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# Early Reduction in Proteinuria with Voclosporin Treatment Across Lupus Nephritis Biopsy Classes: Pooled Data from the AURA-LV and AURORA 1 Trials

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# Disclosures

Clinical trial investigator in studies for Aurinia, AstraZeneca, GSK, and Eli Lilly.
Participated in advisory boards of Aurinia, AstraZeneca, and GSK.

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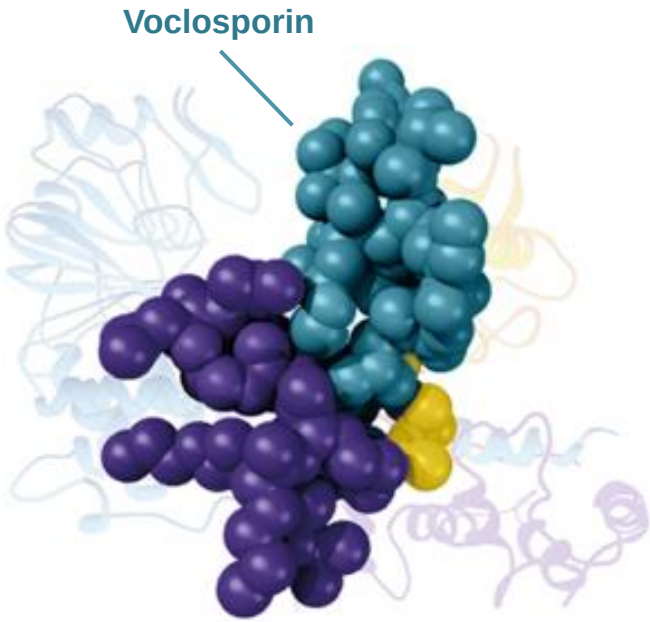
# Voclosporin

- Voclosporin is a novel calcineurin inhibitor (CNI) approved in the United States in January 2021 for the treatment of adults with active lupus nephritis in combination with background immunosuppressive therapy[1]
- As a CNI, voclosporin has two complementary mechanisms of action pertinent to the treatment of lupus nephritis[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]




1. LUPKYNIS [package insert]. Rockville, MD: Aurinia Pharma U.S., Inc., 2021. 2. van Gelder T et al. J Am Soc Nephrol. 2020;31:594. 3. Busque S et al. Am J Transplant. 2011;11(12):2675-2684.
4. Kolic J et al. Endocrinology. 2020(161)11. 5. van Gelder T et al. Nephrol Dial Transplant. 2021;gfab022. 6. Ardoin S et al. Kidney Int Rep. 2022;7:S99. 7. Rovin BN et al. Lancet. 2021;397(10289):2070-2080.

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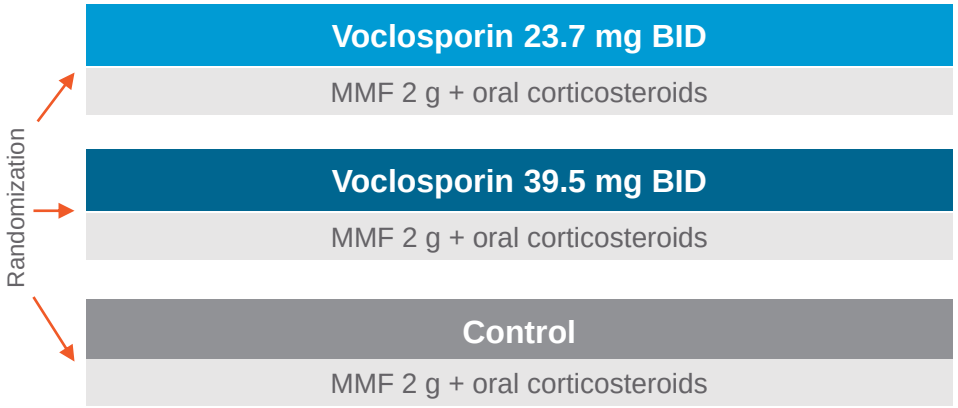
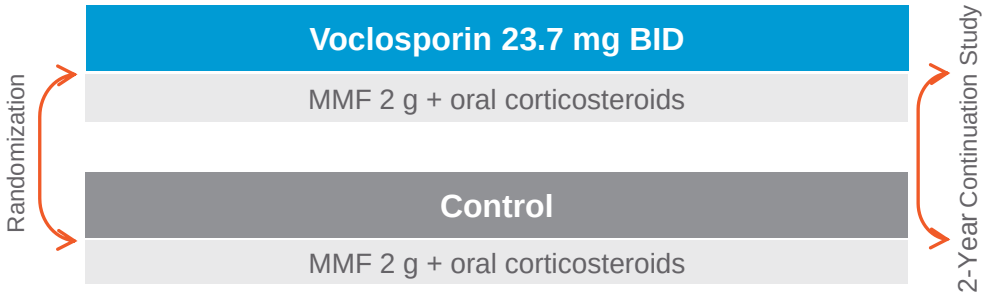
# Voclosporin Clinical Program: AURA-LV & AURORA 1

