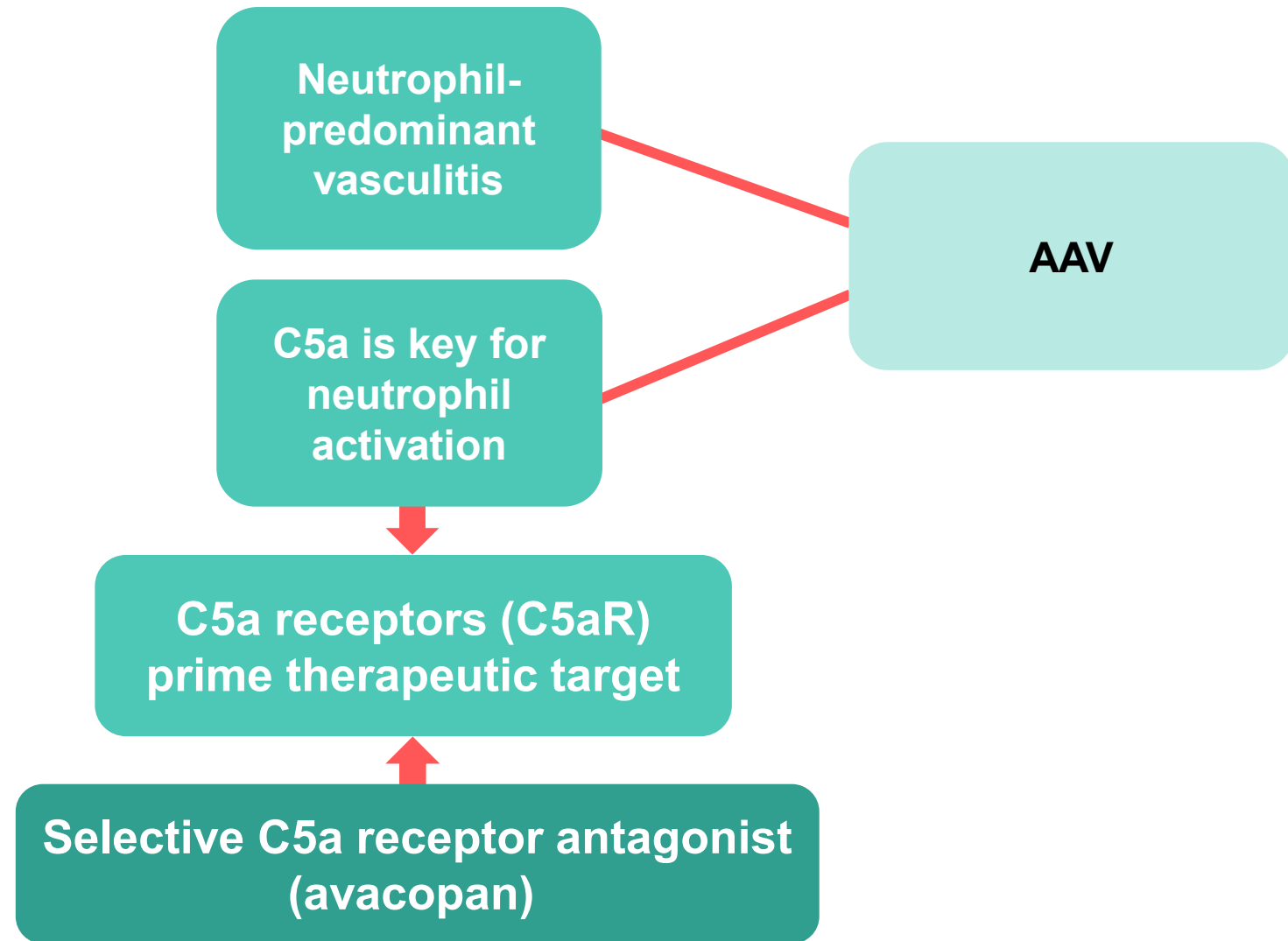


Alternative Complement Pathway



ADVOCATE Trial

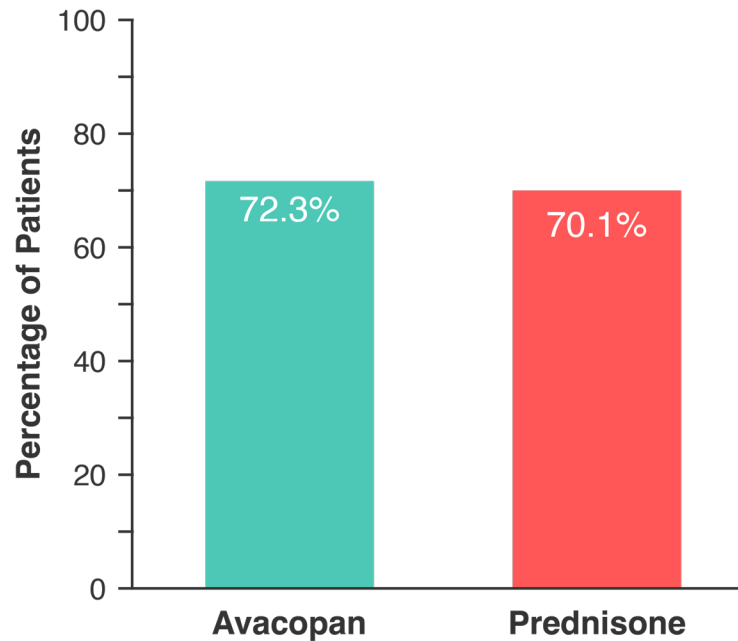
- 330 patients analyzed
 - 166 received:
 - Avacopan 30 mg bd
 - 1.7 g prednisone
 - RTX 375 mg/m² x 4 (n = 107, 64.5%) or CYC/AZA (n = 59, 35.5%)
 - 164 received:
 - 3.8 g prednisone
 - RTX 375 mg/m² x 4 (n = 107, 65.2%) or CYC/AZA (n = 57, 34.8%)
- Primary endpoint/Remission at 26 weeks (BVAS)
