Background: The novel calcineurin inhibitor voclosporin was approved in 2021 for the treatment of adult patients with active lupus nephritis (LN) in combination with background immunotherapy. Voclosporin has a favorable metabolic profile and a consistent dose-concentration relationship, eliminating the need for therapeutic drug monitoring.

The Phase 2 AURA-LV and Phase 3 AURORA 1 studies demonstrated that the addition of voclosporin to mycophenolate mofetil (MMF) and low-dose steroids led to significantly higher complete renal response rates in AURA-LV at 24 weeks (32.6% vs 19.3%; odds ratio [OR] 2.03; p=0.046) and in AURORA 1 at 52 weeks (40.8% vs 22.5%; OR 2.65; p<0.0001) of treatment in patients with LN.

Objectives: The European League Against Rheumatism and European Renal Association (EULAR/ERA) published updated treatment recommendations for LN 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 these updated response criteria.

Methods: AURA-LV and AURORA 1 enrolled patients with biopsy-proven active lupus nephritis (Class III, IV, or Va III/IV) and proteinuria ≥1.5 mg/mg for Class V). Pooled data included 288 patients in the voclosporin (23.7 mg BID) group and 286 patients in the control group, with all patients receiving MMF (target dose 1 g BID) 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) by 3 months, ≥50% reduction in UPCR by 6 months, UPCR ≤0.7 mg/mg by 12 months, and steroid dose ≤7.5 mg/day by 3, 6, and 12 months.

Results: Within the first 3 months of treatment, 79.4% of patients in the voclosporin group and 62.9% of those 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 by 6 months was also significantly greater in the voclosporin group compared to control (66.0% vs 47.0%, respectively; OR 2.24; CI 1.57, 3.21; p<0.0001). After 12 months of treatment, 52.6% and 33.1% of patients receiving voclosporin and control, respectively, had achieved a UPCR ≤0.7 mg/mg (OR 2.52; CI 1.75, 3.63; p<0.0001). Given the protocol-defined steroid taper, at both 3 and 6 months, a similar proportion (≥90%) of patients in both groups had achieved the recommended steroid dose, with 89.6% and 82.8% in the voclosporin and control groups, respectively, on the recommended dose at 12 months.

The proportion of patients meeting all three UPCR targets during the one-year study period and having a steroid dose ≤75 mg/day at 12 months was 37.3% in the voclosporin group and 23.3% in the control group (OR 1.43; CI 1.13, 1.80; p=0.0001).

Conclusion: 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.

References:
