Voclosporin is Effective in Achieving Complete Renal Response in Severe Lupus Nephritis

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Disclosures

Affiliation/Financial Interest	Organization
Consultancy	Aurinia Pharmaceuticals
Consultancy, Medical Education Board	GlaxoSmithKline (GSK)
Clinical trials, Co-PI	Astra-Zeneca
Clinical trials, Co-PI	Biogen
Clinical trials, Co-PI	Human Genome Sciences
Clinical trials, Co-PI	Pfizer
Clinical trials, Co-PI	Merck Pharmaceuticals

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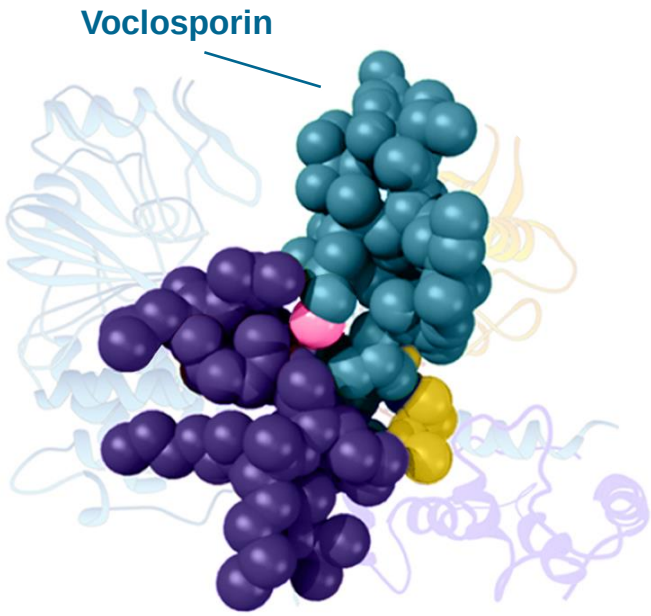
Voclosporin

- Voclosporin is a novel calcineurin inhibitor (CNI) recently approved for the treatment of adults with lupus nephritis[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 and glucose profile and no drug-drug interaction with mycophenolate mofetil (MMF)[3-5]



Voclosporin has two separate mechanisms of action

1. Inhibition of calcineurin reduces activation of T-cells
2. Inhibition of calcineurin stabilizes podocytes, reducing proteinuria

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):bqaa162. 5. van Gelder T et al. Nephrol Dial Transplant. 2021;gfab022.

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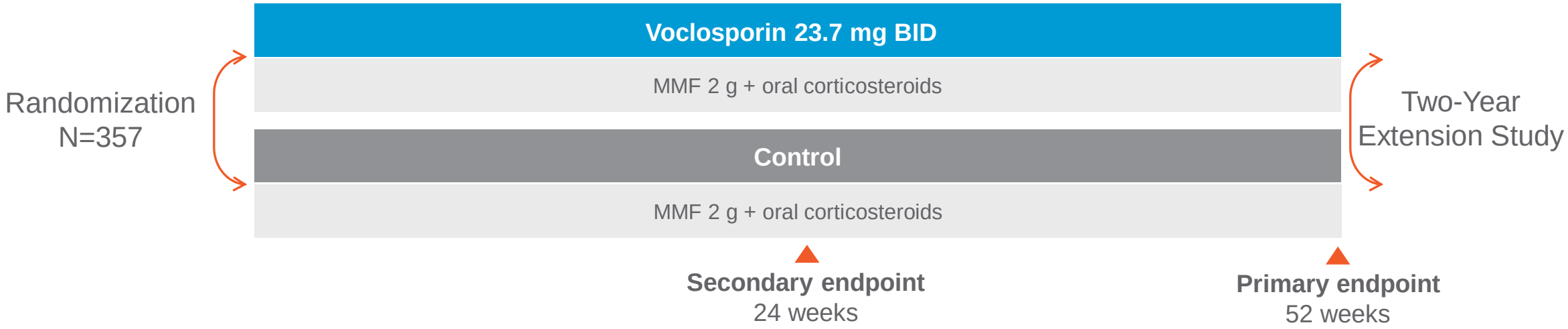
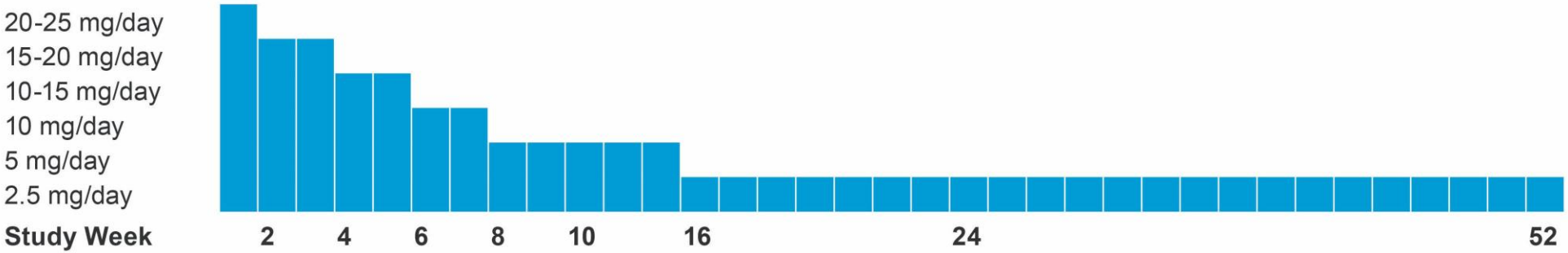
AURORA 1 Study Design

