Management of Lupus Nephritis with Voclosporin: An Update from a Pooled Analysis of 534 Patients

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Disclosures

BHR reports consultancy agreements (Aurinia, Bristol Myers Squibb, Biogen, Pfizer, Lilly, Genentech, GlaxoSmithKline, Mallinckrodt, EMD Serono, Omeros, Calliditas, Retrophin, BioMarin), research funding (National Institute of Diabetes and Digestive and Kidney Diseases, Lupus Foundation of America) and participation in clinical trials (Aurinia).

SVP reports consultancy agreements (Aurinia, GlaxoSmithKline, Bristol Myers Squibb), research funding (National Institutes of Diabetes and Digestive and Kidney Disease, EMD Serono, Aurinia, Mallinckrodt) and participation in clinical trials (Aurinia).

RBH, NS, SR are employees and stockholders of Aurinia Pharmaceuticals Inc.

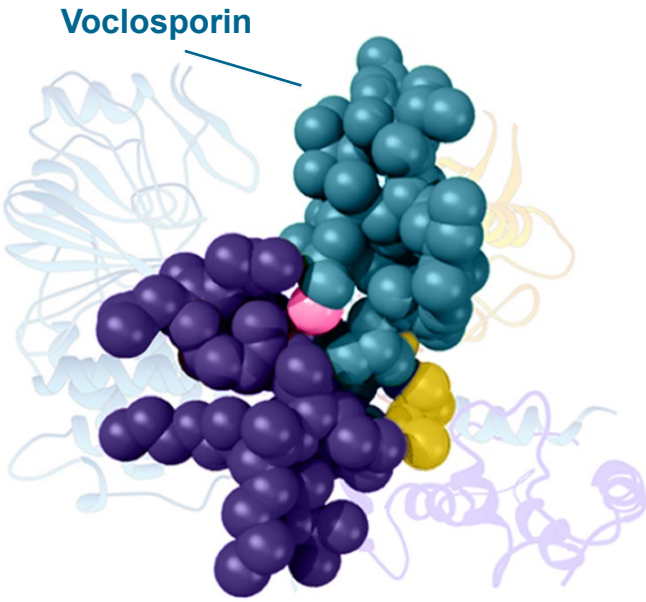
Aurinia provided funding for the study and presentation.

Voclosporin, an Investigational Calcineurin Inhibitor (CNI)

- Voclosporin is structurally similar to cyclosporine A, except for a single carbon bond extension with a double-bond at amino acid-1

This modification:

- Changes how voclosporin binds to calcineurin
- Results in a consistent dose-response, potentially eliminating the need for therapeutic drug monitoring
- Increases potency and results in an improved lipid and glucose metabolic profile compared to other CNIs



Voclosporin has two mechanisms of action potentially relevant to the treatment of LN

1. Inhibition of calcineurin reduces cytokine activation of T-cells
2. Inhibition of calcineurin stabilizes podocytes, protecting against proteinuria

Aurinia Data on File.
Busque S et al. *Am J Transplant.* 2011;11(12):2675-2684.
Kuglstatter A et al. *Acta Crystallogr D Struct Biol*. 2011(67)2:119-123.

