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

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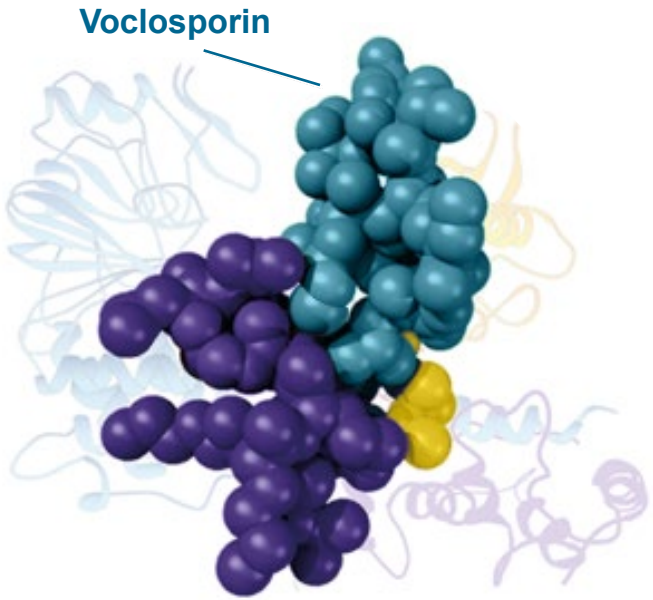
Voclosporin

- 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]
- Compared to other CNIs, voclosporin is associated with an improved lipid and glucose profile and no drug-drug interaction with mycophenolate mofetil (MMF)[3-6]



1. LUPKYNIS [package insert]. Rockville, MD: Aurinia Pharma U.S., Inc., 2021. 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. Endocrinology. 2020(161)11. 5. van Gelder T et al. Nephrol Dial Transplant. 2021;gfab022. 6. Rovin BN et al. Lancet. 2021;397(10289):2070-2080.

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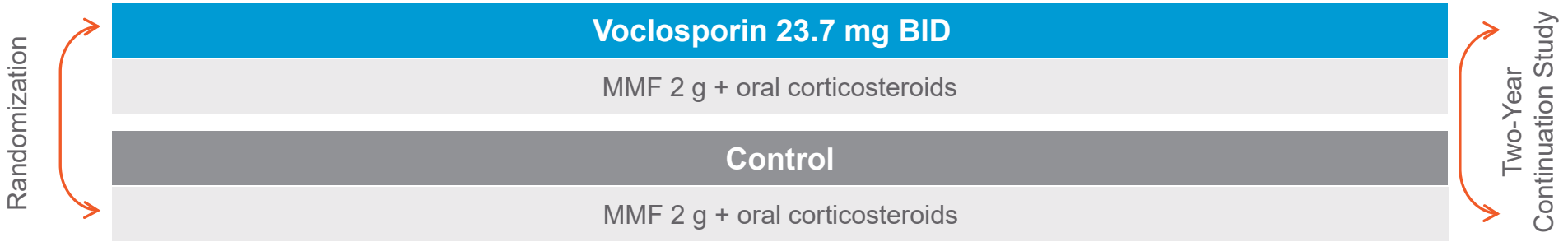
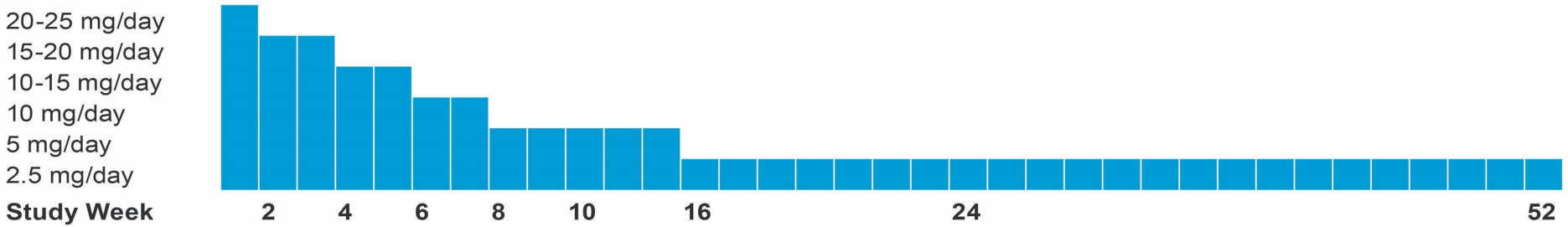
AURORA 1 Study Design