 - Avacopan: 120 out of 166 patients (72.3%)
 - Prednisone: 115 out of 164 patients (70.1%)
- Primary endpoint/Sustained remission at 52 weeks (BVAS)
 - Avacopan: 109 out of 166 patients (65.7%)
 - Prednisone: 90 out of 164 patients (54.9%)



ADVOCATE Trial

Clinical Remission at Week 26

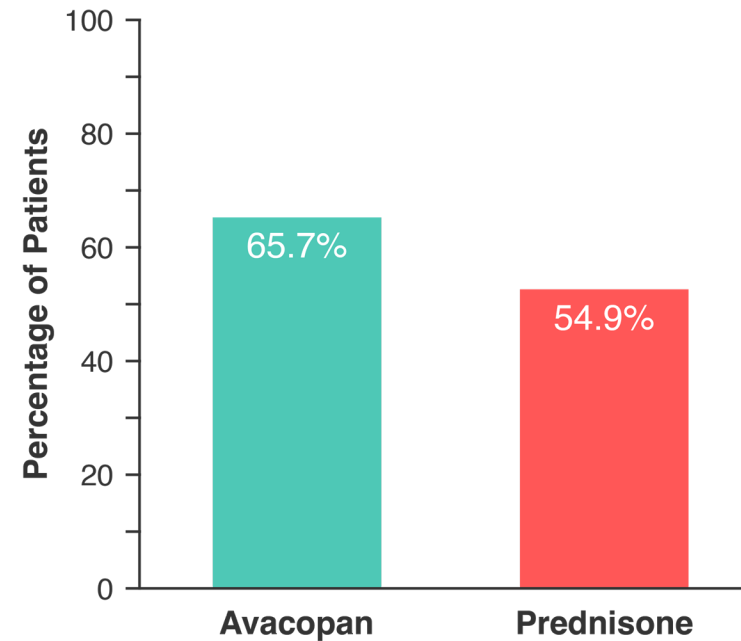
Estimated common difference, 3.4 percentage points
95% CI, -6.0 to 12.8
 $P < 0.001$ for noninferiority; $P = 0.24$ for superiority



