Voclosporin for Lupus Nephritis: Results of the Two-Year AURORA 2 Continuation Study

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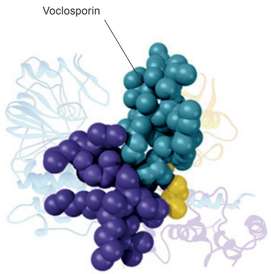
BACKGROUND

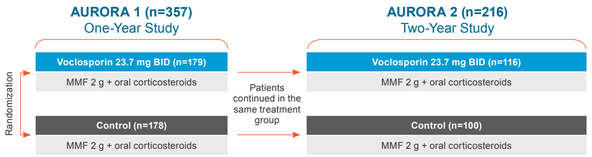
- Voclosporin is a novel calcineurin inhibitor (CNI) approved in the United States in January 2021 for the treatment of adults with active lupus nephritis (LN) in combination with background immunosuppressive therapy[1]
- As a CNI, voclosporin has two complementary mechanisms of action pertinent to the treatment of LN[1]:
  - Reduces activation of T-cells
  - Stabilizes podocytes, reducing proteinuria
- Voclosporin has a consistent dose-concentration relationship, eliminating the need for therapeutic drug monitoring[1,2]
- Unlike other CNIs, voclosporin has shown no increased safety signal for diabetes or dyslipidemia, and has no drug-drug interaction with mycophenolate mofetil (MMF)[3-7]

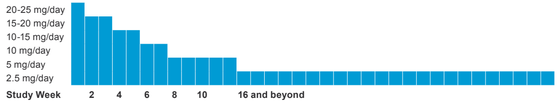


METHODS

AURORA 2 STUDY DESIGN

- AURORA 2 was a global, multi-center, double-blind, two-year continuation study of the Phase 3 AURORA 1 study and evaluated the long-term safety and efficacy of voclosporin compared to control in patients with LN
- AURORA 1 enrolled patients with biopsy-proven active LN and proteinuria ≥1.5 mg/mg (>2 mg/mg for Class V)
- AURORA 2 patients continued the same randomized treatment as in AURORA 1 (voclosporin or control) in combination with MMF and low-dose steroids for up to an additional two years
- Presented here is an analysis of AURORA 2 patients from pre-treatment baseline of AURORA 1, the one-year treatment period in AURORA 1 and up to two years of treatment in AURORA 2
- A total of 116 patients in the voclosporin arm and 100 patients in the control arm enrolled into AURORA 2





BID, twice daily; MMF, mycophenolate mofetil. *In AURORA 1, intravenous (IV) methylprednisolone 0.5 g/day was 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 and beyond. At AURORA 1 Week 16, over 80% of patients in both the voclosporin and control arms were on oral prednisone ≤2.5 mg/day. Low-dose oral steroids continued without interruption in AURORA 2.

RESULTS

AURORA 2 BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

- Baseline characteristics were generally balanced between treatment arms except for an increased number of black patients in the voclosporin arm

	Control n=100	Voclosporin n=116
Age, years		
Mean (SD)	35.4 (11.6)	32.3 (10.3)
Sex, n (%)		
Female	88 (88.0)	105 (90.5)
Race, n (%)		
White	40 (40.0)	44 (37.9)
Asian	30 (30.0)	30 (25.9)
Black	7 (7.0)	18 (15.5)
Other	23 (23.0)	24 (20.7)
Corrected eGFR, mL/min/1.73 m²*		
Mean (SD) AURORA 1 Baseline	78.7 (16.6)	79.0 (15.1)
Mean (SD) AURORA 2 Baseline	83.3 (12.6)	80.7 (13.5)
UPCR, mg/mg		
Mean (SD) AURORA 1 Baseline	3.9 (2.5)	3.9 (2.6)
Mean (SD) AURORA 2 Baseline	1.47 (1.64)	0.86 (1.36)

eGFR, estimated glomerular filtration rate; SD, standard deviation; UPCR, urine protein to creatinine ratio. *Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a pre-specified ceiling of 90 mL/min/1.73 m².

SUMMARY OF ADVERSE EVENTS

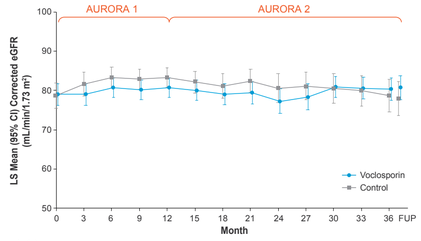
- Over three years of treatment, no unexpected adverse events (AEs) were reported and overall rates of AEs decreased over time
- Coronavirus infection occurred in twelve patients in the control arm and seven patients in the voclosporin arm; five and two events, respectively, were serious
- There were four deaths in the control arm due to pulmonary embolism (n=1) and coronavirus infection (n=3); there were no deaths in the voclosporin arm

