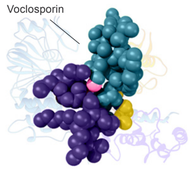
Efficacy of Voclosporin Across Lupus Nephritis Biopsy Classes: Pooled Data from the AURORA 1 and AURA-LV Trials

Anca Askanase[1], Simrat Randhawa[2], Laura Lisk[2], Paola Mina-Osorio[2]

[1]Columbia University Lupus Center, New York, NY, United States, [2]Aurinia Pharmaceuticals Inc., Victoria, Canada

BACKGROUND

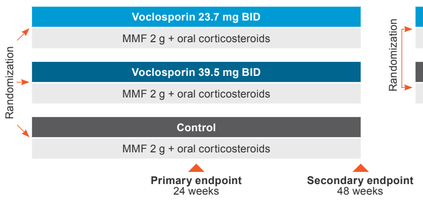


- Voclosporin is a novel calcineurin inhibitor (CNI) recently approved for the treatment of adults with lupus nephritis[1]
- As a CNI, voclosporin has two complementary mechanisms of action pertinent to the treatment of lupus nephritis: Inhibition of calcineurin 1) reduces cytokine activation of T-cells, and 2) stabilizes podocytes, protecting against proteinuria[1]
- Voclosporin has a consistent dose-concentration relationship, eliminating the need for therapeutic drug monitoring[1,3]
- Compared to other CNIs, voclosporin has an improved lipid and glucose profile[2] and no drug-drug interaction with mycophenolate mofetil (MMF)[4]
- In clinical trials, compared to MMF and steroids alone, the addition of oral voclosporin 23.7 mg BID increased complete renal response (CRR) by 26% in AURA-LV (OR 3.21, p <0.001) and 18% in AURORA 1 (OR 2.65, p <0.001) at one year[5,6]

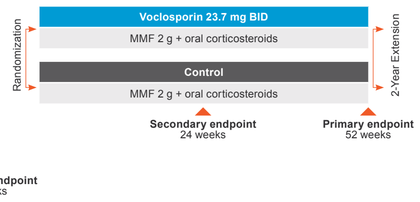
METHODS

- AURA-LV and AURORA 1 were double-blind, randomized controlled trials with similar designs and endpoints that evaluated efficacy and safety of voclosporin used in combination with MMF and rapidly tapered low-dose oral steroids* for the treatment of lupus nephritis
- A pooled data set from AURA-LV and AURORA 1 was analyzed to provide more information on the treatment effect of voclosporin with an intent-to-treat population of 268 patients in the voclosporin 23.7 mg BID treatment arm and 266 patients in the control arm
- In both studies, patients with a diagnosis of systemic lupus erythematosus, biopsy-proven active lupus nephritis and proteinuria ≥1.5 mg/mg were eligible for inclusion
- The primary endpoint of CRR was defined as urine protein creatinine ratio (UPCR) ≤0.5 mg/mg, stable renal function (estimated glomerular filtration rate [eGFR] ≥60 mL/min/1.73 m² or no decrease >20% from baseline), presence of sustained, low-dose steroids (in the 8 weeks prior to assessment) and no use of rescue medication

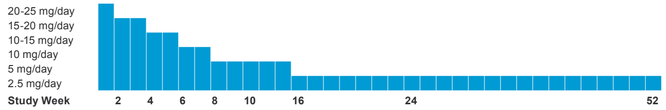
Phase 2 AURA-LV Study Design (n=265)



Phase 3 AURORA 1 Study Design (n=357)



Rapid Low-Dose Oral Steroid Taper*



*IV methylprednisolone 0.5 g/day administered on Days 1 and 2. Oral steroid initiated on Day 3 with 20-25 mg/day prednisone and rapidly tapered to a target dose of 2.5 mg/day at Week 16. At Week 16, over 80% of patients in both the voclosporin and placebo arms were on oral prednisone ≤2.5 mg/day.

RESULTS

POOLED ANALYSIS OF AURA-LV AND AURORA 1

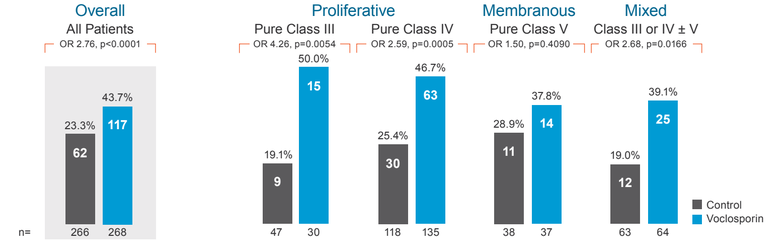
KEY DEMOGRAPHIC AND BASELINE CHARACTERISTICS

	Control (n=266)	Voclosporin (n=268)
Age, years	n=266	n=268
Mean (SD)	33.5 (10.7)	32.3 (11.2)
Median (Min, Max)	32.0 (18, 72)	30.0 (18, 66)
BMI, kg/m²	n=265	n=267
Mean (SD)	25.1 (5.6)	25.1 (5.8)
Race, n (%)	n=266	n=268
White	103 (38.7)	98 (36.6)
Asian	92 (34.6)	105 (39.2)
Black	24 (9.0)	29 (10.8)
Other	47 (17.7)	36 (13.4)
Region, n (%)	n=266	n=268
North and Latin America	93 (35.0)	87 (32.5)
USA	32 (12.0)	31 (11.6)
Asia	87 (32.7)	104 (38.8)
Europe + South Africa	86 (32.3)	77 (28.7)
eGFR, mL/min/1.73 m²	n=266	n=267
Mean (SD)	93.6 (28.6)	93.2 (29.7)
Median (Min, Max)	98.0 (25.0, 153.0)	92.0 (39.0, 168.0)
UPCR, mg/mg	n=266	n=267
Mean (SD)	4.1 (2.8)	4.5 (3.3)
Median (Min, Max)	3.1 (0.8, 19.3)	3.5 (0.2, 29.7)
Biopsy Class, n (%)	n=266	n=268
Pure Class III	47 (17.6)	32 (11.9)
Pure Class IV	118 (44.4)	135 (50.4)
Pure Class V	38 (14.3)	37 (13.8)
Class III or IV ± V	63 (23.7)	64 (23.9)
Time since lupus nephritis diagnosis, years	n=266	n=267
Mean (SD)	4.5 (4.6)	4.7 (5.1)
Median (Min, Max)	2.2 (0.6, 28.0)	(0.6, 32.3)
MMF use at screening*	n=266	n=268
Yes, n (%)	127 (47.7)	129 (48.1)