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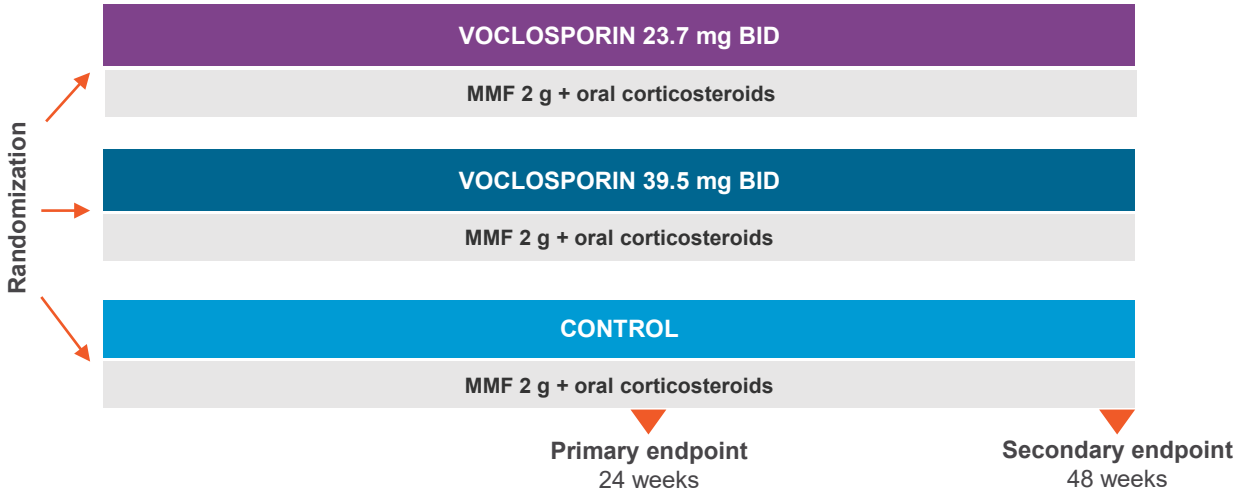
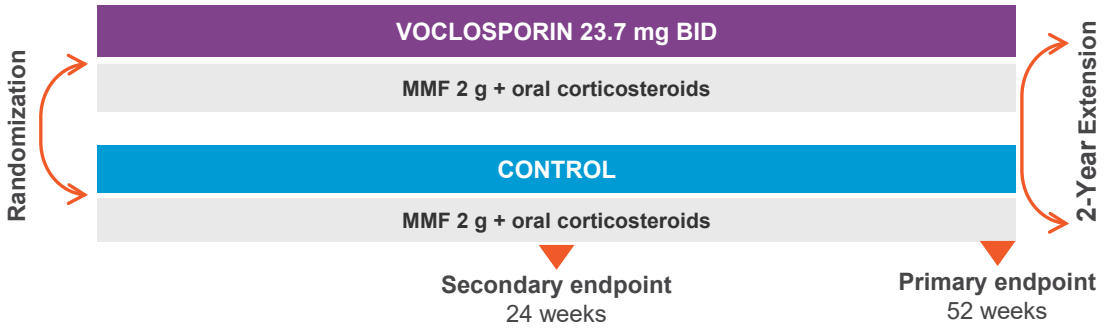
Pooled Analysis of AURA-LV & AURORA

- AURA-LV (Phase 2) and AURORA (Phase 3) were double-blind, randomized controlled trials designed to test whether the addition of voclosporin to background therapy with mycophenolate mofetil (MMF) and corticosteroids improved the complete renal response rate in patients with LN. Both trials employed a low dose of glucocorticoids that were rapidly tapered*
    - Compared to MMF and steroids alone, the addition of oral voclosporin 23.7 mg BID increased renal response by 26% in AURA-LV (OR 3.21, $p < 0.001$) and 18% in AURORA (OR 2.65, $p < 0.001$) at one year
- We pooled and analyzed data from AURA-LV and AURORA to provide more information on the treatment effect of voclosporin with an intent-to-treat population of 268 patients in the voclosporin 23.7 mg BID treatment arm and 266 patients in the control arm.

Phase 2 AURA-LV



Phase 3 AURORA



*IV 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 down to a target dose of 2.5 mg/day at Week 16.

