Voclosporin for Lupus Nephritis: Interim Analysis of the AURORA 2 Extension Study

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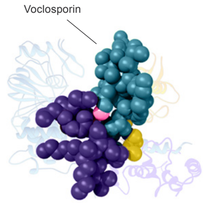
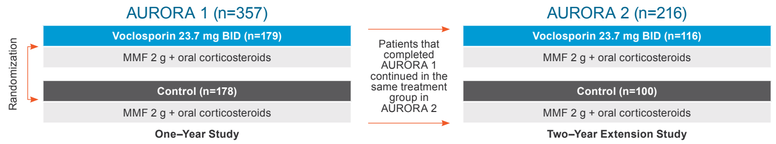
BACKGROUND



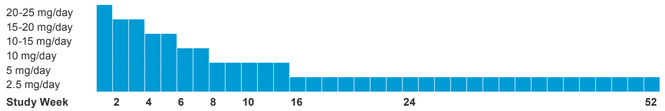
- Voclosporin is a novel calcineurin inhibitor (CNI) recently approved in the US for the treatment of adults with lupus nephritis[1]
- As a CNI, voclosporin has two complementary mechanisms of action pertinent to the treatment of lupus nephritis: inhibition of calcineurin 1) reduces activation of T-cells, and 2) stabilizes podocytes, reducing proteinuria[1]
- Voclosporin has a consistent dose-concentration relationship, eliminating the need for therapeutic drug monitoring[1,2]
- Compared to other CNIs, voclosporin has an improved lipid[3] and glucose profile and no drug-drug interaction with mycophenolate mofetil (MMF)[3-5]
- In clinical trials, compared to MMF and low-dose steroids alone, the addition of oral voclosporin 23.7 mg BID increased complete renal response (CRR) by 26% in Phase 2 AURA-LV (OR 3.21, p<0.001) and 18% in Phase 3 AURORA 1 (OR 2.65, p<0.001) at one-year of treatment[6,7]

METHODS

- AURORA 2 is an ongoing, global, multi-center, double-blind, two-year Phase 3 extension study of AURORA 1, evaluating efficacy and safety of voclosporin compared to placebo in patients with lupus nephritis
  - Phase 3 AURORA 1 enrolled patients with a diagnosis of systemic lupus erythematosus, biopsy-proven active lupus nephritis and proteinuria ≥1.5 mg/mg (>2 mg/mg for Class V). Patients were randomized to receive voclosporin (23.7 mg BID) or placebo, in combination with MMF (1 g BID) and rapidly tapered low-dose oral steroids for one-year of treatment
- AURORA 2 patients continued the same randomized treatment as in AURORA 1 for up to an additional two-years
- Presented here is an interim analysis of patents that enrolled into AURORA 2 including integrated data of AURORA 1 and AURORA 2 from pre-treatment baseline of AURORA 1, the one-year treatment period in AURORA 1 and up to a one-year treatment period in AURORA 2
  - A total of 116 patients in the voclosporin arm and 100 patients in the control arm enrolled in the extension study, of which 73 patients in the voclosporin arm and 51 patients in the control arm received two-years of total treatment (AURORA 1 and AURORA 2) at the time of the interim analysis



Rapid Low-Dose Oral Steroid Taper*



MMF, mycophenolate mofetil. *In AURORA 1, intravenous 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. At AURORA 1 Week 16, over 80% of patients in both the voclosporin and placebo arms were on oral prednisone ≤2.5 mg/day. Low-dose oral steroids continued without interruption in AURORA 2.