AURORA 1 was a global, double-blind, randomized-control Phase 3 trial evaluating the efficacy and safety of voclosporin compared to placebo in achieving complete renal response in patients with active lupus nephritis when used in combination with MMF and rapidly tapered low-dose oral steroids



Rapid Low-Dose Oral Steroid Taper*



MMF, mycophenolate mofetil. *Intravenous methylprednisolone 0.25-0.5 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 52, 70.2% and 66.0% of control- and voclosporin- treated patients with severe disease were on a dose ≤2.5 mg/day compared with 70.2% and 84.4%, respectively, of patients with non-severe disease.

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AURORA 1 Study

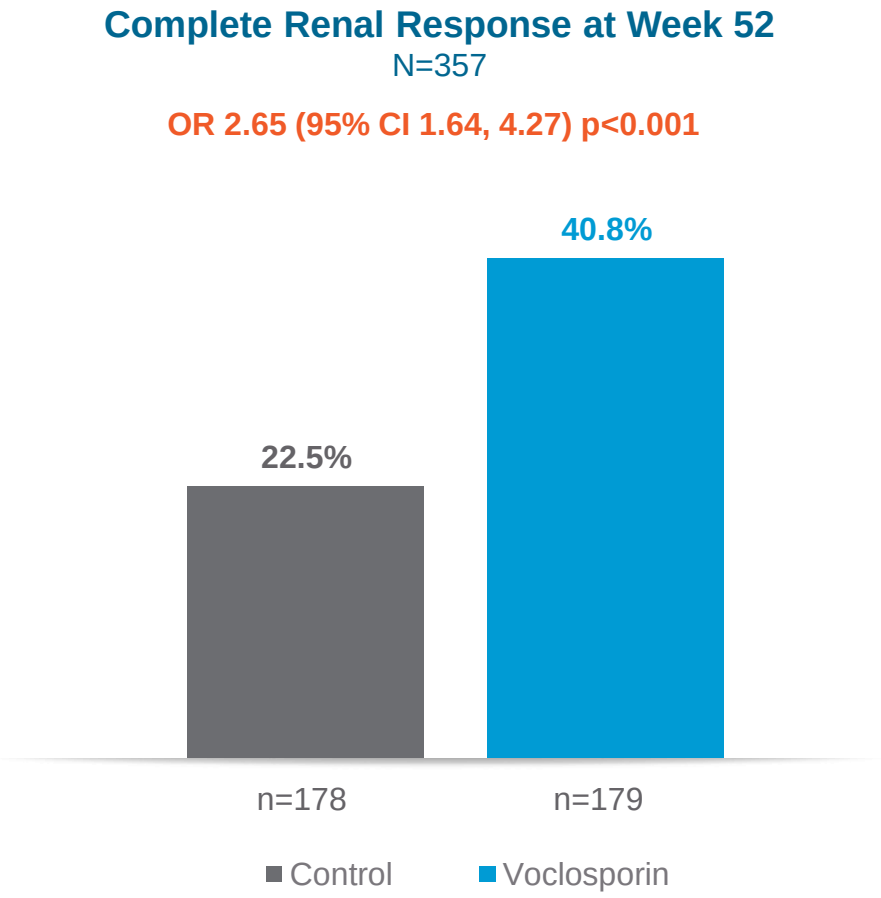
Key Inclusion Criteria

- Biopsy-proven active lupus nephritis (Class III, IV or V)
- Proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V)
- eGFR >45 mL/min/1.73 m^2

Composite Primary Outcome

Complete Renal Response at Week 52

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



CI, confidence interval; eGFR, estimated glomerular filtration rate; LN, lupus nephritis; 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.