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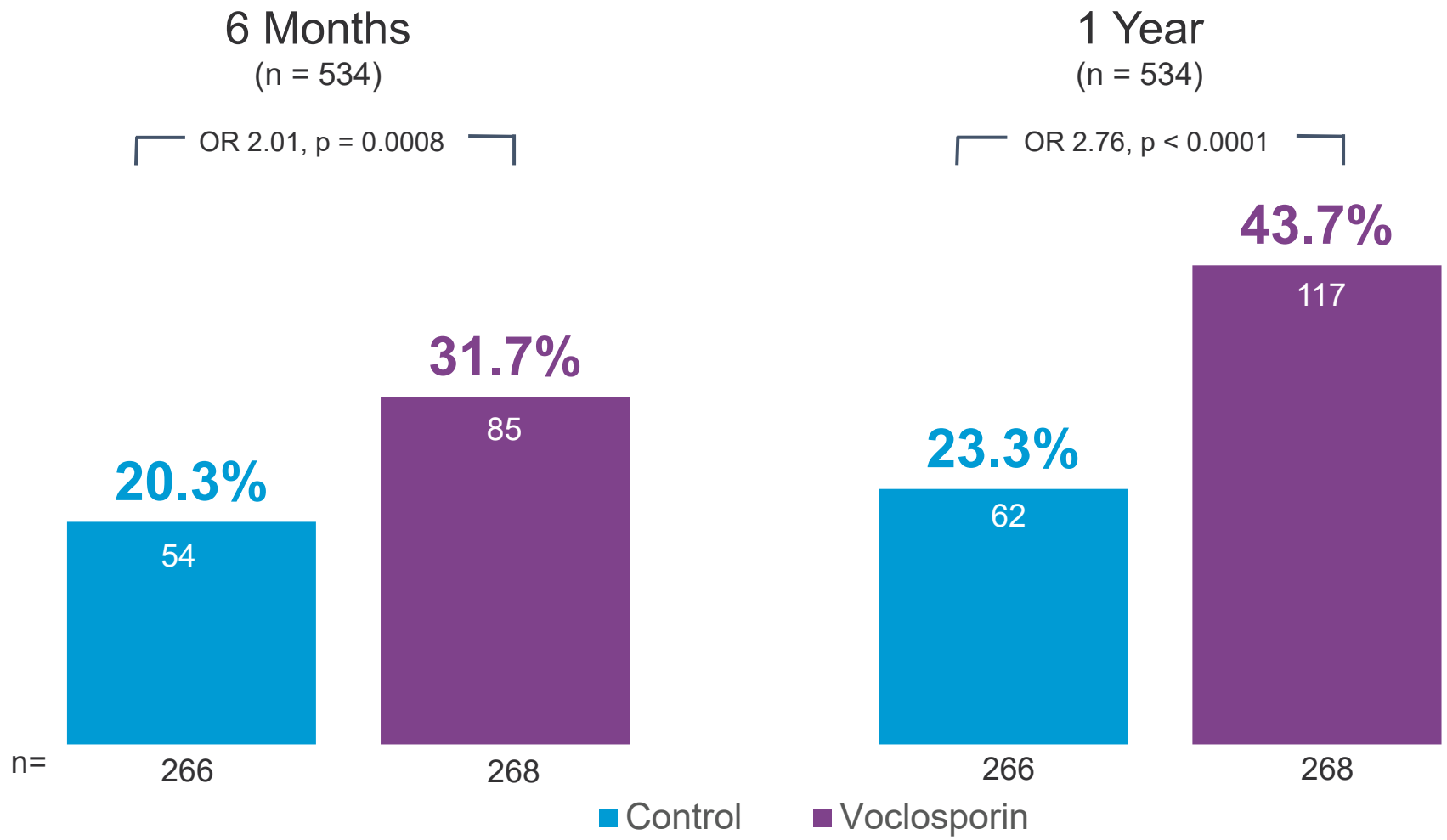
Pooled Analysis of AURA-LV & AURORA: Key Baseline and Demographic Characteristics

	Control n=266	Voclosporin n=268
Age, years	n=266	n=268
Mean (SD)	34 (11)	32 (11)
Median	32	30
Ethnicity, n (%)	n=266	n=268
Hispanic or Latino	72 (27)	66 (25)
Not Hispanic or Latino	193 (73)	202 (75)
eGFR, mL/min/1.73 m^2	n=266	n=267
Mean (SD)	94 (29)	93 (30)
Median	98	92
UPCR, mg/mg	n=266	n=267
Mean (SD)	4.1 (2.8)	4.5 (3.3)
Median	3.1	3.5
Biopsy Class, n (%)	n=266	n=268
Class III or IV (+/- V)	228 (86)	231 (86)
Pure Class V	38 (14)	37 (14)
Time since lupus nephritis diagnosis, years	n=266	n=267
Mean (SD)	4.5 (4.6)	4.7 (5.1)
Median	2.2	2.2

eGFR, estimated glomerular filtration rate; SD, standard deviation; UPCR, urine protein to creatinine ratio.

Pooled Analysis of AURA-LV & AURORA: Renal Response



OR, odds ratio. Renal response defined as UPRC ≤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 rescue medication. Pooled analysis of AURA-LV and AURORA for renal response at approximately 1 year included Week 52 data from AURORA and Week 48 data from AURA-LV.