Avacopan was noninferior to prednisone with respect to remission at week 26

Clinical Remission at Week 52

Estimated common difference, 12.5 percentage points
95% CI, 2.6 to 22.3
 $P < 0.001$ for noninferiority; $P = 0.007$ for superiority

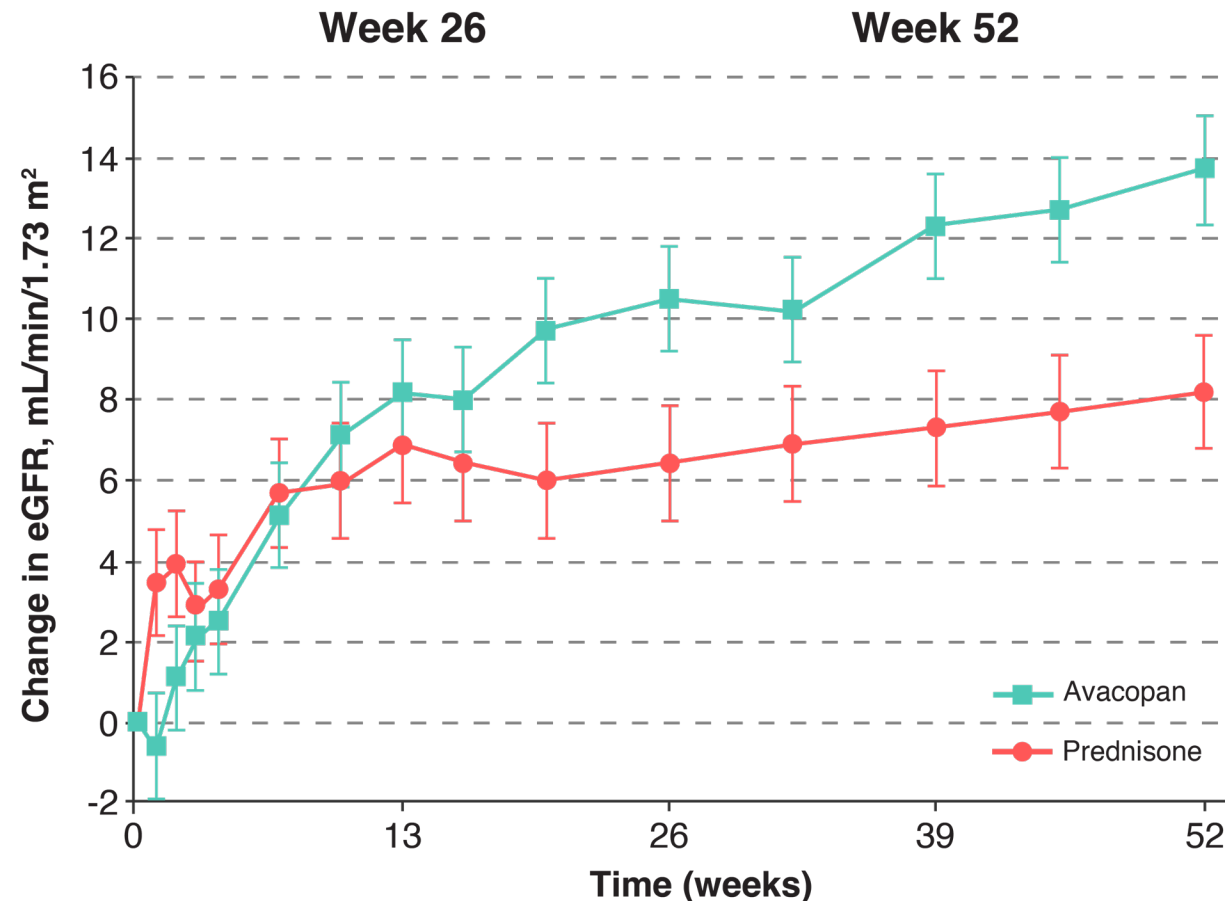


Avacopan was superior to prednisone with respect to sustained remission at week 52