- AURORA 1 was a Phase 3, global, double-blind, one-year randomized-control trial evaluating voclosporin compared to placebo in achieving complete renal response when used in combination with MMF and low-dose oral steroids
- AURORA 1 enrolled patients with biopsy-proven active lupus nephritis, eGFR >45 mL/min/1.73 m^2 and proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V)



Rapid Low-Dose Oral Steroid Taper*



BID, twice daily; eGFR, estimated glomerular filtration rate; MMF, mycophenolate mofetil. *Protocol-defined steroid taper included intravenous methylprednisolone 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.

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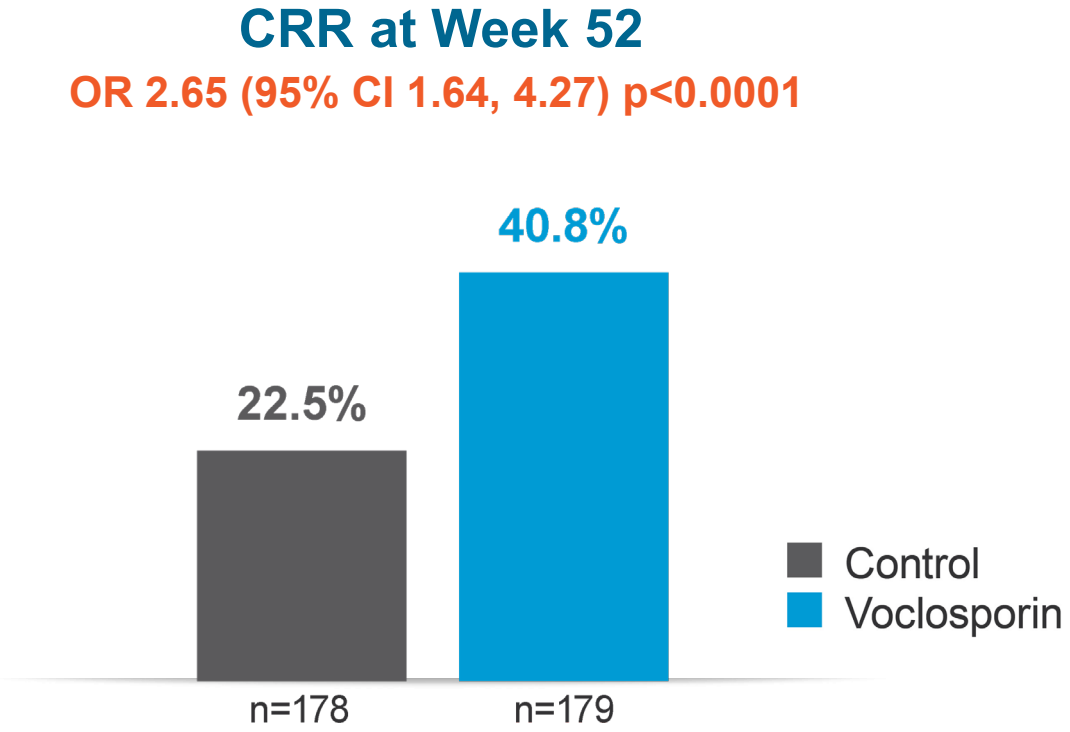
AURORA 1 Primary Outcome

- Compared to MMF and steroids alone, the addition of voclosporin increased complete renal response by 18% at Week 52