AURA-LV and AURORA 1 were global, double-blind, randomized clinical trials with similar designs and endpoints that evaluated the efficacy and safety of 23.7 mg BID voclosporin compared to control when used in combination with MMF and low-dose oral steroids* in patients with active lupus nephritis[1,2]

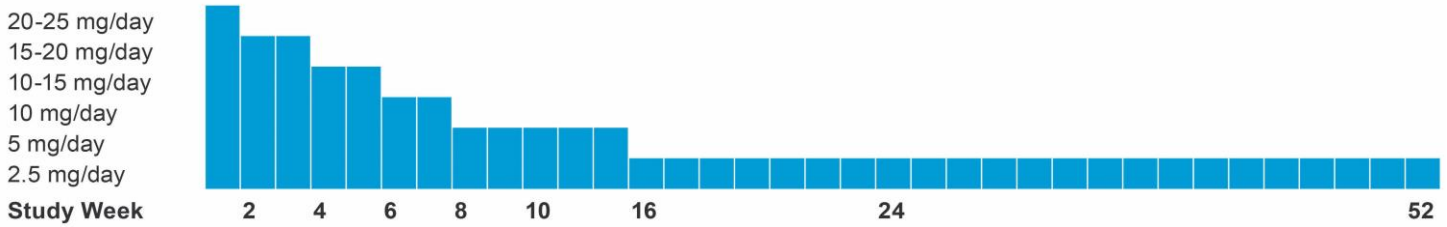
## Phase 2 AURA-LV (n=265)




## Phase 3 AURORA 1 (n=357)




### Rapid Low-Dose Oral Steroid Taper*




BID, twice daily; MMF, mycophenolate mofetil. *Protocol-defined steroid taper included intravenous methylprednisolone 0.25-0.5 g/day administered on Days 1 and 2. Oral steroid was initiated on Day 3 with 20-25 mg/day prednisone and tapered to a target dose of 2.5 mg/day at Week 16. 1. Rovin BH et al. Lancet. 2021;397:2070. 2. Rovin BH et al. Kidney Int. 2019;95:219.

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# Pooled Analysis of AURA-LV & AURORA 1: Key Baseline Characteristics

- Key inclusion criteria included biopsy-proven active lupus nephritis (Class III, IV, or V ± III/IV), proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V), and eGFR >45 mL/min/1.73 $m^2$

| | Control n=266 | Voclosporin n=268 |
|---|---|---|
| **Age, years** | | |
| Mean (SD) | 33.5 (10.7) | 32.3 (11.2) |
| **Region, n (%)** | | |
| North and Latin America | 93 (35.0) | 87 (32.5) |
| Europe and South Africa | 86 (32.3) | 77 (28.7) |
| Asia | 87 (32.7) | 104 (38.8) |
| **eGFR, mL/min/1.73 $m^2$** | | |
| Mean (SD) | 93.6 (28.6) | 93.2 (29.7) |
| **UPCR, mg/mg** | | |
| Mean (SD) | 4.1 (2.8) | 4.5 (3.3) |

eGFR, estimated glomerular filtration rate; SD, standard deviation; UPCR, urine protein creatinine ratio. Pooled analysis of AURA-LV and AURORA 1 includes data from the voclosporin 23.7 mg BID and control treatment groups.

