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.

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

1110 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...
(MMF) and low-dose steroids resulted in significantly higher complete renal response rates at 24 weeks in AURA-LV (32.6% vs 19.3%; odds ratio [OR] 2.03; p=0.045) and 52 weeks in AURORA 1 (40.8% vs 22.5%; OR 2.65; p<0.0001) in patients with lupus nephritis.

The European League Against Rheumatism and European Renal Association (EULAR/ERA) published updated treatment recommendations for lupus nephritis with targeted reductions in proteinuria over the course of the first year of therapeutic intervention. Here we report on a post-hoc analysis of pooled data from the similarly-designed 48-week AURA-LV and 52-week AURORA 1 studies based on the recommended treatment targets.

Methods AURA-LV and AURORA 1 enrolled patients with biopsy-proven active lupus nephritis (Class III, IV, or V ± III/IV) and proteinuria >1.5 mg/mg (>2 mg/mg for Class V). Pooled data included 268 patients in the voclosporin arm and 266 patients in the control arm; all patients received MMF (target dose 2 g/day) and low-dose steroids (target dose 2.5 mg/day by week 16 according to protocol-defined steroid taper). We assessed the following EULAR/ERA treatment targets: ≥25% reduction in urine protein creatinine ratio (UPCR) at 3 months, ≥50% reduction in UPCR at 6 months, UPCR ≤0.7 mg/mg at 12 months, and steroid dose ≤7.5 mg/day at 12 months.

Results After 3 months of treatment, 78.4% of patients in the voclosporin group and 62.4% of patients in the control group achieved ≥25% reduction in UPCR (odds ratio [OR] 2.25; 95% confidence interval [CI] 1.52, 3.33; p<0.0001). The percentage of patients achieving a reduction of ≥50% in UPCR at 6 months was significantly greater in the voclosporin arm (66.0% vs 47.0%, respectively; OR 2.24; CI 1.57, 3.21; p<0.0001). At 12 months, 52.6% and 33.1% of the voclosporin and control arms, respectively, had achieved a UPCR ≤0.7 mg/mg (OR 2.52; CI 1.75, 3.63; p<0.0001). A total of 89.6% and 82.8% of patients in the voclosporin and control arms, respectively, had reached the recommended steroid dose of ≤7.5 mg/day at 12 months. The proportion of patients achieving a UPCR ≤0.7 mg/mg and having a steroid dose ≤7.5 mg/day at 12 months was 44.4% in the voclosporin arm and 27.1% in the control arm (OR 2.42; CI 1.66, 3.53; p<0.0001).

Conclusions The addition of voclosporin to a background regimen of MMF and low-dose steroids in patients with LN significantly increased the likelihood of achieving the 3-, 6-, and 12-month UPCR targets of therapy recommended by EULAR/ERA.

Lupus Nephritis

**1111 TYPE I INTERFERON AND NEUTROPHIL TRANSCRIPTS IN LUPUS NEPHRITIS RENAL BIOPSIES: CLINICAL AND HISTOPATHOLOGICAL ASSOCIATIONS**

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**Objectives** To investigate the expression of type I interferon (IFN-I) and neutrophil transcripts in kidney tissue from patients with distinct classes of lupus nephritis and their association with clinical and histopathological features.

**Patients and Methods** Quantitation of IFN-I and defensin-α3 transcripts was performed in kidney biopsies from 24 patients with various classes of lupus nephritis (6 class III, 14 class IV, 4 class V) and 3 control samples by real-time PCR. Demographic characteristics, creatinine levels, and histopathological characteristics, including activity and chronicity indices, presence of active glomerular lesions, and tubulointerstitial or vascular involvement were analyzed.

**Results** IFNα2 and β transcripts were overexpressed in renal tissues from patients with proliferative forms of lupus nephritis (III/IV) compared to patients with membranous nephritis and control kidneys. Such difference was not detected between membranous nephritis and control biopsies. Defensin-α3 transcripts, overexpressed in lupus nephritis biopsies – particularly those with segmental necrotizing lesions - were correlated with higher activity index (r=0.61, p=0.02). Patients with proliferative lupus nephritis with impaired renal function, as attested by elevated creatinine levels, displayed higher relative expression of IFNα2 transcripts in renal tissues compared to those with normal renal function (26.6 ±18.0 vs. 7.1 ±6.2, p=0.013).

**Conclusion** IFN-I transcripts are produced locally in kidneys from patients with the proliferative, but not membranous, forms of lupus nephritis in association with impaired renal function. Neutrophil transcript defensin-α3 is a potential biomarker for increased renal pathologic activity. These findings provide insight into mechanisms of proliferative lupus nephritis and could impact therapeutic decisions in clinical practice.