Complete Renal Response at Week 52

Composite Primary Outcome

- UPCR ≤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; UPCR, urine protein creatinine 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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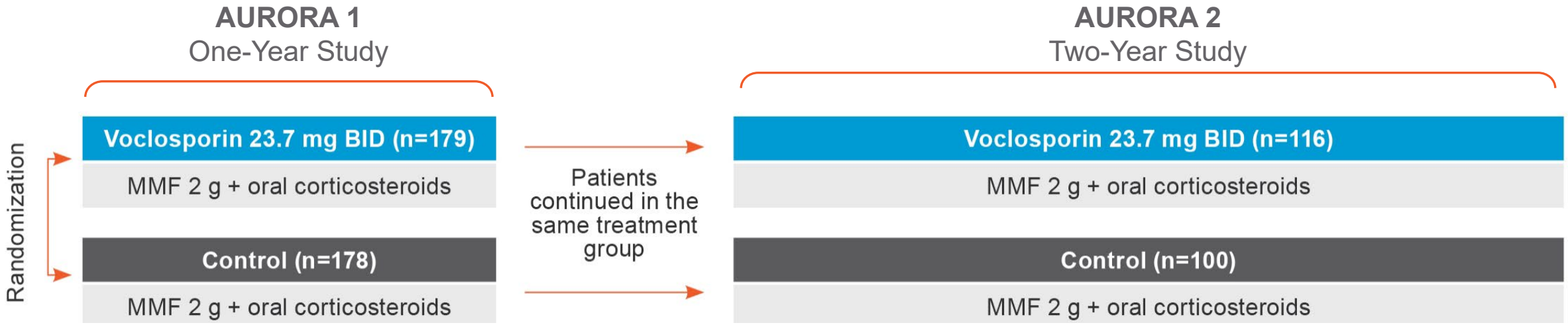
AURORA 2 Study Design

- AURORA 2 was a Phase 3, global, double-blind, two-year continuation study of AURORA 1 comparing voclosporin to placebo, in combination with MMF and low-dose steroids, in patients with lupus nephritis
- This analysis includes 216 patients that enrolled into AURORA 2 providing overall exposure data of three years from AURORA 1 and AURORA 2



BID, twice daily. Analysis of AURORA 2 patients (n=216) includes pooled data from AURORA 1 and AURORA 2.

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AURORA 2 Study Design

Study Objectives

AURORA 2 was designed to assess long-term safety and tolerability of voclosporin compared with placebo in patients with lupus nephritis

Primary End point

The primary endpoint was safety and included assessments of adverse events, deaths, and biochemistry and hematological assessments during the treatment period

Key Secondary End points

Renal response, renal flare, renal outcomes, and changes in UPCR and eGFR

AURORA 2 Baseline Characteristics

- Baseline characteristics were generally balanced between treatment groups except for increased number of black patients in the voclosporin group

	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)
Pre-treatment corrected eGFR, mL/min/1.73 m^2		
Mean (SD)	78.9 (16.6)	79.6 (15.2)
Pre-treatment UPCR, mg/mg		
Mean (SD)	3.9 (2.5)	3.9 (2.6)

AURORA 2 patient characteristics at pretreatment baseline of AURORA 1.
Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m^2.

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Summary of Adverse Events

- No unexpected new AEs were reported in the voclosporin arm compared to the control arm
- Coronavirus infection occurred in 12 patients in control group and 7 patients in voclosporin group; 2 patients in the voclosporin group and 5 patients in the control group had serious events

	Control n=100	Voclosporin n=116
Any AE, n (%)	95 (95.0)	107 (92.2)
Treatment-related AE	31 (31.0)	58 (50.0)
Serious AE	28 (28.0)	31 (26.7)
Serious Treatment-related AE	4 (4.0)	5 (4.3)
AE Leading to Study Drug Discontinuation	17 (17.0)	11 (9.5)
Death	4 (4.0)*	0

AE, adverse event. Includes adverse events starting on or after the first dose of study drug in AURORA 1 up to 30 days after the last dose and all events of death reported during study follow-up.
*The four deaths in the control arm were due to pulmonary embolism (n=1) and coronavirus infection (n=3).

