Mapping Disease Severity and Progression of Renal Involvement in Patients with Systemic Lupus Erythematosus

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Introduction

- A pragmatic review (GSK study LS3178) was conducted to better understand the association between systemic lupus erythematosus (SLE), lupus nephritis (LN), and end-stage renal disease (ESRD) as well as the degree of severity and the transitions between severity states, risk factors, laboratory predictors of disease progression, and overall disease progression
- A pragmatic review method was chosen in order to develop an overall picture of the available information as well as any gaps in the literature, with a view to addressing more specific questions in the future

Objectives

To map disease severity and progression of renal involvement in SLE, focusing on three research categories:

1. **Development of LN among patients with SLE**
2. **Within-LN progression**
3. **Progression to ESRD**

Methods

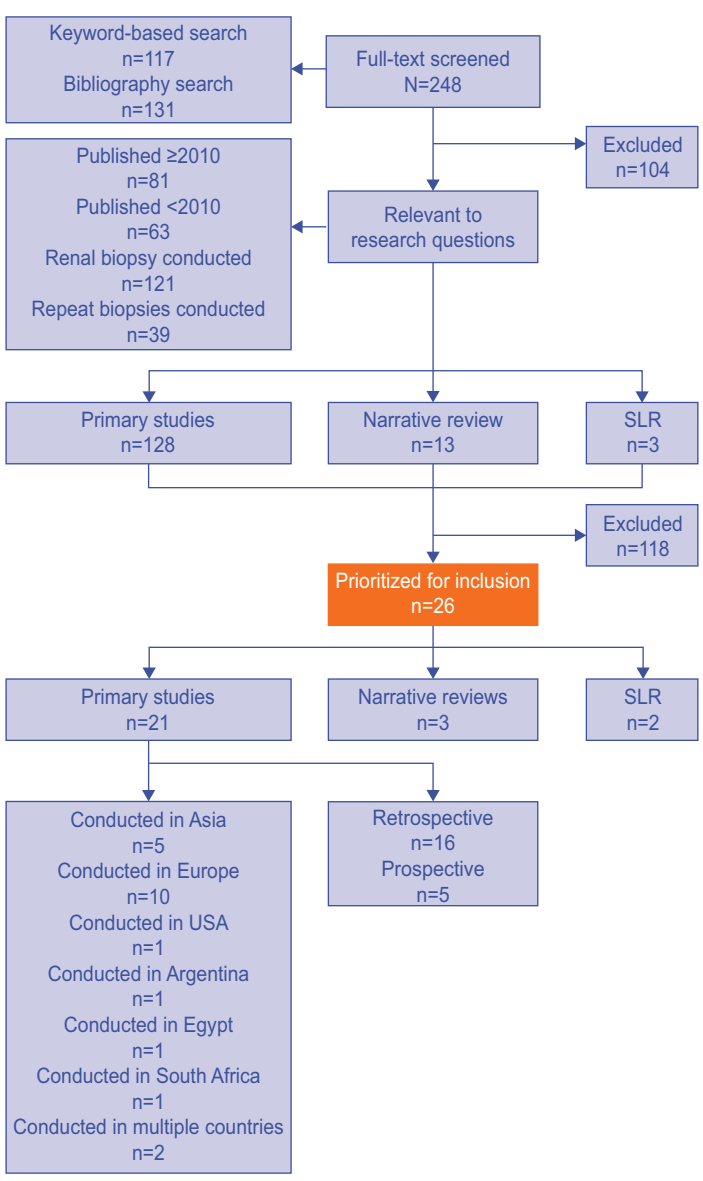
Literature search and data extraction

- A keyword-based literature search was conducted using PubMed, Google, and Google Scholar and supplemented with a bibliography search relevant to the focus area
- Publications were screened and prioritized for inclusion: high quality; published after 2010; addressed a topic of focus or an information gap; data were from the USA or Europe (high-quality pre-2010 and non-USA/Europe publications were permitted)

Results

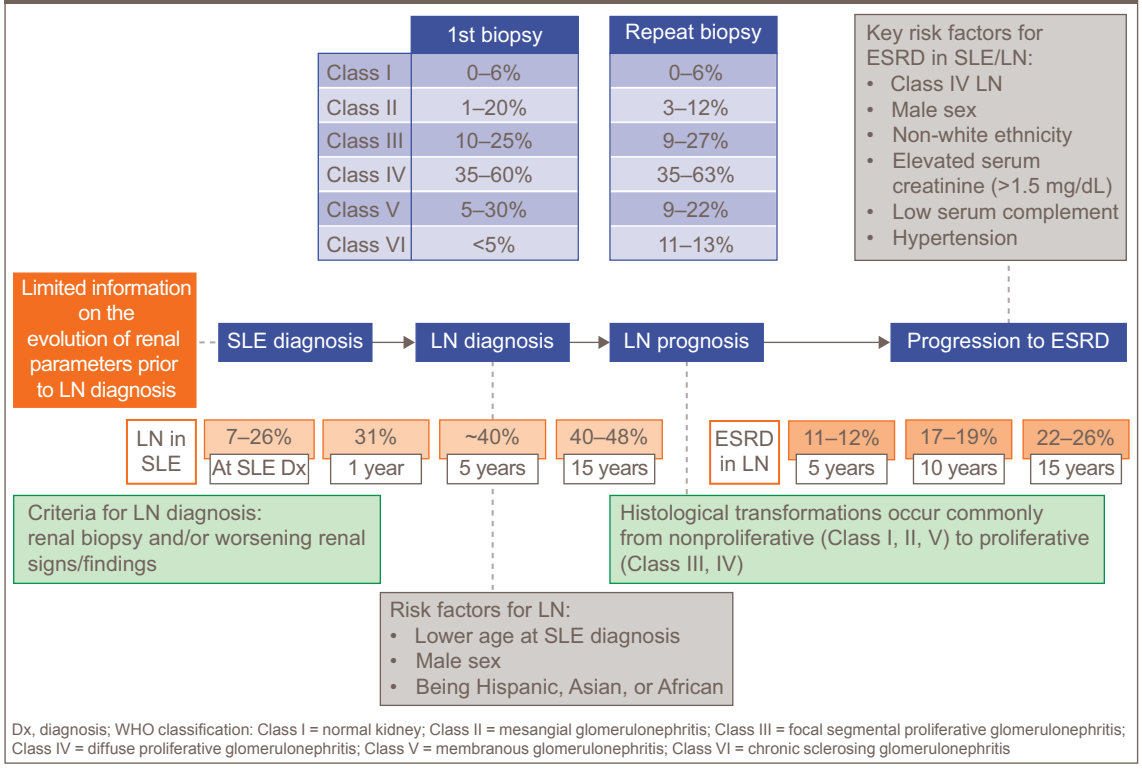
- Literature screening and selection are shown in **Figure 1**
- An overview of the results is provided in **Figure 2**

Figure 1. Literature screening metrics



SLR, systematic literature review; USA, United States of America

Figure 2. Mapping of disease progression from SLE to LN and ESRD



Dx, diagnosis; WHO classification: Class I = normal kidney; Class II = mesangial glomerulonephritis; Class III = focal segmental proliferative glomerulonephritis; Class IV = diffuse proliferative glomerulonephritis; Class V = membranous glomerulonephritis; Class VI = chronic sclerosing glomerulonephritis

- 7–26% of patients had LN at the time of SLE diagnosis
- 31–48% of patients with SLE developed LN in the disease course, most (80–90%) within 5 years of diagnosis
- Risk factors for developing LN included male sex; younger age at SLE diagnosis; and African, Asian, or Hispanic ethnicity
- Data on renal symptoms prior to LN diagnosis were limited; in general, worsening renal parameters were indicated in most of the studies as the primary reason for biopsy
- Class IV nephritis was the most common LN class found at first biopsy (35–60%)
- Data on time to progression within LN were scarce, most likely because transformation between LN classes is not sequential and because progression is determined by renal function parameters without the need for second biopsy
  - A single study suggested that median (range) time to histological transformation with LN was 32 months (11–305 months)

Conclusions

- **Early diagnosis and management of LN are important to delay progression**
- **Early elevation of serum creatinine was identified as a predictor of worsening disease state and potentially a useful laboratory predictor of progression within LN classes and from SLE/LN to ESRD**
- **This review enhanced our understanding of renal involvement within SLE and revealed gaps in the literature, including information on early renal symptoms, robust data in class transformations due to lack of repeat biopsies, and the timing of progression within LN stages and from SLE/LN to ESRD**
- **Male patients, patients of non-white race, and patients of a younger age at SLE diagnosis were at higher risk of developing LN and progressing from SLE/LN to ESRD**
- **When LN develops, it usually does so soon after SLE diagnosis; transformation to proliferative lesions is common and can occur rapidly**
- **Limitations: This review did not address patient experience of nephritis, nor did it assess the proportion of patients with Class I/II (as these are not biopsied) or the extent to which progression to Class III/IV could be delayed through treatment**

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Disclosures

- **JA**, **KG**, **DB**, **RAL**, and **DR** are employees of GSK and hold shares in the company. **AM** and **GK** are employees of Bridge Medical Pvt. Ltd and have nothing to disclose.

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