Lupus nephritis is a severe cause of acute kidney injury and an important cause of end-stage renal failure in some regions such as Asia. It is characterised by aberrant innate and adaptive immune responses, autoantibody production and their deposition in the kidney parenchyma, triggering complement activation, increased proliferation of resident renal cells and upregulation of pro-inflammatory molecules leading to inflammatory cell infiltration, all of which culminate in the destruction of normal nephrons and their replacement by fibrous tissue. Anti-dsDNA antibodies are specific to SLE and their level often correlates with disease activity. Apart from mediating pathogenic processes through the formation of immune complexes, there is evidence that pathogenic anti-dsDNA antibodies can bind to resident renal cells and induce downstream inflammatory and fibrotic processes. Though clinically effective, current treatment for lupus nephritis entails the use of non-specific immunosuppressive agents and the anti-inflammatory action of high-dose corticosteroids. The clinical and historical impact of novel biologics targeting pro-inflammatory molecules remain to be fully defined. Insight into the underlying mechanisms that induce inflammatory and fibrotic processes in the kidney in lupus nephritis could offer opportunities for novel therapeutic options to improve clinical outcome.

This lecture will discuss recent advances in the understanding of pathogenic mechanisms leading to inflammation and fibrosis in the kidney in lupus nephritis, with particular focus on the contribution of resident renal cells.

Lupus nephritis (LN), complete remission (CR) or partial remission is associated with better patient and renal survival. Subjects who do not achieve a 25% reduction in proteinuria within 8 weeks of starting induction immunosuppression are unlikely to achieve even a PR. Voclosporin (VCS) is a novel CNI demonstrating less pharmacokinetic variability and a potentially improved safety profile compared with other CNIs.

Published and unpublished data in studies in experimental models of these forms of renal vasculitis will be discussed, focusing on the role of cell mediated responses and renal injury in these diseases. The potential relevance of these studies to SLE and lupus nephritis will be highlighted.

**Background and Aims**

In lupus nephritis (LN), complete remission (CR) or partial remission is associated with better patient and renal survival. Subjects who do not achieve a 25% reduction in proteinuria within 8 weeks of starting induction immunosuppression are unlikely to achieve even a PR. Voclosporin (VCS) is a novel CNI demonstrating less pharmacokinetic-pharmacodynamic variability and a potentially improved safety profile compared with other CNIs.

**Methods**

**Entry criteria**

- Renal biopsy within 24 months (Class III; IV-S, IV-G (A) or (A/C)); V, III/V, IV/V, ISN/RPS);
- Urine protein:creatinine ratio (UPCR) ≥ 1.0 mg/mg (III/IV) or UPCR ≥ 1.5 mg/mg (V);
- Serum evidence of active LN; and eGFR > 45 mL/min/1.73 m².

AURION assessed the ability of biomarkers at 8 weeks to predict clinical response over 24 and 48 weeks when taking voclosporin (VCS) 23.7 mg po BID in combination with non-specific immunosuppressive agents and the anti-inflammatory agent MMF and prednisolone.