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AURORA 2 Selected Adverse Events of Interest

	Control			Voclosporin		
	Year 1 n=100	Year 2 n=100	Year 3 n=85	Year 1 n=116	Year 2 n=116	Year 3 n=103
GFR Decreased, n (%)	6 (6.0)	3 (3.0)	2 (2.4)	22 (19.0)	10 (8.6)	4 (3.9)
Hypertension	6 (6.0)	5 (5.0)	2 (2.4)	24 (20.7)	7 (6.0)	3 (2.9)
Acute Kidney Injury	0	0	0	3 (2.6)	0	0
Headache	7 (7.0)	3 (3.0)	2 (2.4)	22 (19.0)	6 (5.2)	2 (1.9)
Tremor	0	0	0	4 (3.4)	0	0
Hyperglycemia	0	0	0	0	1 (0.9)	0
Infections and Infestations AEs	60 (60.0)	30 (30.0)	21 (24.7)	70 (60.3)	45 (38.8)	35 (34.0)
Neoplasms Benign, Malignant and Unspecified AEs	2 (2.0)	0 (0.0)	2 (2.4)	2 (1.7)	1 (0.9)	1 (1.0)

Includes adverse events starting on or after the first dose of study drug in AURORA 1 up to 30 days after the last dose and all events of death reported during study follow-up. Adverse events were aggregated by System Organ Class and Preferred Term and coded using Medical Dictionary for Regultory Activities (MedDRA) Version 20.0.

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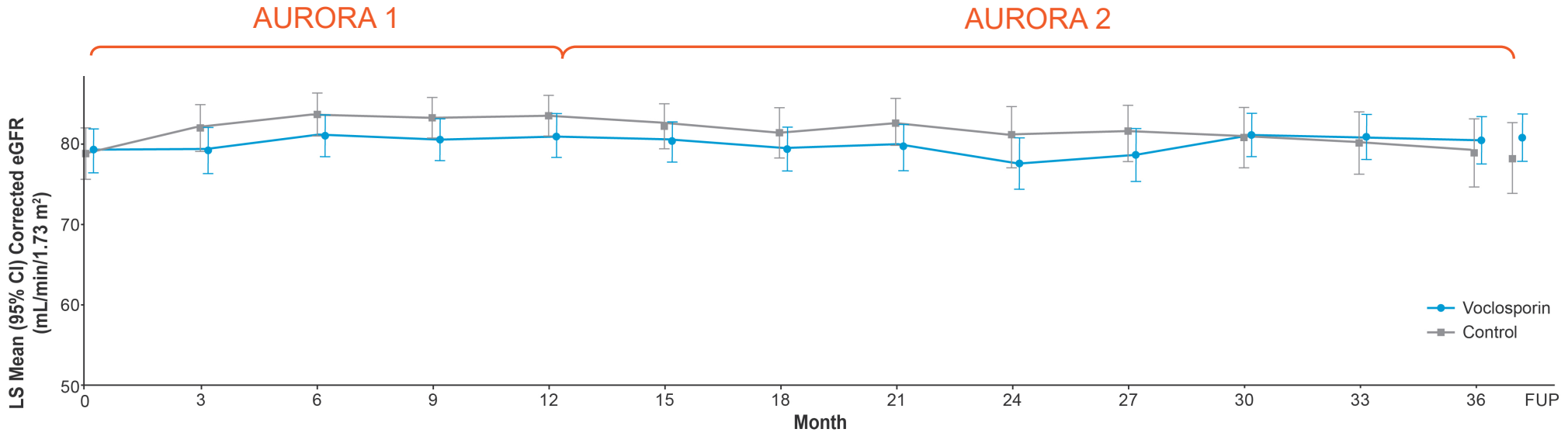
Mean Corrected eGFR

- 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 study
- The difference between the voclosporin and control arms in LS mean change from baseline in eGFR was 2.7 mL/min/1.73 m^2 (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	86	85	84	87	85

eGFR, estimated glomerular filtration rate. LS, least squares. 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 of AURORA 2 patients includes pooled data from AURORA 1 and AURORA 2 and including a follow up (FUP) visit four weeks after study drug discontinuation.