*MMF use determined by nominal yes/no question at screening visit.

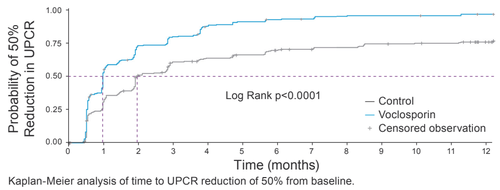
COMPLETE RENAL RESPONSE AT ONE YEAR

- CRR was significantly greater at 1 year of treatment in the voclosporin arm compared to the control arm
- The treatment benefit of voclosporin was seen in all biopsy subgroups



OR, odds ratio. Complete renal response defined as UPCR ≤0.5 mg/mg, stable renal function (eGFR ≥60 mL/min/1.73 m² or no decrease >20% from baseline), presence of sustained, low-dose steroids (in the 8 weeks prior to assessment) and no rescue medication. Pooled analysis of AURA-LV and AURORA 1 at approximately 1 year included Week 48 data from AURA-LV and Week 52 data from AURORA 1.

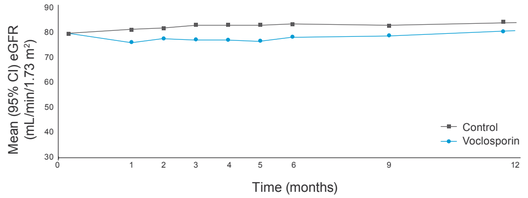
TIME TO UPCR REDUCTION OF ≥50%



Kaplan-Meier analysis of time to UPCR reduction of 50% from baseline.

- A ≥50% reduction in UPCR was achieved by 93.7% of patients in the voclosporin arm and 75.2% of patients in the control arm
- The median time to ≥50% reduction of 29 days was significantly shorter for the voclosporin arm compared to 58 days in the control arm (HR 1.96, p<0.0001)

MEAN eGFR OVER ONE YEAR OF TREATMENT



Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². Pooled analysis of AURA-LV and AURORA 1 at approximately 1 year included Week 52 data from AURORA 1 and Week 48 data from AURA-LV. In AURA-LV, mean eGFR returned to baseline at the follow-up visit (two weeks after study drug discontinuation). In AURORA 1, many patients did not discontinue study drug at the end of AURORA 1 study (patients continued treatment in the extension study).

- Mean eGFR remained in the normal range (≥60 mL/min/1.73 m²) for both treatment arms
- As expected, there was a slight early decrease in mean eGFR of -3.4 mL/min/1.73 m² at Week 4 in the voclosporin arm
- Mean eGFR remained stable throughout the study with change from baseline of -1.0 mL/min in the voclosporin arm at one year

ADVERSE EVENTS

Serious adverse events were similar between treatment arms and there were no unexpected safety events

	Control (n=266) n (%)	Voclosporin (n=267) n (%)
Adverse Event (AE)	232 (87.2)	244 (91.4)
Serious Adverse Event (SAE)	50 (18.8)	61 (22.8)
SAE of Infections and Infestations	27 (10.2)	27 (10.1)
Treatment-related SAE	9 (3.4)	12 (4.5)
AE leading to study drug discontinuation	35 (13.2)	36 (13.5)
Death*	6 (2.3)	11 (4.1)
Treatment-related AE leading to death	0	0

*Includes all deaths post-randomization until completion of study follow-up.

CONCLUSIONS

- The positive benefit-risk profile observed in this pooled analysis confirms the treatment effect seen in AURA-LV and AURORA 1 when comparing voclosporin to control, in combination with MMF and low-dose steroids
- The odds of achieving a complete renal response in the voclosporin arm were 2.76-fold greater than control, while maintaining a comparable safety profile and with minimal impact on mean eGFR at one year of treatment
- In this pooled analysis, the voclosporin arm had improved complete renal response rates (OR>1) across all biopsy classes, with the highest OR seen in pure class III
- Adult patients with lupus nephritis treated with oral voclosporin in combination with MMF and low-dose steroids achieved meaningful reductions in proteinuria and achieve that reduction faster compared to patients treated with MMF and low-dose steroids alone

REFERENCES

1. Voclosporin (LUPKYNIS) Full Prescribing Information.
2. Busque S, et al. Am J Transplant. 2011;11(12):2675-2684.
3. Kuglstatter A, et al. Acta Crystallogr D Biol. 2011;(67)2:119-123.
4. van Gelder T, et al. Arthritis Rheumatol. 2020;72(Suppl10).
5. Rovin BN, et al. Kidney Int. 2019;95(1):219-231.
6. Gibson K, et al. Am J Kidney Dis. 2020;75(5):818.

DISCLOSURES

AA is a consultant for Aurinia. SR, LL, PMO are employees and stockholders of Aurinia Pharmaceuticals Inc.

Editorial support provided by MedEvent Partners Ltd.

Aurinia provided funding for the study and presentation.