Voclosporin Increases Renal Response at Commonly Used UPCR Thresholds in Patients with Lupus Nephritis

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Disclosures

Dr. Paola Mina-Osorio is an employee and stockholder of Aurinia.

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Lupus Nephritis

- Lupus nephritis is a severe manifestation of systemic lupus erythematosus (SLE) that presents with proteinuria and impaired kidney function[1]
- In lupus nephritis, an early reduction in proteinuria is critical to the preservation of kidney function and improvement in long-term outcomes, including reduced risk of disease flare, end-stage kidney disease, and death[2-5]
- Lupus nephritis treatment guidelines recommend a target of ≥50% reduction from baseline in urinary protein to creatinine ratio (UPCR) at 6 months of treatment and a target UPCR <0.5-0.7 mg/mg within the first year of treatment[6]
- The majority of patients are unable to achieve guideline targets with previously available treatments, most of which are used off label[4,5,7]

1. Parikh SV et al. *Am J Kidney Dis*. 2020;76(2):265-81. 2. Dall'Era et al. *Arthritis Rheum.* 2015;67(5):1305-13. 3. Davidson et al. *J Rheumatol.* 2018;45(5):671-7. 4. Rovin et al. *Arthritis Rheum.* 2012;64(4):1215-26. 5. Tamirou et al. *Ann Rheum Dis.* 2016;75(3):526-31. 6. Fanouriakis A et al. *Ann Rheum Dis.* 2019;78(6):736-45. 7. Zeher et al. *Lupus.* 2011;20(14):1484-93.

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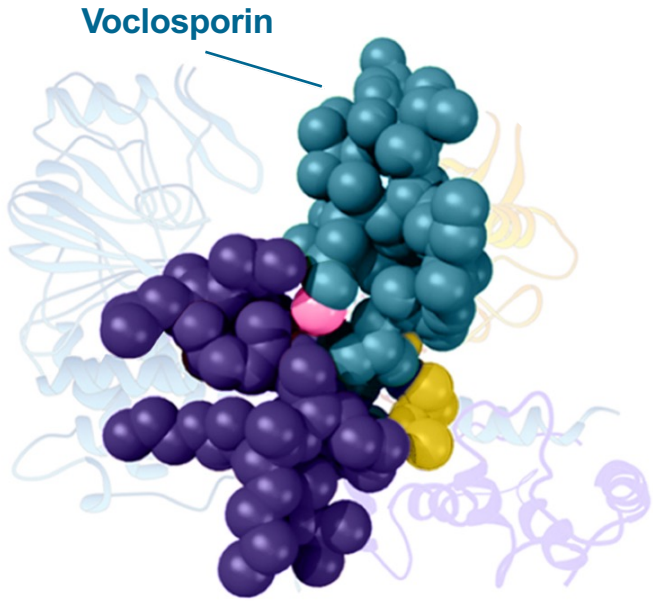
Voclosporin

- Voclosporin is a novel calcineurin inhibitor (CNI) recently approved in the US 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[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. Voclosporin (LUPKYNIS) Full Prescribing Information. 2. van Gelder T et al. *JASN*. 2020;31:594. 3. Busque S et al. *Am J Transplant*. 2011;11(12):2675-2684. 4. Kolic J et al. *Endocrin*. 2020(161)11. 5. van Gelder T et al. *Nephrol Dial Transplant*. 2021;gfab022.

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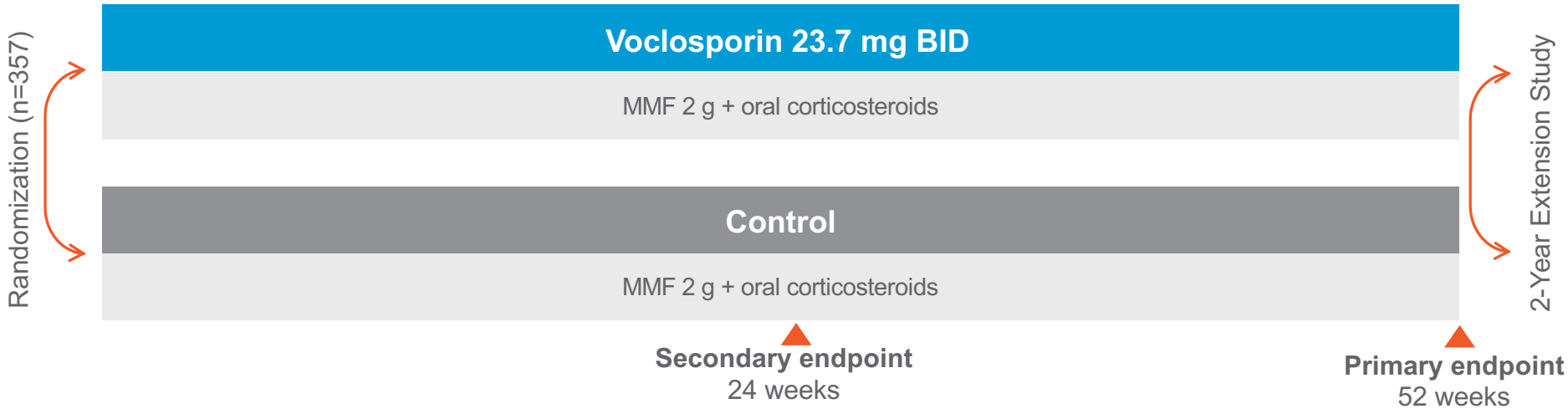
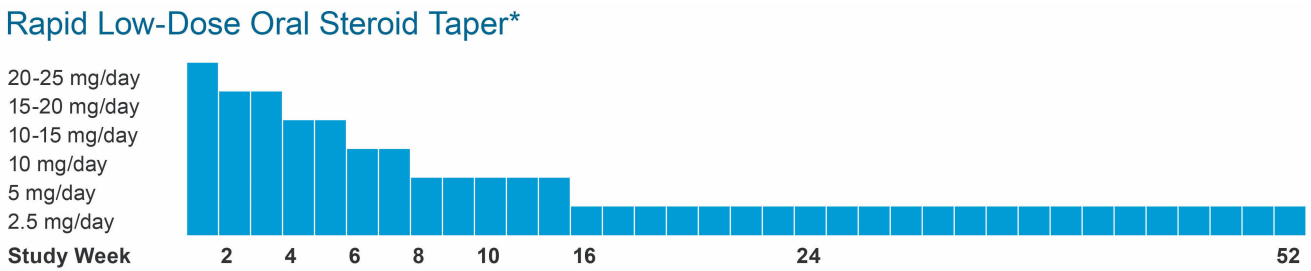
AURORA 1 Study Design

Global, multi-center, double-blind, randomized-control Phase 3 trial evaluating 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 low-dose oral steroids





MMF, mycophenolate mofetil.
*Intravenous 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.

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AURORA 1 Study Design

KEY INCLUSION CRITERIA

Diagnosis of SLE ACR criteria	Biopsy-proven active LN (Class III, IV or V)	Proteinuria of ≥1.5 mg/mg (≥2 mg/mg for Class V)

PRIMARY OUTCOME

Complete Renal Response at Week 52

Complete Renal Response (CRR) defined as:

- Urinary protein to 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 (in the 8 weeks prior to assessment)
- No rescue medications

Post-Hoc Sensitivity Analysis

Post-hoc analysis evaluating CRR with additional UPCR targets at 0.2 mg/mg intervals above and below the primary outcome target of ≤0.5 mg/mg at six months and one year of treatment in AURORA 1

ACR, American College of Rheumatology; eGFR, estimated glomerular filtration rate; LN, lupus nephritis.

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AURORA 1 Demographics and Baseline Characteristics

	Control n=178	Voclosporin n=179	Total n=357
Age, years			
Mean (SD)	33.6 (11.0)	32.8 (10.9)	33.2 (11.0)
Median (Min, Max)	31.5 (18.0, 72.0)	31.0 (18.0, 62.0)	31.0 (18.0, 72.0)
Sex, n (%)			
Male	26 (14.6)	18 (10.1)	44 (12.3)
Female	152 (85.4)	161 (89.9)	313 (87.7)
Race, n (%)			
White	61 (34.3)	68 (38.0)	129 (36.1)
Black	19 (10.7)	26 (14.5)	45 (12.6)
Asian	56 (31.5)	53 (29.6)	109 (30.5)
Other	42 (23.6)	32 (17.9)	74 (20.7)
eGFR, ml/min/1.73 m^2			
Mean (SD)	90.4 (29.0)	92.1 (30.6)	91.2 (29.8)
Median (Min, Max)	97.0 (25.0, 140.0)	91.0 (39.0, 168.0)	93.5 (25.0, 168.0)
UPCR, mg/mg			
Mean (SD)	3.9 (2.4)	4.1 (2.7)	4.0 (2.5)
Median (Min, Max)	3.1 (0.8, 14.5)	3.4 (0.2, 15.0)	3.2 (0.2, 15.0)
Biopsy class, n (%)			
Class V	25 (14.0)	25 (14.0)	50 (14.0)
Other	153 (86.0)	154 (86.0)	307 (86.0)

eGFR, estimated glomerular filtration rate; UPCR, urinary protein to creatinine ratio.