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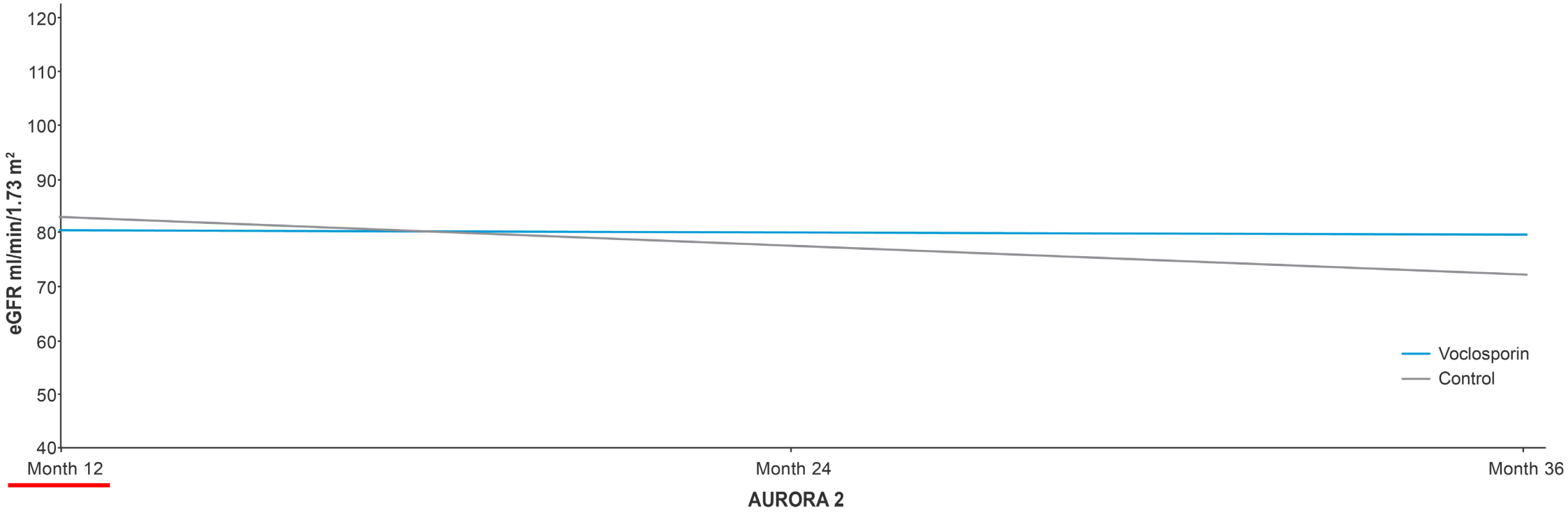
Mean Corrected eGFR Slopes

- The slopes of the LS mean change in corrected eGFR from AURORA 2 baseline to Month 36 were -0.2 mL/min/1.73 m^2 (95% CI -3.0, 2.7) in the voclosporin arm and -5.4 mL/min/1.73 m^2 (95% CI -8.4, -2.3) in the control arm



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 of mean corrected eGFR slope in AURORA 2 patients includes the 24-month treatment period in AURORA 2.

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Renal Flare

	Control n=100	Voclosporin n=116
Adequate response, % (n/n)	73.0% (73/100)	87.1% (101/116)
Renal flare in patients with adequate response % (n/n) Odds ratio vs control (95% CI) p-value	26.0% (19/73)	23.8% (24/101) 0.85 (0.42, 1.73) 0.662

Adequate response and incidence of flare were adjudicated by independent and blinded CEC. Percentages for patients with flares are based on the number of patients who achieved adequate response prior to the flare event. A sustained reduction in UPCR to ≤0.7 mg/mg was considered an adequate response. Renal flare was defined as an increase to UPCR >1 mg/mg from a post-response baseline of <0.2 mg/mg, or an increase to UPCR >2 mg/mg from a post-response baseline between 0.2 to 1.0 mg/mg, or a doubling of UPCR from pretreatment baseline values of UPCR >1 mg/mg. The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region; an odds ratio <1 indicates benefit of voclosporin.

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Good Renal Outcome

	Control n=100	Voclosporin n=116
Good Renal Outcome		
Patients with adequate response and without flare, % (n/n)	54.0% (54/100)	66.4% (77/116)
Odds ratio vs control (95% CI)		0.56 (0.32, 0.99)
p-value		0.045

Adequate response and incidence of flare were adjudicated by independent and blinded CEC. A sustained reduction in UPCR to ≤0.7 mg/mg was considered an adequate response. Renal flare was defined as an increase to UPCR >1 mg/mg from a post-response baseline of <0.2 mg/mg, or an increase to UPCR >2 mg/mg from a post-response baseline between 0.2 to 1.0 mg/mg, or a doubling of UPCR from pretreatment baseline values of UPCR >1 mg/mg. The model is based on a logistic regression with terms for treatment, baseline UPCR, biopsy class, MMF use at baseline and region; an odds ratio <1 indicates benefit of voclosporin.

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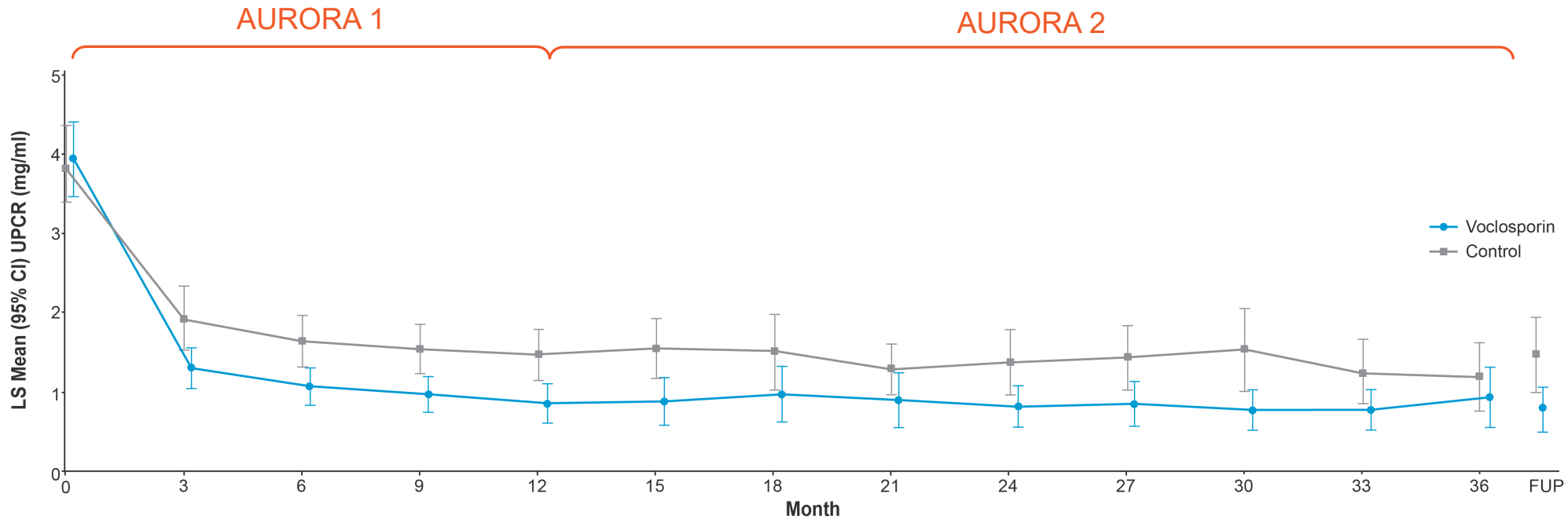
UPCR

- The mean reductions in UPCR observed in AURORA 1 were maintained with continued treatment in AURORA 2
- There was no increase in UPCR at the follow-up visit 4 weeks after study drug discontinuation



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

Analysis of AURORA 2 patients includes pooled data from AURORA 1 and AURORA 2 including a follow up (FUP) visit four weeks after study drug discontinuation.
LS, least squares; UPCR, urine protein creatine ratio.

