(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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10.1136/lupus-2022-lupus21century.76

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.

1112 CHANGE IN URINARY BIOMARKERS AT THREE MONTHS PREDICTS 1-YEAR TREATMENT RESPONSE OF LUPUS NEPHRITISBETTER THAN PROTEINURIA

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10.1136/lupus-2022-lupus21century.77

Intro/Background A decline of urine protein-to-creatinine ratio (UPCR) to < 0.5 is associated with better long-term preservation of kidney function in lupus nephritis (LN). UPCR < 0.5 defines complete response in guidelines and clinical trials when achieved after 1 or 2 years. Biomarkers of early response are needed to guide early treatment changes. We studied longitudinal urine proteomic profiles in LN to identify early predictors of proteinuric response.

Methods We quantified 1200 biomarkers (Kiloplex, RayBiotech) in urine samples collected on the day of (73%) or within 3 weeks (27%) of kidney biopsy and week 12, 24, or 52 in LN patients (ISN class III, IV, V, or mixed) with proteinuria > 1 g/d. Response was defined at one year from renal biopsy: Complete = UPCR <0.5, serum creatinine (sCr) <125% of baseline, prednisone ≤ 10mg/d; Partial = UPCR < 50% from baseline but >0.5, sCr <125% of baseline, but