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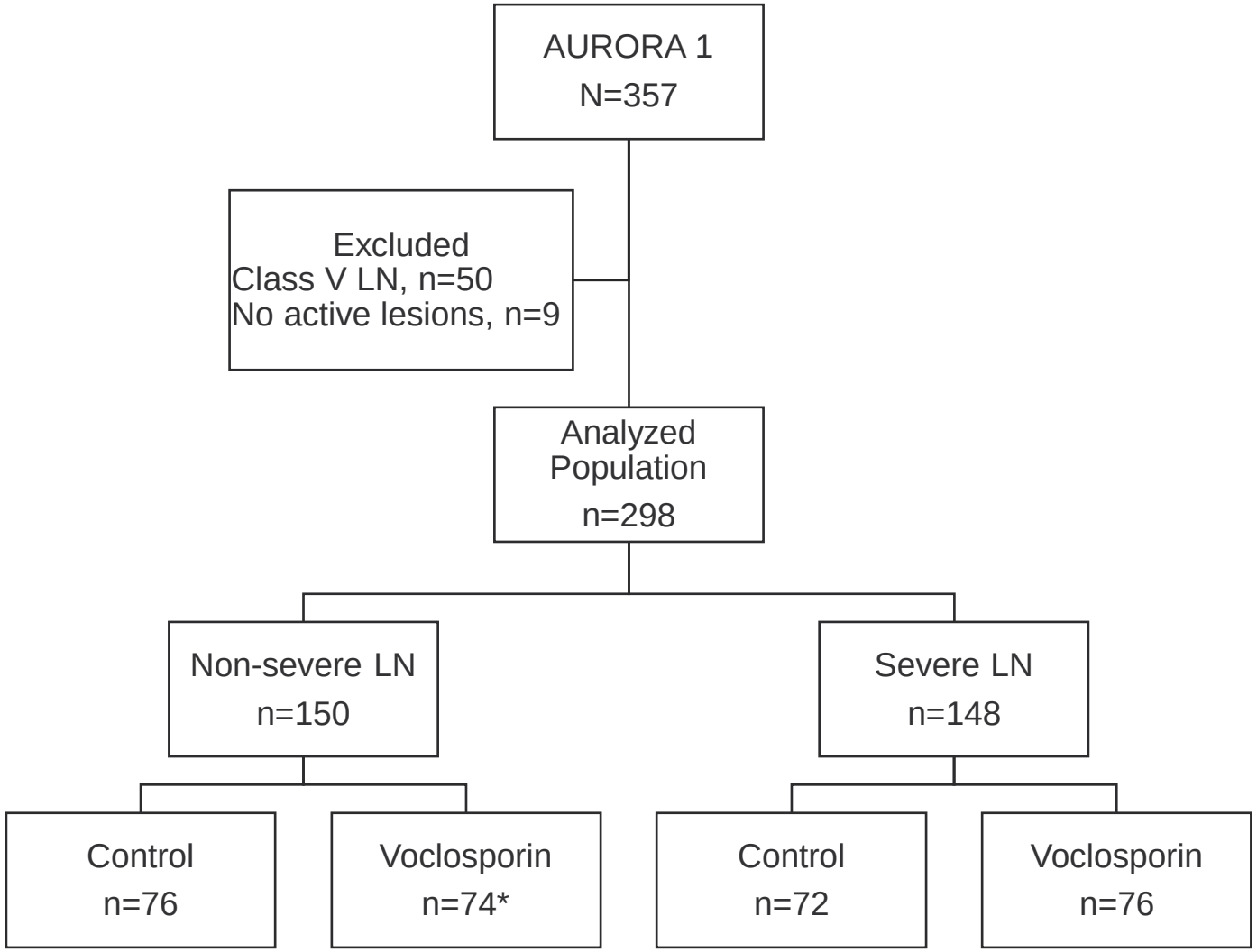
AURORA 1 Post-hoc Analysis of Patients with Severe Disease



Severe lupus nephritis defined as:

- Baseline UPCR ≥3 mg/mg
- Class III or IV biopsy (± Class V) with active lesions
- Pure Class V lupus nephritis excluded

Renal function and serology evaluated to ensure population representative of that seen in clinical practice

Hypothesis

- The addition of voclosporin to MMF and steroids significantly impacts CRR rates in patients with severe disease

CRR, complete renal response; LN, lupus nephritis; UPCR, urine protein creatinine ratio.
*One patient in the voclosporin arm discontinued the study before receiving study treatment; the patient is included in the intent-to-treat population for the efficacy analysis and excluded from the safety analysis.