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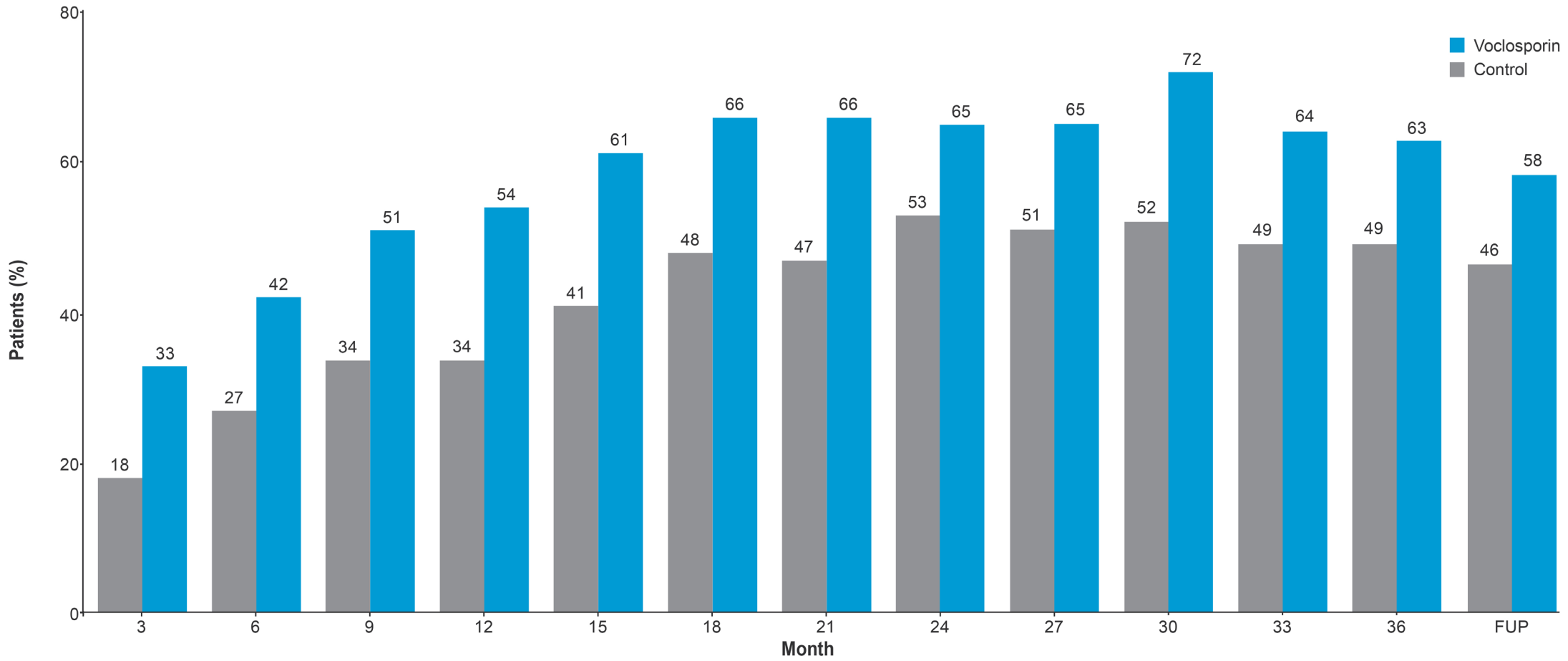
AURORA 2 Proportion of subjects with UPCR ≤ 0.5