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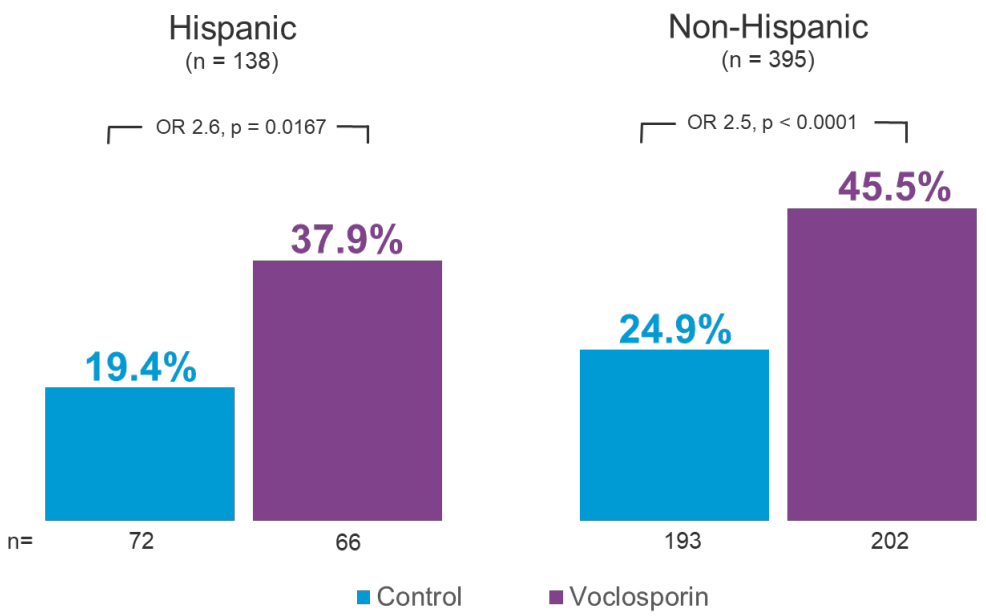
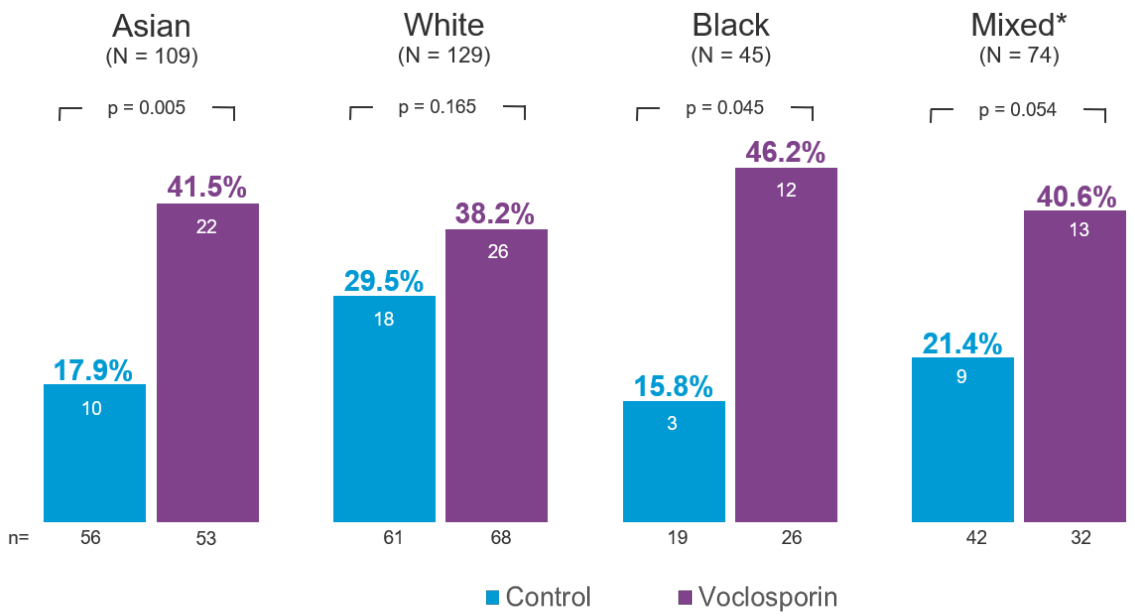
Pooled Analysis of AURA-LV & AURORA: One Year Renal Response by Ethnicity



AURORA: One Year Renal Response by Race



*Mestizo, Mulato, Other. OR, odds ratio. Renal response defined as UPRC ≤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 rescue medication. Pooled analysis of AURA-LV and AURORA for renal response at approximately 1 year included Week 52 data from AURORA and Week 48 data from AURA-LV.