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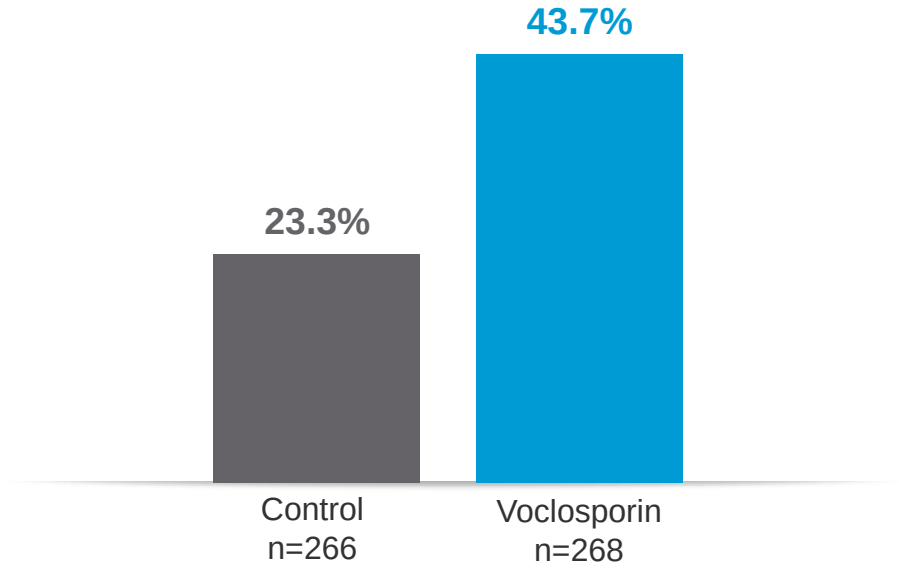
# Pooled Analysis of AURA-LV & AURORA 1: Efficacy

## CRR at 1 Year

**OR 2.76 (95% CI 1.88, 4.05)**
**p<0.0001**

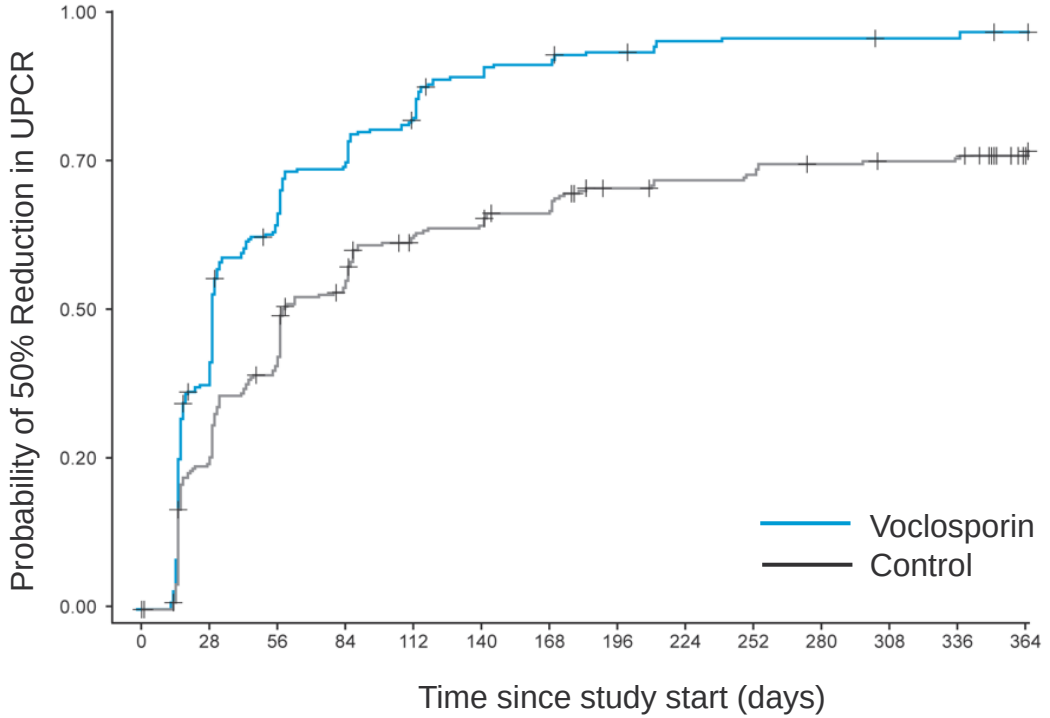



**CRR defined as**:

- Urine protein creatinine ratio (UPCR) of ≤0.5 mg/mg
- eGFR ≥60 mL/min/1.73 $m^2$ or no decrease >20% from baseline
- Presence of sustained, low-dose steroids*
- No rescue medications