	Control				Voclosporin			
	Year 1 n=100	Year 2 n=100	Year 3 n=85	Overall n=100	Year 1 n=116	Year 2 n=116	Year 3 n=103	Overall n=116
AE, n (%)	84 (84.0)	66 (66.0)	46 (54.1)	95 (95.0)	103 (88.8)	85 (73.3)	67 (65.0)	107 (92.2)
SAE, n (%)	13 (13.0)	18 (18.0)	8 (9.4)	28 (28.0)	13 (11.2)	13 (11.2)	8 (7.8)	31 (26.7)
Treatment-related SAEs, n (%)	2 (2.0)	2 (2.0)	0	4 (4.0)	4 (3.4)	1 (0.9)	0	5 (4.3)
Select AEs, n (%)								
eGFR Decreased	6 (6.0)	3 (3.0)	2 (2.4)	9 (9.0)	22 (19.0)	10 (8.6)	4 (3.9)	28 (24.1)
Hypertension	6 (6.0)	5 (5.0)	2 (2.4)	13 (13.0)	24 (20.7)	7 (6.0)	3 (2.9)	31 (26.7)
Renal Impairment	1 (1.0)	1 (1.0)	1 (1.2)	2 (2.0)	5 (4.3)	3 (2.6)	0	6 (5.2)
Acute Kidney Injury	0	0	0	0	3 (2.6)	0	0	3 (2.6)
Coronavirus infection	0	2 (2.0)	11 (12.9)	12 (12.0)	0	2 (1.7)	5 (4.9)	7 (6.0)

AE, adverse events; eGFR, estimated glomerular filtration rate; SAE, serious adverse events. Includes AEs of AURORA 2 patients starting on or after the first dose of study drug in AURORA 1 and up to 30 days after the last dose in AURORA 2. AEs were aggregated by Preferred Term using Medical Dictionary for Regulatory Activities (MedDRA) Version 20.0.

CORRECTED eGFR

- There was a small, expected, and early decrease in mean eGFR in the voclosporin arm in the first four weeks of treatment in AURORA 1, after which eGFR remained stable through to the end of the follow-up
- The difference between the voclosporin and control arms in least squares (LS) mean change from baseline in eGFR was 2.7 mL/min/1.73 m² (p=0.23) at 4 weeks following study drug discontinuation

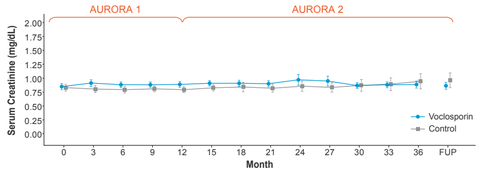


Voclosporin (n)	116	116	116	116	116	114	114	109	103	102	99	100	100	96	
Control (n)	100	100	100	100	100	98	96	90	81	84	85	84	87	85	

CI, confidence interval; eGFR, estimated glomerular filtration rate; FUP, follow-up (occurred 4 weeks after study drug was discontinued); LS Mean, least squares mean. Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². Analysis of AURORA 2 patients includes data from pre-treatment baseline of AURORA 1, 12 months in AURORA 1 and up to 25 months in AURORA 2. Error bars represent 95% CI.

SERUM CREATININE

- Mean levels of serum creatinine over time were stable in both treatment arms

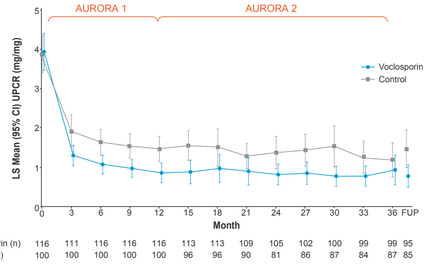


Voclosporin (n)	116	116	116	116	116	114	114	109	103	102	99	100	100	96	
Control (n)	100	100	100	100	100	98	96	90	81	84	85	84	87	85	

FUP, follow-up (occurred 4 weeks after study drug was discontinued). Analysis of AURORA 2 includes data from pre-treatment baseline of AURORA 1, 12 months in AURORA 1, and up to 25 months of follow-up in AURORA 2. Error bars represent standard deviation.

UPCR OVER TIME

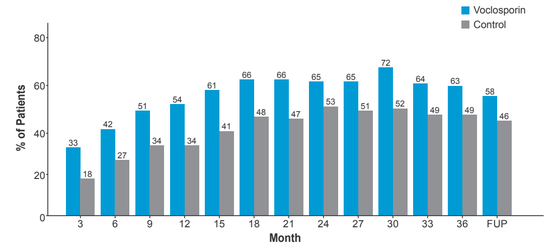
- The mean reductions in UPCR observed in voclosporin-treated patients in AURORA 1 were maintained in AURORA 2 with no increase in UPCR noted at the follow-up visit 4 weeks after study drug was discontinued



Voclosporin (n)	116	111	116	116	116	113	113	109	105	102	100	99	99	95	
Control (n)	100	100	100	100	100	96	96	90	81	86	87	84	87	85	

CI, confidence interval; FUP, follow-up (occurred 4 weeks after study drug was discontinued); LS, least squares; UPCR, urine protein to creatinine ratio Analysis of AURORA 2 includes data from pre-treatment baseline of AURORA 1, 12 months in AURORA 1, and up to 25 months of follow-up in AURORA 2. Error bars represent 95% confidence intervals.

UPCR ≤ 0.5 mg/mg OVER TIME



Voclosporin (n)	111	116	116	116	113	113	109	105	102	100	99	99	95		
Control (n)	100	100	100	100	96	96	90	81	86	87	84	87	85		

FUP, follow-up. Analysis of AURORA 2 patients includes data from AURORA 1 and AURORA 2 including a follow-up visit four weeks after study drug discontinuation.

CONCLUSIONS

- Voclosporin was well-tolerated over three years of treatment with no unexpected safety signals detected
- AE profiles were comparable in both arms with declining rates of events observed year over year. eGFR and serum creatinine remained stable throughout the study period
- The significant and meaningful reductions in proteinuria achieved in AURORA 1 were maintained in AURORA 2
- The data from AURORA 2 support the long-term treatment benefit of voclosporin in patients with LN

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