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AURORA 1 Clinical Characteristics at Baseline and 52 Weeks in Severe and Non-severe Disease

Patients with severe disease had baseline mean UPCR of 5.9 mg/mg compared to 2.1 mg/mg in non-severe patients

	Baseline		52 Weeks	
	Severe (N=148)	Non-severe (N=150)	Severe (N=148)	Non-severe (N=150)
Time since LN diagnosis, years				
Mean (SD)	3.2 (4.1)	4.5 (5.8)	-	-
eGFR, mL/min/1.73 m^2				
Mean (SD)	87.6 (29.5)	91.6 (29.8)	89.6 (32.8)	93.2 (29.8)
Serum creatinine, mg/dL				
Mean (SD)	0.93 (0.33)	0.86 (0.31)	1.10 (0.96)	0.97 (0.79)
UPCR, mg/mg				
Mean (SD)	5.9 (2.4)	2.1 (0.4)	2.3 (2.9)	1.0 (1.4)
Complement 3, mg/dL				
Mean (SD)	77.9 (34.0)	86.6 (35.4)	97.6 (32.8)	96.5 (32.5)
Low <90 mg/dL, n (%)	96 (64.9)	80 (53.3)	52 (35.1)	58 (38.7)
Anti-double stranded DNA, IU/mL				
Mean (SD)	110.9 (129.3)	109.9 (129.9)	48.3 (60.7)	54.7 (83.2)

eGFR, estimated glomerular filtration rate; LN, lupus nephritis; SD, standard deviation; UPCR, urine protein creatinine ratio.
Severe lupus nephritis was defined as baseline UPCR ≥3 mg/mg with Class III or IV biopsy (± Class V) with active lesions.

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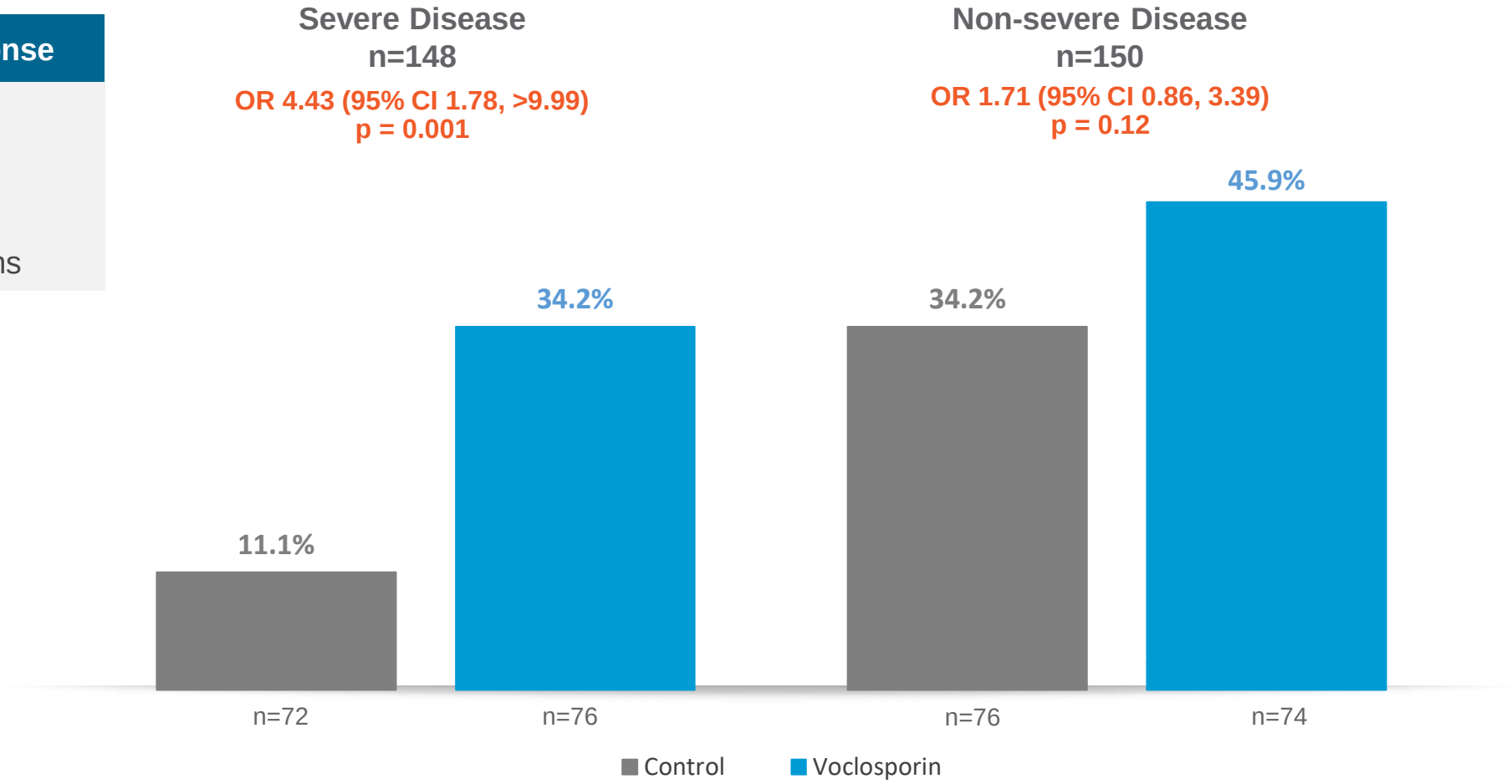
AURORA 1 CRR at Week 52 in Severe and Non-severe Disease