## Time to 50% Reduction in UPCR

**HR 1.96 (95% CI 1.61, 2.38)**
**p<0.0001**




CI, confidence interval; CRR, complete renal response; eGFR, estimated glomerular filtration rate; HR, hazard ratio; OR, odds ratio. *Low-dose steroids defined as no more than 10 mg prednisone equivalent per day for ≥3 consecutive days or for ≥7 days in the 8 weeks prior to the primary endpoint assessment. CRR analysis includes pooled data from voclosporin 23.7 mg BID and control treatment groups at 48 weeks in AURA-LV and 52 weeks in AURORA 1.

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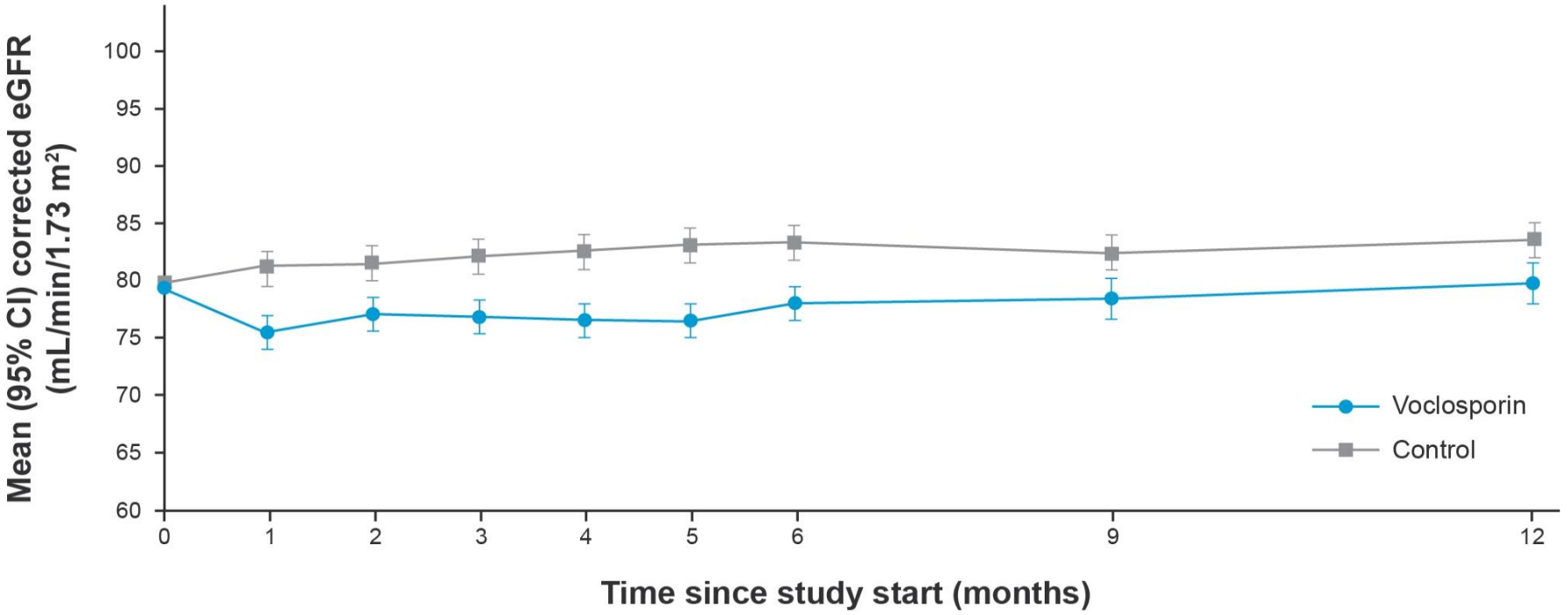
# Pooled Analysis of AURA-LV & AURORA 1: Corrected eGFR

- Mean corrected eGFR remained in the normal range (≥60 mL/min/1.73 $m^2$) for both treatment arms
- As expected, there was a slight early decrease in mean eGFR (-3.4 mL/min/1.73 $m^2$ at Week 4) in the voclosporin arm after which mean eGFR remained stable throughout the study with change from baseline of -1.0 mL/min in the voclosporin arm at one year




CI, confidence interval; eGFR, estimated glomerular filtration rate. Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 $m^2$. Analysis includes pooled data from voclosporin 23.7 mg BID and control treatment groups up to 48 weeks in AURA-LV and 52 weeks in AURORA 1.