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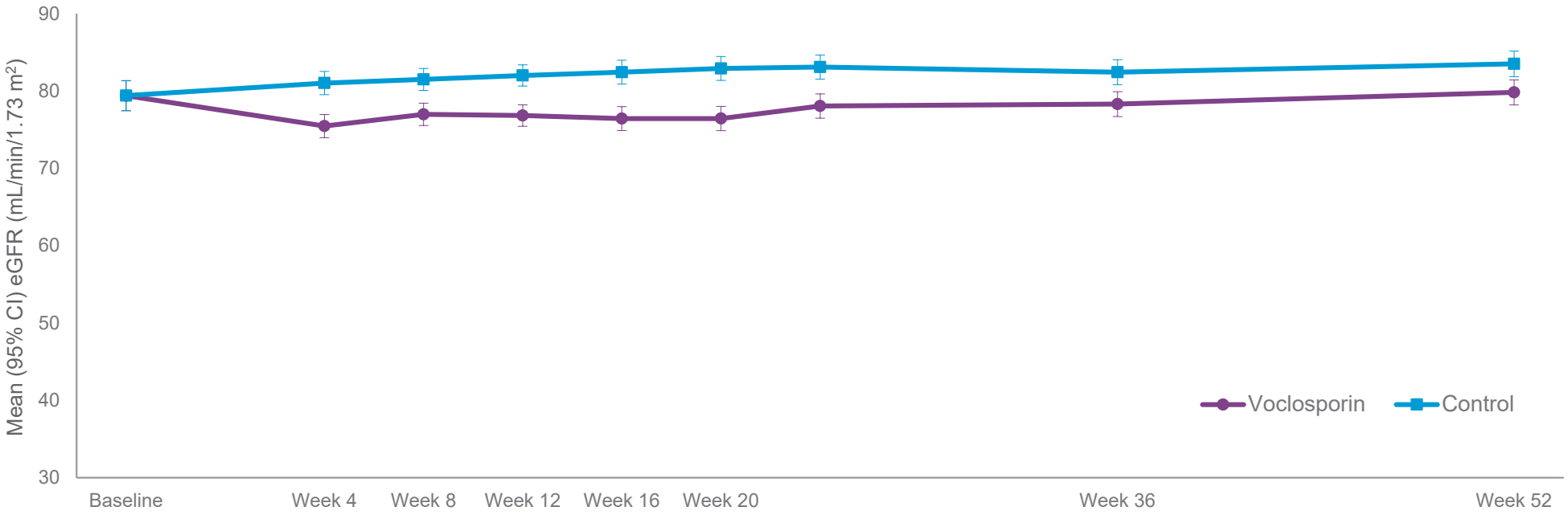
Pooled Analysis of AURA-LV & AURORA: Mean eGFR



- Mean 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 of -3.4 mL/min/1.73 m^2 at Week 4 in the voclosporin arm; mean eGFR remained stable throughout the study with change from baseline of -1.0 mL/min in the voclosporin arm at Week 52

eGFR, estimated glomerular filtration rate. Pooled analysis of AURA-LV and AURORA includes safety population, n=533.
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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Pooled Analysis of AURA-LV & AURORA: Adverse Events

Serious adverse events were similar between treatment arms and there were no unexpected safety signals

	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 System Organ Class of Infection	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

*Includes all deaths post-randomization until completion of study follow-up.

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Conclusions

- The positive benefit-risk profile observed in this pooled analysis confirms the treatment effect seen in AURA-LV and AURORA when comparing voclosporin to placebo treatment, in combination with MMF and low-dose steroids
- In this pooled analysis, adult patients with lupus nephritis treated with voclosporin achieved meaningful rapid reductions in proteinuria, including patients in the Hispanic subgroup, a high-risk lupus nephritis population
- The odds of achieving a renal response in the voclosporin arm were 2.76-fold greater than control, while maintaining a comparable safety profile and with minimal impact on mean eGFR at one year of treatment
- These results are encouraging as the rapid reduction of proteinuria within the first year of treatment is a critical clinical response associated with preserving renal function and improving long-term outcomes for patients with lupus nephritis