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IMPROVING TREATMENT FOR LUPUS NEPHRITIS: NEW DATA RELEASED AT EULAR

Findings support recommendations targeting early remission

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Lupus nephritis (LN) is a frequent complication of systemic lupus erythematosus (SLE), and one of the most severe organ manifestations, affecting up to 40% of patients. It constitutes an important cause of morbidity and death among patients with SLE, and leads to end stage kidney disease (ESKD) in 17–33% after 10 years. The renal injury is the result of an immune-mediated process which involves leukocytes, immune complexes, complement, and cytokines. Data shared at the 2022 EULAR Congress include the development of chronic kidney disease (CKD), a post-hoc analysis of voclosporin data based on updated response criteria, and an integrated multilevel omics analysis that reveals pathways of potential interest for future drug targets.

Dr Konstantinos Tselios presented work on the impact of time to remission and flares on the development of advanced CKD in LN. Using data from the Toronto Lupus Clinic database, the group showed that 15.8% developed advanced CKD after 9.5 years. At baseline, these patients had a higher SLICC/Damage Index, lower estimated glomerular filtration rate, higher prevalence of hypertension, proliferative nephritis, and were more often treated with ACE inhibitors or angiotensin receptor blockers.

Importantly, complete remission within the first year from LN diagnosis strongly protected against advanced CKD. However, experiencing just one flare was associated with 2.7-fold increased risk for advanced CKD. Longer time on immunosuppressives after remission was associated with decreased risk for advanced CKD. These findings emphasize the importance of early remission as well as flare prevention with prolonged immunosuppressive to maximize renal survival in LN.

Severe (proliferative) forms of LN are treated with induction immunosuppressive therapy (IST), followed by maintenance IST. The optimal duration of maintenance IST for proliferative LN is unknown. Professor Dr Noemie Jourde-Chiche shared results of the WIN-Lupus trial, which tested whether maintenance IST discontinuation after 2–3 years in patients in remission after a proliferative LN is non-inferior to IST continuation for 2 more years.

In the per-protocol population, a relapse occurred in 10.4% with IST continuation, and 25% with IST discontinuation. Non-inferiority was not demonstrated for relapse rate. Time to renal relapse did not differ between groups, and severe SLE flares (renal or extra-renal) were less frequent in patients with IST continuation compared to discontinuation, but adverse events did not differ between groups.

An abstract on integrated multilevel omics analysis revealed a set of enriched pathways of potential interest for future drug investigation in LN, with implications for proteasome inhibition. Dr Ioannis Parodis and colleagues analysed differentially expressed genes (DEGs), pathways and their druggability via the Drug Gene Interaction database (DGIdb) in 41 patients with active LN

versus healthy controls. In total, 6,869 significant and validated DEGs were identified in active LN. These genes could be targeted by 203 different drugs, with the proteasome inhibitor bortezomib interfering with cathepsin B (CTSB) regulation and cyclophosphamide interfering with the regulation of tumour necrosis factor receptor superfamily member 1A (TNFRSF1A) being of particular interest.

In 2020 EULAR – the European Alliance of Associations for Rheumatology – and the European Renal Association (ERA) published updated treatment recommendations for LN. The outline targeted reductions in proteinuria over the course of the first year of therapeutic intervention. Dr Hans-Joachim Anders reported on a post-hoc analysis of pooled voclosporin data from the AURA-LV and AURORA-1 studies based on these updated response criteria.

The novel calcineurin inhibitor voclosporin was approved in 2021 in the USA for the treatment of adult patients with active LN in combination with background immunotherapy. Within the first 3 months of treatment, 78.4% of patients on voclosporin and 62.4% in the control group achieved ≥25% reduction in urine protein creatinine ratio (UPCR). After 12 months, 52.6% and 33.1% of those receiving voclosporin and control, respectively, had achieved UPCR ≤0.7 mg/mg.

The results suggest that addition of voclosporin to a background regimen of mycophenolate mofetil and low-dose steroids in patients with LN significantly increased the likelihood of achieving the UPCR targets of therapy recommended by EULAR/ERA.

Source

Jourde-Chiche J, et al. Weaning of Maintenance Immunosuppressive Therapy in Lupus Nephritis (WIN-Lupus): a multicenter randomized controlled trial. Presented at EULAR 2022; abstract OP0280.

Parodis I, et al. Drug repurposing for treating lupus nephritis based on transcriptome profiling and autoimmunity-related serological markers. Presented at EULAR 2022; abstract POS0187.

Tselios K, et al. Impact of time to remission, flares and exposure to immunosuppressives on the development of advanced chronic kidney disease (stage IV or worse) in lupus nephritis. Presented at EULAR 2022; abstract POS0740.

Anders H-J, et al. Voclosporin is Effective in Achieving Proteinuria Treatment Targets in Lupus Nephritis Defined by EULAR/ERA Recommendations. Presented at EULAR 2022; abstract OP0285.

About EULAR

EULAR – the European Alliance of Associations for Rheumatology – is the European umbrella organisation representing scientific societies, health professional associations and organisations for people with rheumatic and musculoskeletal diseases (RMDs). EULAR aims to reduce the burden of RMDs on individuals and society and to improve the treatment, prevention and rehabilitation of RMDs. To this end, EULAR fosters excellence in education and research in the field of rheumatology. It promotes the translation of research advances into daily care and fights for the recognition of the needs of people with RMDs by the EU institutions through advocacy action.

About the EULAR European Congress of Rheumatology

Since its introduction in 2000, the annual EULAR European Congress of Rheumatology has become the primary platform for exchange of scientific and clinical information in Europe. It is also a renowned forum for interaction between medical doctors, scientists, people with arthritis/rheumatism, health professionals and representatives of the pharmaceutical industry worldwide. The EULAR congress is usually held in June in one of the major cities in Europe.

The scientific programme covers a wide range of topics on clinical innovations, clinical, translational and basic science. Meetings set up by associations of people with arthritis/rheumatism, health professionals and the health care industry complement the programme. The poster sessions, offering lively interaction between presenters and participants, are regarded by many as the heart of the congress.

Over the years, the EULAR Congress has gained a reputation of being a most innovative platform for the practicing physician particularly with respect to the acquisition of information on novel clinical research. The congress attracts more than 18,000 delegates from more than 130 countries.

The aim of the EULAR European Congress of Rheumatology is to provide a forum of the highest standard for scientific, both clinical and basic, educational, and social exchange between professionals involved in rheumatology, liaising with patient organisations, in order to achieve progress in the clinical care of people with rheumatic diseases.

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Notes to Editors
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