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# Pooled Analysis of AURA-LV & AURORA 1: 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 |

Adverse events are defined as an adverse event that occurs on or after the day of the first dose and up to 30 days after the last dose of voclosporin or control, except for death; includes all deaths post-randomization until completion of study follow-up.

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# Pooled Analysis of AURA-LV & AURORA 1: Biopsy Class Analysis

- Several studies have reported that reduced proteinuria at one year is the best predictor of improved long-term renal outcomes in lupus nephritis[1,2]
- Given the treatment benefit of voclosporin observed in the pooled AURA-LV and AURORA 1 population,[3,4] this post-hoc analysis investigated the impact of voclosporin on time to proteinuria reduction by biopsy class

## Pooled AURA-LV and AURORA 1 Population by Biopsy Class

| Biopsy Class, n (%) | Control n=266 | Voclosporin 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) |
| Mixed Class V and III or IV | 63 (23.7) | 64 (23.9) |

1. Fanouriakis A et al. Ann Rheum Dis. 2020;79(1):713–723. 2. Tamirou F et al. Lupus Sci Med. 2015;2(1): e000123. 3. Rovin BH et al. Lancet. 2021;397:2070. 4. Rovin BH et al. Kidney Int. 2019;95:219.

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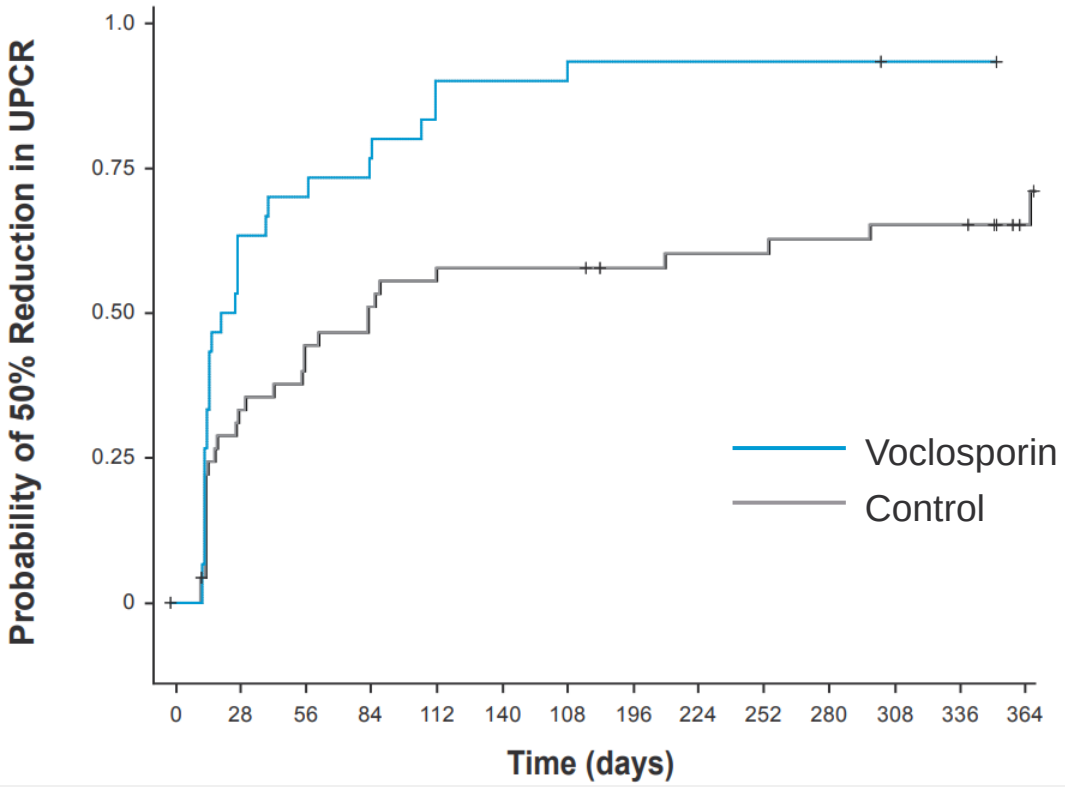
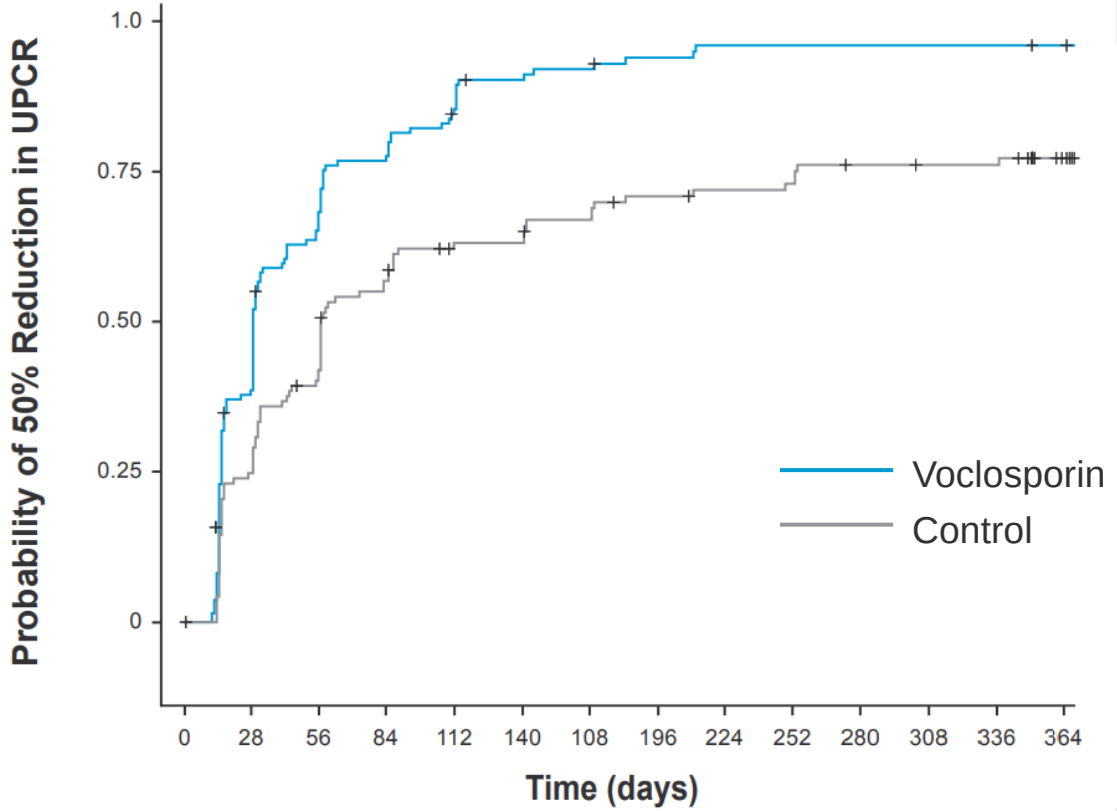
# Pooled Analysis of AURA-LV and AURORA 1: Probability of a 50% Reduction from Baseline in UPCR in Proliferative Disease

- For Class III disease, time to 50% reduction from baseline was achieved in a median of 84 days for control compared to 25 days for the voclosporin arm (HR 2.00, p=0.0146)
- For Class IV patients, the median times were 57 and 29 days for the control and voclosporin arms, respectively (HR 1.98, p<0.0001)

Pure Class III




Pure Class IV




UPCR, urine protein creatinine ratio; HR, hazard ratio. Analysis includes pooled data from voclosporin 23.7 mg BID and control treatment groups in AURA-LV and AURORA 1.