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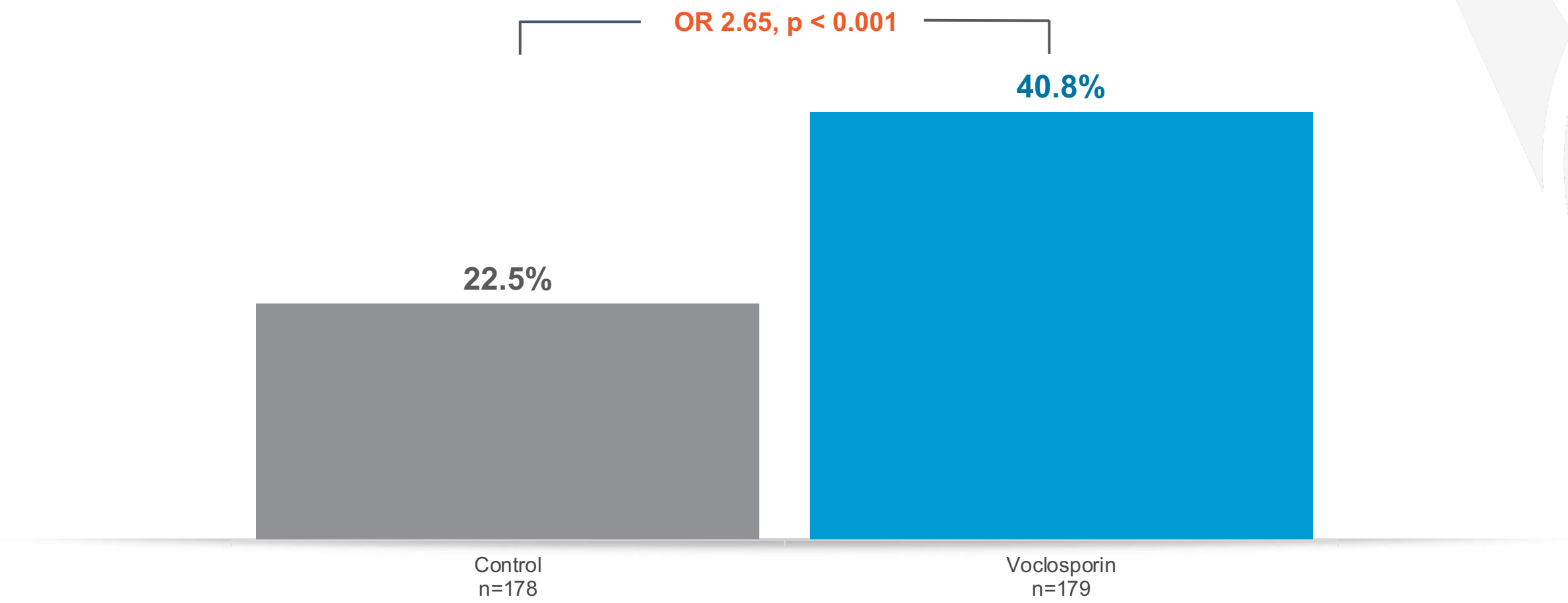
AURORA 1 Primary Outcome of CRR at One Year



OR, odds ratio. Complete renal response (CRR) defined as UPCR ≤0.5 mg/mg, stable renal function (eGFR ≥60 mL/min/1.73 m^2 and no decrease >20% from baseline), presence of sustained, low-dose steroids (in the 8 weeks prior to assessment) and no use of rescue medication. Complete renal response analysis at approximately one year included Week 52 data from AURORA 1.

