points is modest. Have low threshold for renal biopsy. If you think about it, do it (unless contraindicated)
- In the kidney biopsy report, look for crescents/fibrinoid necrosis and tubular atrophy and interstitial fibrosis. Stratify according to severity (histologic and clinical factors) and treat accordingly (see Table 1)
- Changes in serological tests are more important predictors of concurrent or impending flare than their absolute levels. Pre-emptive treatment based on serology alone is not indicated
- Haematuria and active urine sediment are reliable for the diagnosis of renal disease or its but not for monitoring of treatment or prognosis
- In contrast to haematuria, proteinuria is useful for both diagnosing and monitoring of lupus nephritis. In patients under treatment, proteinuria is a good prognostic factor -if below 0.7 mg/dl- irrespective of haematuria