The treatment benefit of voclosporin (OR >1) was observed in patients with severe and non-severe disease

Complete Renal Response

- UPCR of ≤0.5 mg/mg
- Stable renal function
- Low-dose steroids
- No rescue medications



CRR, complete renal response; CI, confidence interval; OR, odds ratio. Severe lupus nephritis was defined as baseline UPCR ≥3 mg/mg with Class III or IV biopsy (± Class V) with active lesions.

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Summary of Adverse Events in Severe and Non-severe Disease

Similar safety outcomes were reported across patient groups

	Severe Disease		Non-severe Disease	
	Control (n=72) n (%)	Voclosporin (n=76) n (%)	Control (n=76) n (%)	Voclosporin (n=73) n (%)
Adverse Event (AE)	66 (91.7)	73 (96.1)	66 (86.8)	63 (86.3)
Serious Adverse Event (SAE)	17 (23.6)	14 (18.4)	17 (22.4)	13 (17.8)
SAE of Infections and Infestations	8 (11.1)	5 (6.6)	9 (11.8)	9 (12.3)
Treatment-related SAE	4 (5.6)	2 (2.6)	4 (5.3)	4 (5.5)
AE leading to study drug discontinuation	15 (20.8)	11 (14.5)	9 (11.8)	7 (9.6)
Death	3 (4.2)	0	1 (1.3)	1 (1.4)
Treatment-related AE leading to death	0	0	0	0

Safety analysis includes adverse events that occur on or after the day of the first dose of study drug including up to 30 days after the last dose and all events of death reported during study follow-up. One patient in the non-severe voclosporin arm discontinued the study before treatment; the patient is excluded from the safety analysis. Severe lupus nephritis was defined as baseline UPCR ≥3 mg/mg with Class III or IV biopsy (± Class V) with active lesions.

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Conclusions

- Patients with severe lupus nephritis treated with voclosporin in combination with MMF and low-dose steroids had clinically meaningful reductions in proteinuria and achieved significantly higher rates of complete renal response compared to patients treated with MMF and low-dose steroids alone
- The likelihood of achieving a complete renal response at one year was higher in the voclosporin arm compared to the control arm for patients with severe disease (OR 4.43, 95% CI 1.78, >9.99; p=0.001) and non-severe disease (OR 1.71, 95% CI 0.86, 3.39; p=0.12)
- Similar safety outcomes were reported in patients treated with control and voclosporin regardless of disease severity
- This is a post-hoc analysis; the original AURORA 1 study was not designed or powered to address efficacy in this selected population