RESULTS

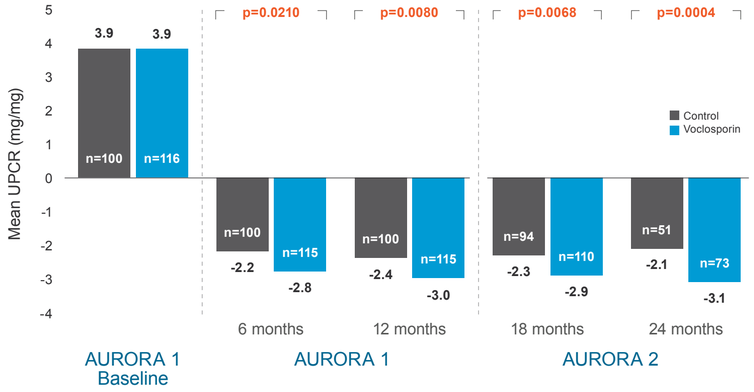
KEY DEMOGRAPHICS AND BASELINE CHARACTERISTICS OF AURORA 2 PATIENTS*

	Control (n=100)	Voclosporin (n=116)
Age, years		
Mean (SD)	35.4 (11.6)	32.3 (10.3)
Sex, n (%)		
Male	12 (12.0)	11 (9.5)
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)
Region, n (%)		
North and Latin America	36 (36.0)	49 (42.2)
Europe and South Africa	37 (37.0)	38 (32.8)
Asia	27 (27.0)	29 (25.0)
eGFR, mL/min/1.73 m²		
Mean (SD)	78.9 (16.6)	79.6 (15.2)
Median (Min, Max)	90.0 (25.0, 90.0)	90.0 (36.0, 90.0)
UPCR, mg/mg		
Mean (SD)	3.9 (2.5)	3.9 (2.6)
Median (Min, Max)	3.0 (0.8, 14.5)	2.8 (0.2, 13.1)

*Patient characteristics from pre-treatment baseline of AURORA 1.

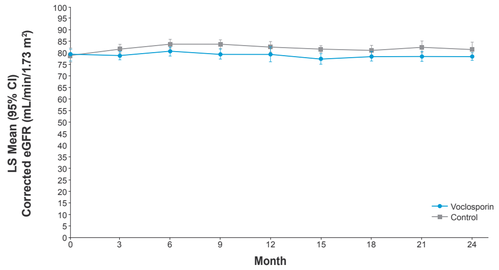
UPCR CHANGE FROM BASELINE

The LS mean change in UPCR from pre-treatment baseline to year two was -3.1 mg/mg for the voclosporin arm (n=73) and -2.1 mg/mg for the control arm (n=51)



LS, least squares; UPCR, urine protein creatinine ratio. Mixed effects model for repeated measures (MMRM) analysis of LS mean change from pre-treatment AURORA 1 baseline for UPCR included terms for baseline covariate, treatment, visit and treatment by visit interaction. Integrated results include data from pre-treatment baseline of AURORA 1, the one-year treatment period in AURORA 1 and up to a one-year treatment period in AURORA 2.

MEAN eGFR OVER TIME



Number at risk

Voclosporin (n)	116	116	116	116	116	113	112	104	73
Control (n)	100	100	100	100	100	98	95	89	51

- There was a small, early and expected decrease in mean eGFR in the voclosporin arm in the first four weeks of treatment in AURORA 1 after which eGFR remained stable throughout year one and year two

Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². Integrated analysis includes data from pre-treatment baseline of AURORA 1, the one-year treatment period in AURORA 1 and up to a one-year treatment period in AURORA 2.

SUMMARY OF ADVERSE EVENTS

No unexpected adverse events were observed in the AURORA 2 extension study

	Control (n=100) n (%)	Voclosporin (n=116) n (%)
Adverse Event (AE)	94 (94.0)	106 (91.4)
Serious Adverse Event (SAE)	25 (25.0)	28 (24.1)
SAE of Infections and Infestations	11 (11.0)	12 (10.3)
AE leading to study drug discontinuation	9 (9.0)	4 (3.4)
Death	2 (2.0)	0 (0.0)
Treatment-related AE leading to death	0	0

Adverse event defined as an adverse event that occurs on or after the day of the first dose of study drug and up to the last dose plus 30 days, except for death. Integrated analysis includes data from the one-year treatment period in AURORA 1 and up to a one-year treatment period in AURORA 2.

CONCLUSIONS

- This interim analysis from the ongoing AURORA 2 extension study showed patients in the voclosporin arm maintained meaningful reductions in proteinuria with no change in mean eGFR at 2 years of continued treatment
- No unexpected AEs were observed in the AURORA 2 extension study
- This analysis provides further support on the positive benefit risk profile of voclosporin seen in both the Phase 2 AURA-LV and Phase 3 AURORA 1 studies, representing the largest LN clinical program to date

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DISCLOSURES

AS has participated in advisory boards for Eli Lilly, Bristol Myers Squibb, Kezar Life Sciences and GlaxoSmithKline and in Aurinia clinical trials. PMO, CM and VB are employees and stockholders of Aurinia Pharmaceuticals Inc.

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