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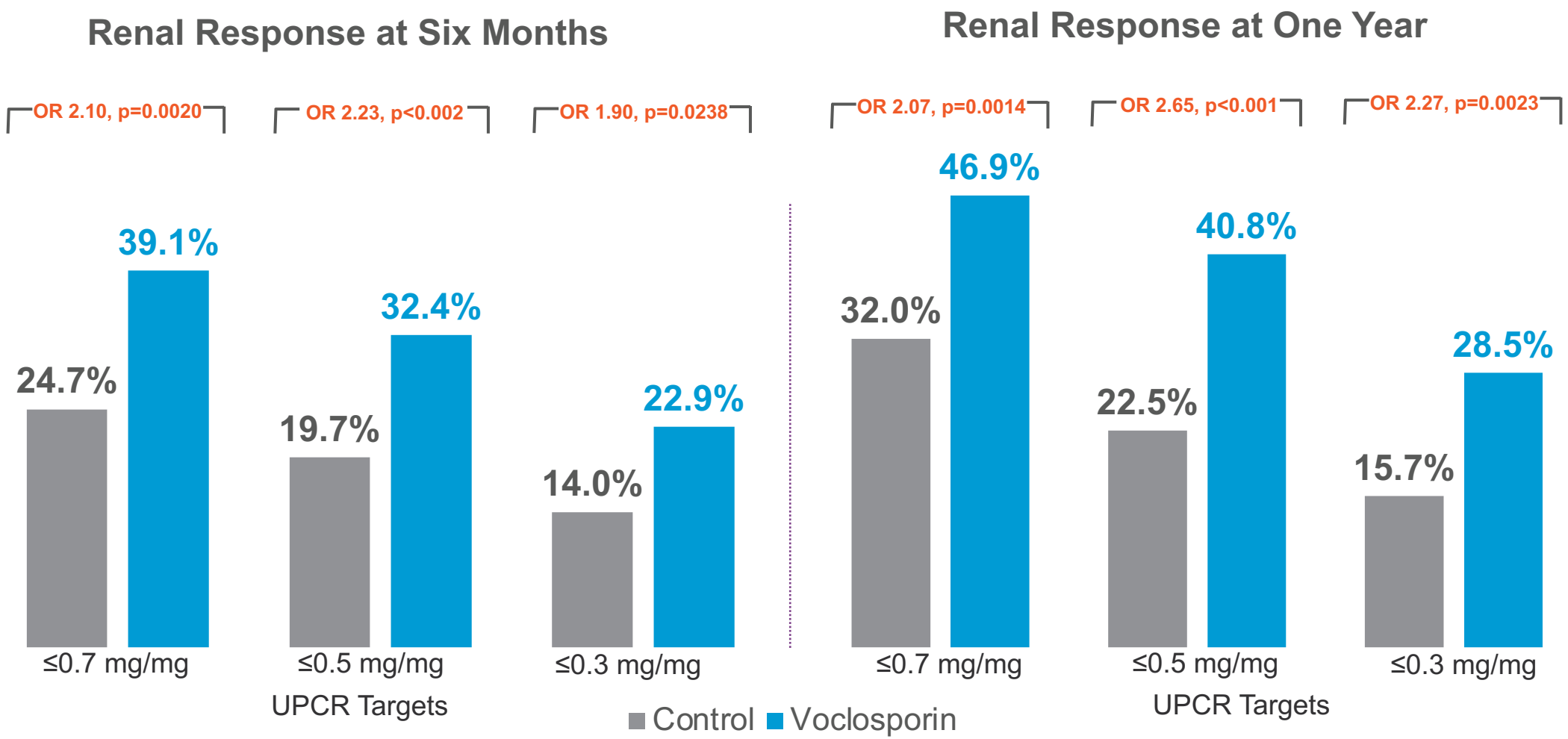
Voclosporin Arm had Increased Rates of Renal Response with UPCR Targets of ≤0.7 mg/mg, ≤0.5 mg/mg and ≤0.3 mg/mg



OR, odds ratio. Renal response defined as achievement of UPCR target with stable renal function (eGFR ≥60 mL/min or no decline >20% from baseline) in the presence of low-dose steroids (in the 8 weeks prior to assessment) and no use of rescue medication. Renal response analysis at approximately one year included Week 52 data from AURORA 1.

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AURORA 1 Summary of Adverse Events

	Control (n=178) n (%)	Voclosporin (n=179) n (%)
Adverse Event (AE)	158 (88.8)	162 (91.0)
Serious Adverse Event (SAE)	38 (21.3)	37 (20.8)
SAE of Infections and Infestations	20 (11.2)	18 (10.1)
Treatment-related SAE	8 (4.5)	8 (4.5)
AE leading to study drug discontinuation	26 (14.6)	20 (11.2)
Death*	5 (2.8)	1 (0.6)
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.
*Includes two deaths in control arm and one death in voclosporin arm that occurred as a result of AEs starting >30 days after discontinuation of study drug.

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Conclusions

- Patients with lupus nephritis administered voclosporin in addition to MMF and low-dose steroids achieved statistically significant increased complete renal response rates compared to the control arm, while maintaining a comparable safety profile
- In this post-hoc analysis, patients in the voclosporin arm had increased renal response rates regardless of the UPCR threshold used, including the more stringent ≤0.3 mg/mg target
- This analysis further supports the efficacy observed with voclosporin in the Phase 3 AURORA 1 and the Phase 2 AURA-LV global trials