ADVOCATE Trial

- 265 patients with ANCA-associated glomerulonephritis
- 50 patients with an eGFR < 20 mL/min/1.73 m²



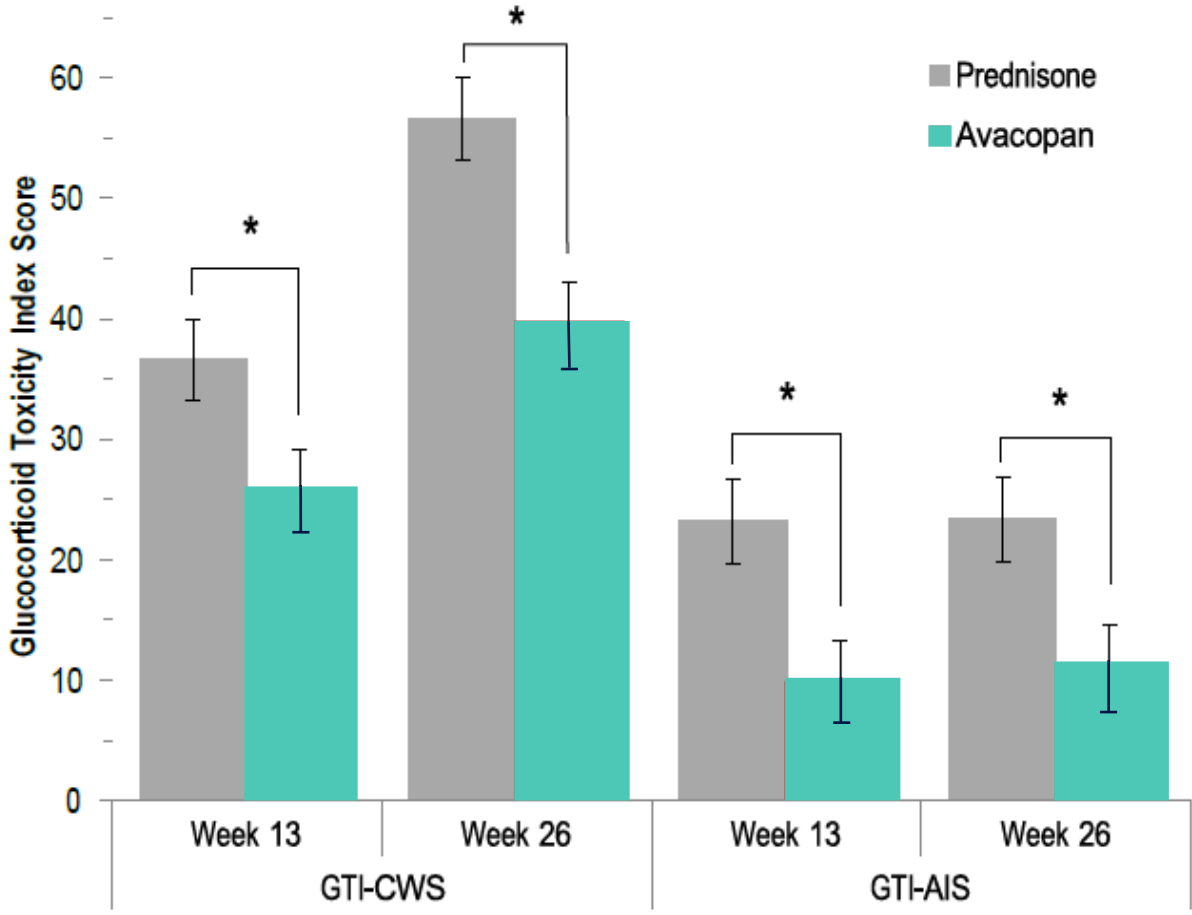
Improvements
in eGFR

eGFR, estimated glomerular filtration rate.