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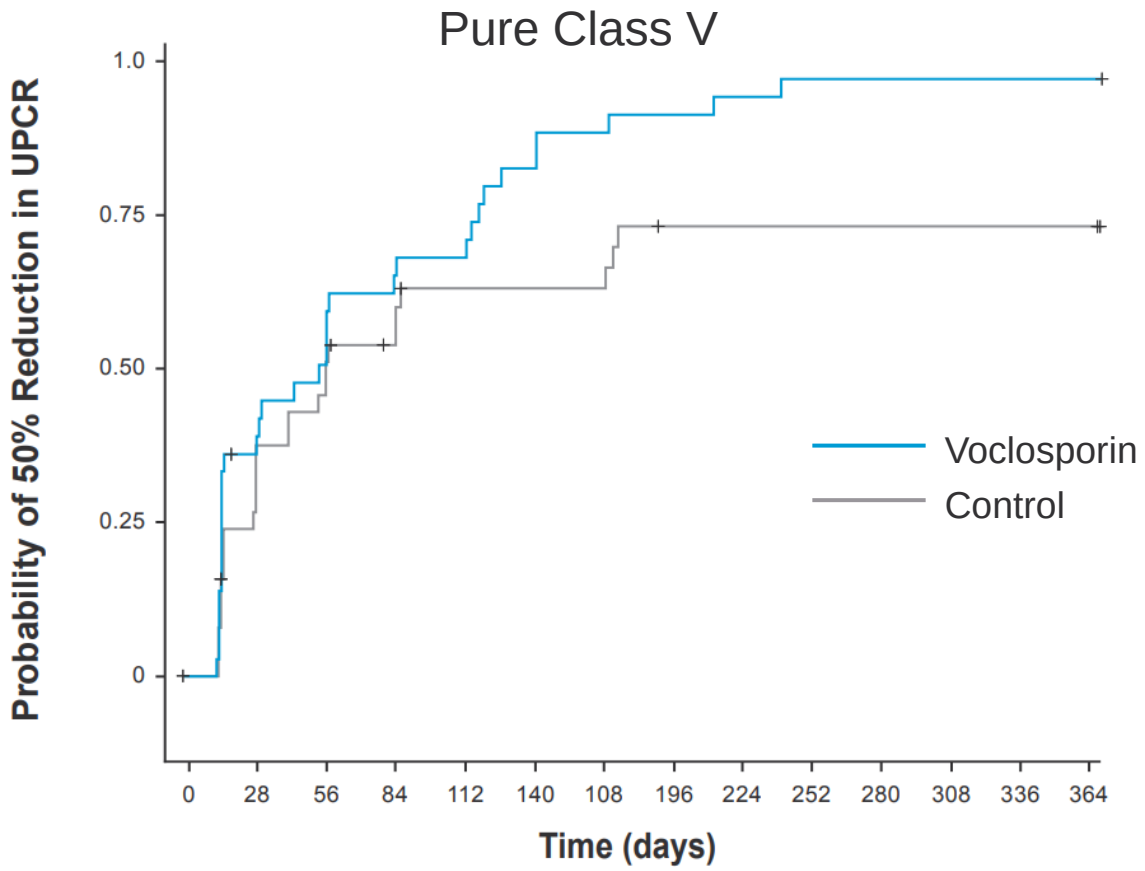
# Pooled Analysis of AURA-LV and AURORA 1: Probability of a 50% Reduction from Baseline in UPCR in Membranous Disease

- Overall, 71% of control and 92% of voclosporin arm achieved UPCR reduction >50%
- Time to 50% reduction from baseline was achieved in a median of 57 days for control and 54 days for voclosporin arm (HR 1.51, p=0.1268)




UPCR, urine protein creatinine ratio; HR, hazard ratio. Analysis includes pooled data from voclosporin 23.7 mg BID and control treatment groups in AURA-LV and AURORA 1.

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# Conclusions

- In these two global clinical trials, patients treated with voclosporin in addition to MMF and low-dose steroids achieved earlier reductions in proteinuria across all biopsy classes
- As expected, patients with membranous disease took longer to reach both UPCR endpoints than patients with proliferative disease, suggesting this population may require a longer duration of treatment
- This post hoc analysis further supports the efficacy results observed in the individual AURA-LV and AURORA 1 trials, indicating a faster time to response when voclosporin is added to standard of care