or surrounding glomeruli. A median (range) of 0 (0–0.82) pDCs/glomerulus and 2.7 (0.77–49) pDC/mm2 of tubulointerstitium were found. There was no evidence of an association between tubulointerstitial pDCs and serum creatinine, proteinuria, activity index, or chronicity index. MX1 immunoreactivity was found in abundance throughout the kidney, including glomerular and tubular epithelial cells, glomerular and tubulointerstitial endothelial cells, vascular wall smooth muscle cells, and infiltrating inflammatory cells.

pDCs are thought to be the major source of IFNα in the kidneys of patients with LN. If this is true, our data suggest that very few infiltrating pDCs are needed to initiate a robust IFNα response within the kidneys.

1007 VOCLOSPORIN FOR LUPUS NEPHRITIS: ASSESSMENT OF LONG-TERM SAFETY AND EFFICACY INCLUDING RENAL OUTCOME OVER THREE YEARS OF TREATMENT IN THE PHASE 3 AURORA 1 AND AURORA 2 STUDIES

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10.1136/lupus-2023-lupus21century.73

Background In AURORA 1, adding voclosporin to mycophenolate mofetil (MMF) and low-dose steroids led to signficant reductions in proteinuria at one year in patients with lupus nephritis (LN). We report on the recently completed AURORA 2 study evaluating voclosporin compared to placebo in patients treated for an additional two years after AURORA 1.

Methods Patients with LN completing AURORA 1 were eligible to continue on the same double-blinded treatment of voclosporin or placebo in AURORA 2; all patients recieved MMF and low-dose steroids. Outcomes assessed over the three year treatment period of both studies included adverse events (AEs), eGFR, urine protein-creatinine ratio (UPCR), good renal outcome and renal flare. Good renal outcome was defined based on achievement of an adequate response (i.e. sustained reduction in UPCR to ≤0.7 mg/mg) and without renal flare (i.e. an increase to UPCR >1 mg/mg from a post-response UPCR of <0.2 mg/mg or an increase to UPCR >2 mg/mg from a post-response UPCR of 0.2 to 1.0 mg/mg), as adjudicated by a blinded Clinical Endpoints Committee.

Results Overall rates of serious AEs in the voclosporin (26.7% of 116 patients) and control arm (28.0% of 100 patients) were similar. There were no deaths in the voclosporin arm during AURORA 2; four deaths occured in the control arm (pulmonary embolism, n=1; coronavirus infection, n=3). Mean corrected eGFR was within the normal range and stable over the study period. The reductions in UPCR achieved in AURORA 1 were maintained in AURORA 2 and significantly more patients in the voclosporin arm achieved a good renal outcome (66.4% in voclosporin vs 54.0% in control; p-value=0.045). Renal flare occurred in 24 of 101 patients with adequate response in the voclosporin arm and 19 of 73 patients in the control arm (23.8% in voclosporin vs 26.0% in control; p-value=0.662); 69.8% of all patients with renal flares completed study treatment.

Conclusions Voclosporin was well-tolerated over three years of treatment. The significant reductions in proteinuria initially achieved in AURORA 1 were maintained throughout AURORA 2 and more patients in the voclosporin arm achieved a good renal outcome. These data provide evidence of a long-term treatment benefit of voclosporin in patients with lupus nephritis.

1009 IN-DEPTH ANALYSIS OF MYELOID CELL SUBSETS IN LUPUS NEPHRITIS KIDNEYS PROVIDES INSIGHTS INTO DISEASE MECHANISMS: LESSONS FROM THE ACCELERATING MEDICINES PARTNERSHIP (AMP) IN RA/SLE CONSORTIUM

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10.1136/lupus-2023-lupus21century.74

We present a detailed analysis of myeloid cell populations found in the kidneys of lupus nephritis (LN) patients, based on the single-cell RNA-sequencing (scRNA-seq) data collected as part of the Accelerating Medicines Partnership (AMP) in RA/SLE consortium. Overall, 23,819 cells isolated from 156 LN patients and 30 healthy donors passed QC. Clustering of these cells (figure 1A) identified populations of CD14 and CD16 monocytes, two subsets of tissue-resident macrophages and several types of dendritic cells (DCs). In addition, we found several transcriptionally-distinct subsets of differentiated macrophages, that were missing from healthy donors (figure 1B- C). The ratio between the frequency of these macrophage subsets and that of infiltrating monocytes positively correlated with the Activity Index (AI) (figure 1D).

To infer the origins of the observed disease-specific macrophages, we compared them to several published scRNA-seq datasets of blood and kidney samples, and performed in addition trajectory analysis. Our results suggested that these subsets likely originate from both infiltrating monocytes and tissue-resident macrophages (figure 2A). Furthermore, our analysis indicated that the differentiation into disease-specific macrophages mostly takes place within the kidney. To identify putative extracellular signals driving the differentiation of infiltrating CD16 monocytes into disease-related activation states, we performed in vitro experiments in which CD16 monocytes were stimulated with a wide array of cytokines and molecules suggested to play role in SLE pathology, such