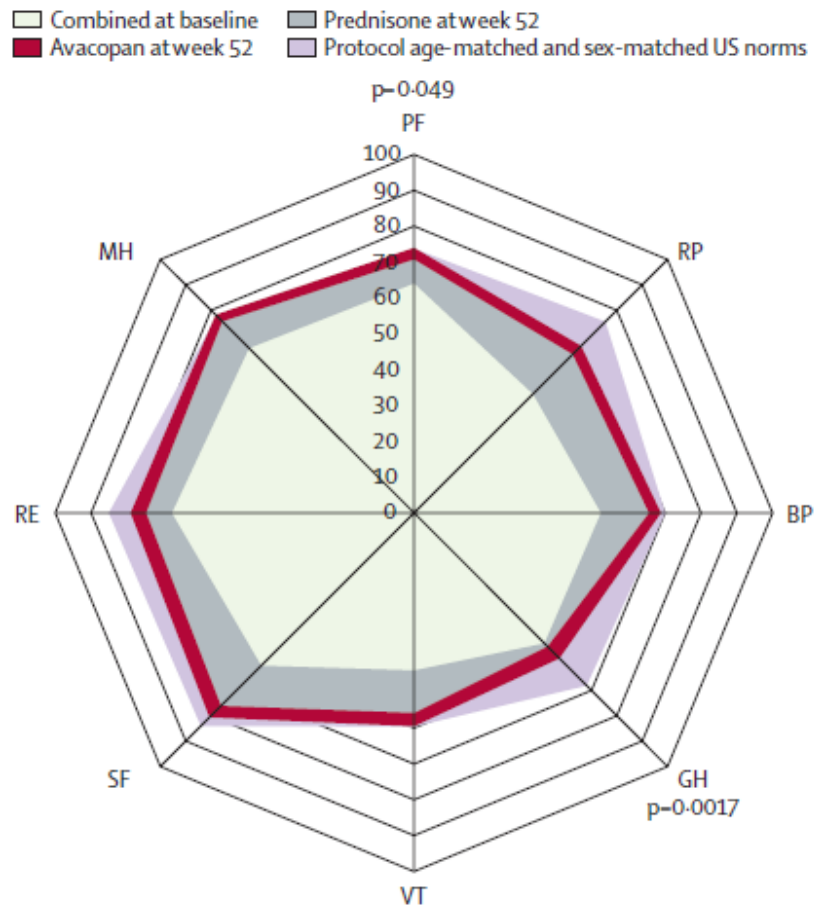
Cortazar FB, et al. *Kidney Int Rep.* 2023;8(4):860-870. Jayne DRW, et al. *N Engl J Med.* 2021;384(7):599-609.

ADVOCATE Trial

Avacopan & GC Toxicity



Avacopan & Quality of Life



Patel NJ, et al. *Lancet Rheumatol.* 2023;5(3):e130-e138.
 Jayne DRW, et al. *N Engl J Med.* 2021;384(7):599-609.



Use of Avacopan in Patients With Antineutrophil Cytoplasmic Antibody-Associated Vasculitis and eGFR <15 mL/min/1.73 m²

