



Abstract 1108 Figure 1 Findings at first biopsy (baseline, at time of nephritis diagnosis) and repeat biopsy (5-7 months into therapy) stratified by clinical response at time of repeat biopsy (CR, complete response; PR, partial response; NR, no response). Shown are medians (lines), means (large circles), and ranges (activity index scored 0 to 24 and chronicity index scored 0 to 12 based on ISN/RPS schema).

clinically. Histologic activity and damage were calculated using National Institutes of Health activity and chronicity indices. Lupus nephritis class transformation and changes in the degree of immune complex deposition were determined. Descriptive statistics and comparison tests were used before and after induction treatment.

Results A total of 44 patients were identified. Complete clinical response was achieved in 43% (19/44) after induction and 69% (29/42) at one year. None of the complete responders after induction had histologic activity index of > 2 on repeat biopsy (figure 1). Activity index after induction in complete responders (median 1, range 0-2) was lower than in partial or non-responders (median 2, range 0-10) (p -value < 0.005). Complete clinical response was associated with transformation to a non-proliferative class in 79% (15/19) and a reduction in immune complex deposition in 68% (13/19) on repeat biopsy.

Conclusions Unlike adult-onset lupus nephritis, clinical and histologic remission are more congruent after induction therapy in childhood-onset disease. There was good correlation between clinical response and activity index.

Lay Summary Lupus nephritis can cause kidney failure. The need to balance risks and benefits of immunosuppression requires stringent monitoring. In adults with lupus, available diagnostics are insufficient to gauge response to initial "induction" therapy and repeat biopsy studies are necessary to rigorously test novel biomarkers. Here we show that repeat biopsy in children performed 1/2 year into therapy correlates well with clinical response, but there is a subset of children with sub-clinical scarring that would be missed without repeat biopsy - this subset may be at risk long-term for kidney failure.

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VISUALIZING *IN SITU* IMMUNE PATHOGENIC MECHANISMS IN HUMAN LUPUS NEPHRITIS

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For over 50 years, systemic lupus erythematosus (SLE) has been thought to result from a break in systemic tolerance and production of pathogenic autoreactive antibodies. In the kidney, the manifestation of systemic autoimmunity is glomerulonephritis (GN). However, tubulointerstitial inflammation (TII)—and not GN—predicts progression to end stage renal disease (ESRD). Lupus TII is associated with a local immune response very different than the inflammation observed in glomeruli. These observations indicate that *in situ* immunity is a central pathogenic mechanism of lupus nephritis. Recently, we developed computational pipelines by training and implementing several deep learning models to identify cells and cellular spatial relationships in biopsies from lupus nephritis patients. When applied to confocal micrographs of renal tissue, this analytic approach revealed discrete *in situ* inflammatory states in lupus nephritis which differed in cellular constituency, spatial architecture and prognosis. These observations demonstrate the utility of studying *in situ* immunity to both identify prognostic groups and therapeutic targets. In follow up studies, we are using high dimensional confocal microscopy to capture the full complexity of lupus nephritis *in situ* immunity innate and adaptive immunity in order to identify those immunological pathways that lead to fibrosis and renal failure.

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Lupus Nephritis

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VOCLOSPORIN IS EFFECTIVE IN ACHIEVING PROTEINURIA TREATMENT TARGETS IN LUPUS NEPHRITIS DEFINED BY EULAR/ERA RECOMMENDATIONS

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Background Pooled data from the Phase 2 AURA-LV and Phase 3 AURORA 1 studies demonstrated that adding voclosporin, a novel calcineurin inhibitor, to mycophenolate mofetil