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

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

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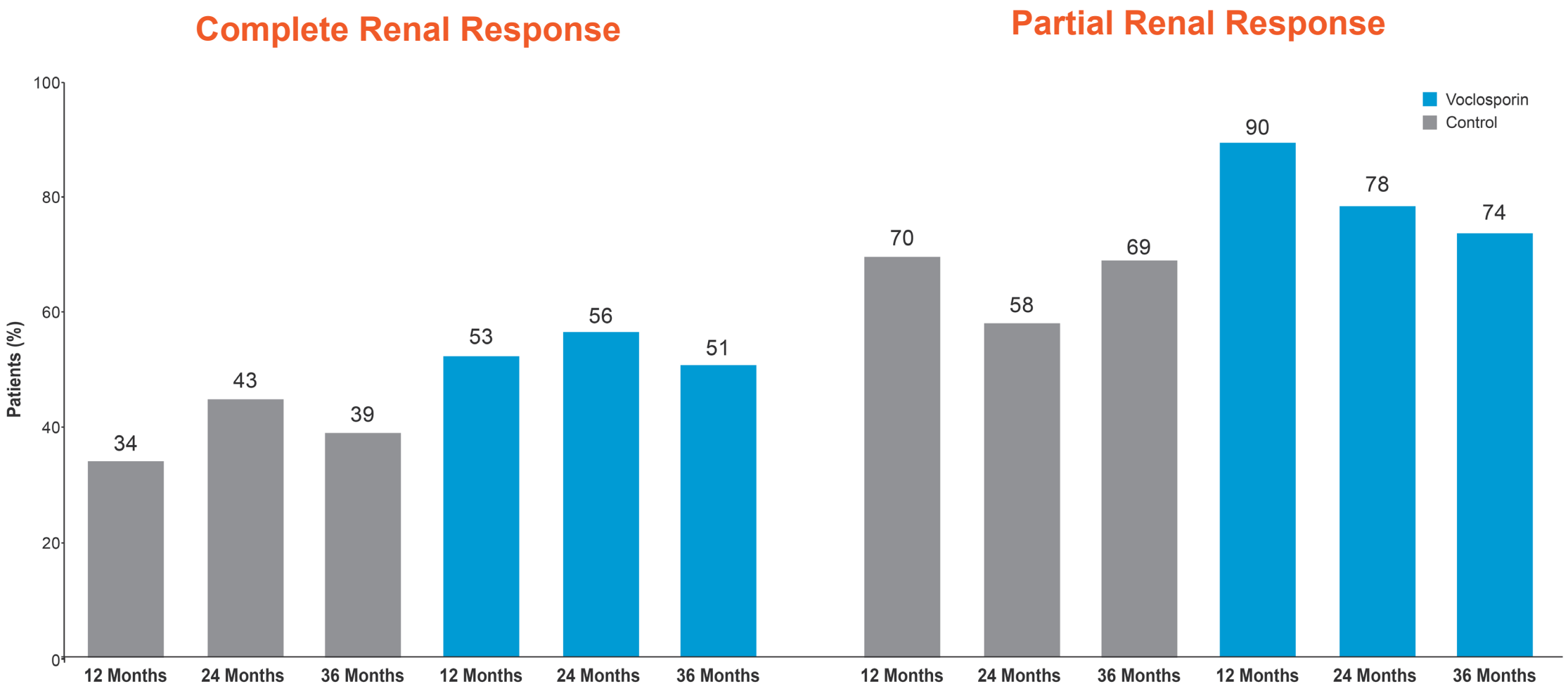
Complete and Partial Renal Response



Analysis of AURORA 2 patients includes pooled data from AURORA 1 and AURORA 2. Complete renal response defined as UPCR ≤0.5 mg/mg with stable renal function (eGFR ≥60 mL/min/1.73 m^2 or no decrease >20% from baseline) in the presence of sustained, low-dose steroids (in the 8 weeks prior to assessment) and no rescue medication. Partial renal response defined as a 50% reduction in UPCR from pretreatment baseline in AURORA 1.

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Study Strengths and Limitations

- + Double-blinded and placebo-controlled design
- + Patients continued the randomized treatment from AURORA 1
- + Overall data provides three years of clinical outcomes for patients receiving voclosporin
- - Study was not designed to assess clinical efficacy (was assessed in AURORA-1)
- - No histological evidence available yet – substudy on repeat biopsies to be expected

Conclusions

- Long-term voclosporin use was safe and well-tolerated with no new safety signals:
  - Overall rates of adverse events were similar in both the control and voclosporin arms
  - No increase in infectious events
  - Incidence of adverse events typically associated with calcineurin inhibition was low and regressed over time
- Long-term voclosporin use led to improved efficacy and preserved kidney function
  - Significant and meaningful reductions in proteinuria achieved in AURORA 1 were maintained
  - Significant difference in eGFR slope in voclosporin arm (-0.2 mL/min/1.73 m^2) compared to control arm (-5.4 mL/min/1.73 m^2)
- AURORA 2 demonstrates a positive benefit-risk profile of voclosporin the treatment of lupus nephritis

Acknowledgements

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