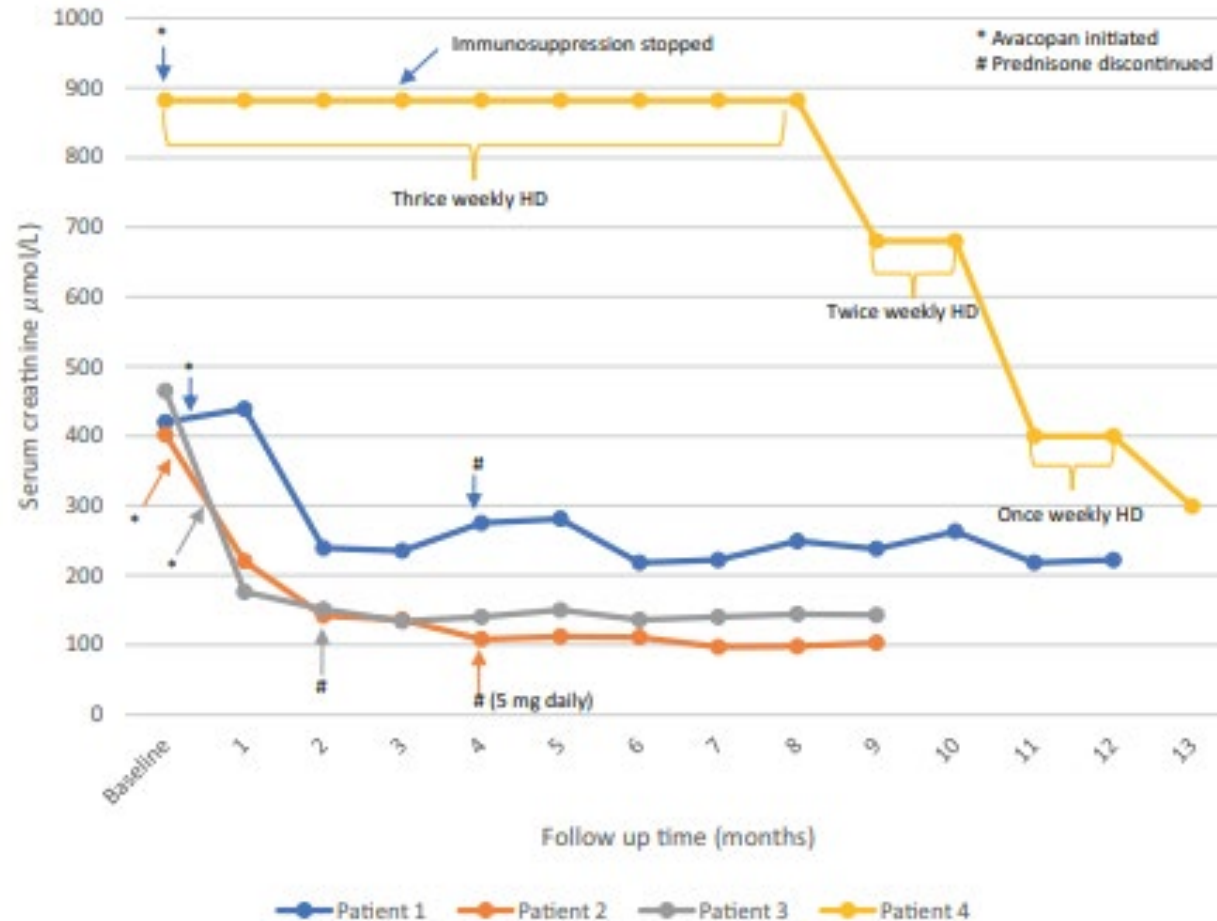


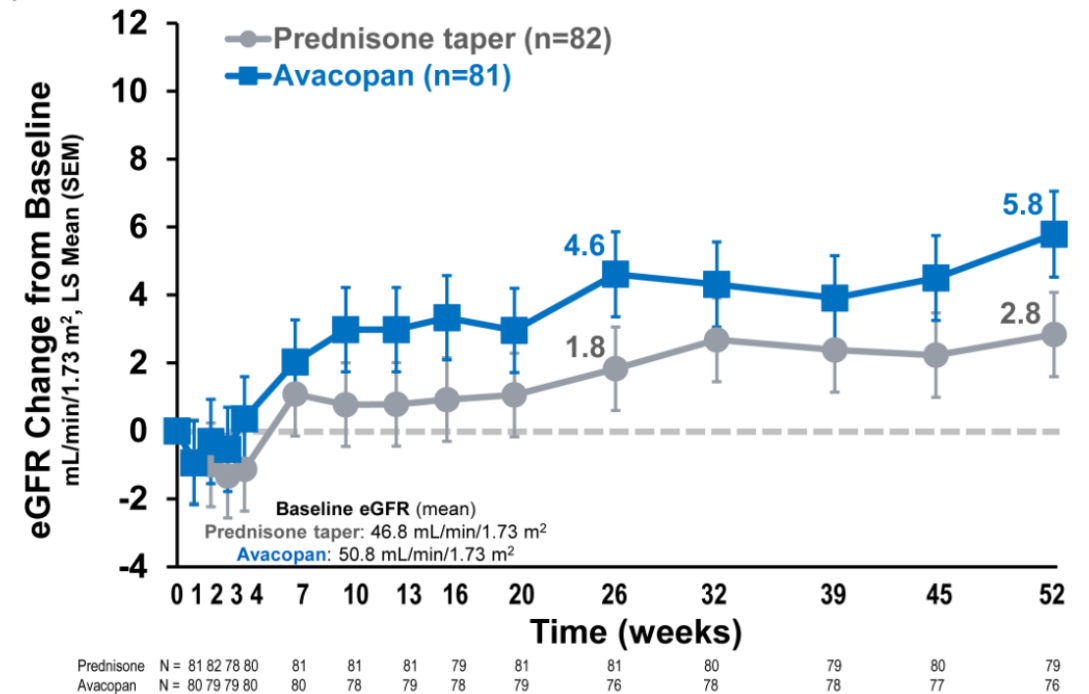
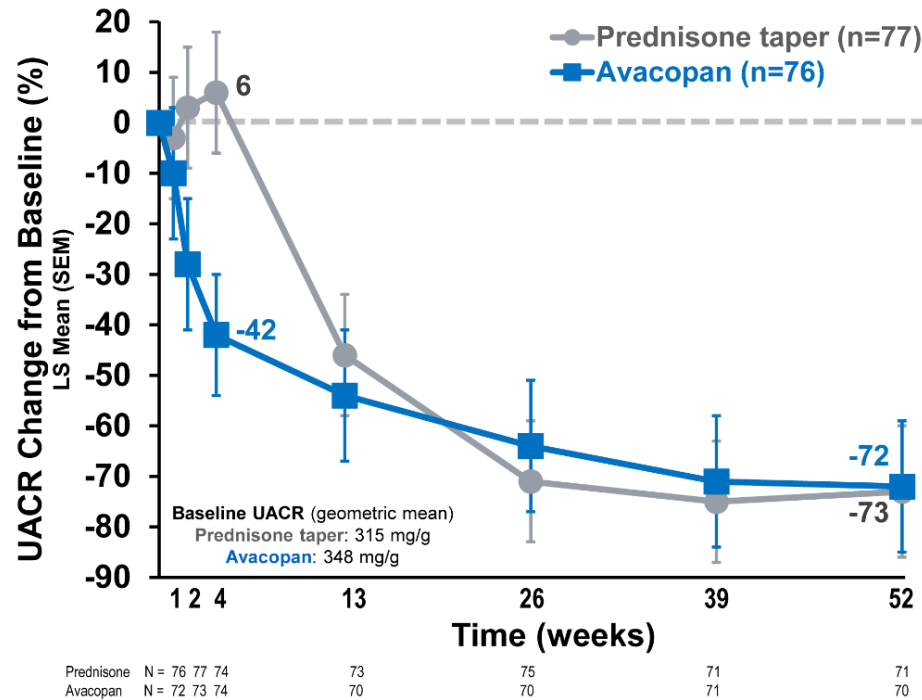
Figure 1. Clinical course of patients treated with avacopan.*Avacopan initiated. #Prednisone discontinued

eGFR, estimated glomerular filtration rate.

Barr B, et al. *Kidney Int Rep.* 2024;9(4):1115-1118.



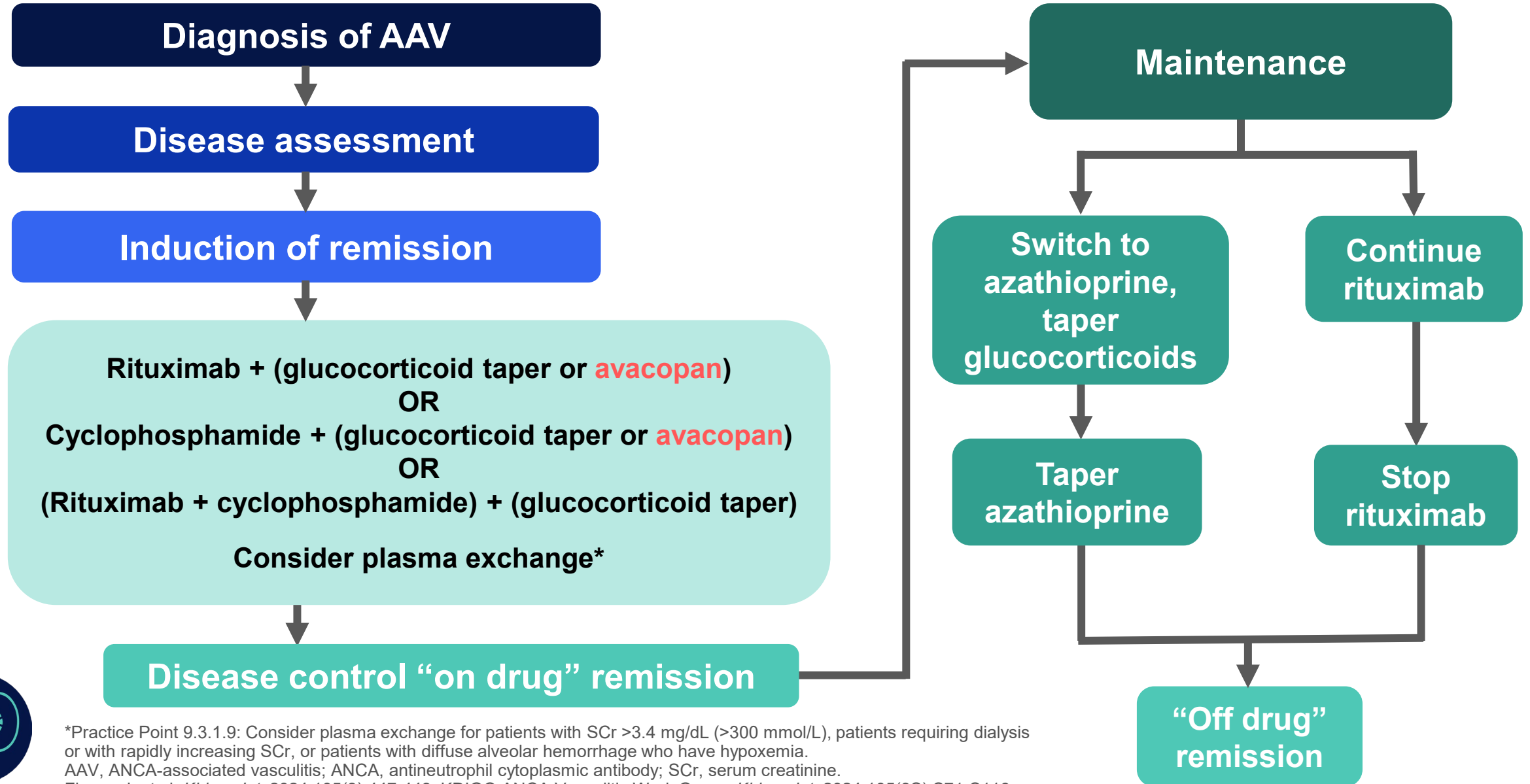
ADVOCATE Trial: Avacopan and Prednisone Taper



eGFR, estimated glomerular filtration rate; UACR, urinary albumin-to-creatinine ratio.
 Geetha D, et al. *Ann Rheum Dis.* 2024;83(2):223-232.



KDIGO: AAV Guidelines 2024



*Practice Point 9.3.1.9: Consider plasma exchange for patients with SCr >3.4 mg/dL (>300 mmol/L), patients requiring dialysis or with rapidly increasing SCr, or patients with diffuse alveolar hemorrhage who have hypoxemia. AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; SCr, serum creatinine. Floege J, et al. *Kidney Int.* 2024;105(3):447-449. KDIGO ANCA Vasculitis Work Group. *Kidney Int.* 2024;105(3S):S71-S116.



Remission Induction: Avacopan as First-Line Alternative to GCs

- Start avacopan 30 mg twice a day as early as possible
- Use avacopan to rapidly reduce glucocorticoid exposure
 - Aim to taper steroids within 1 to 2 weeks
 - Monitor patients for signs of renal recovery, disease remission, or improvement in symptoms



Right Therapy for the Right Patient

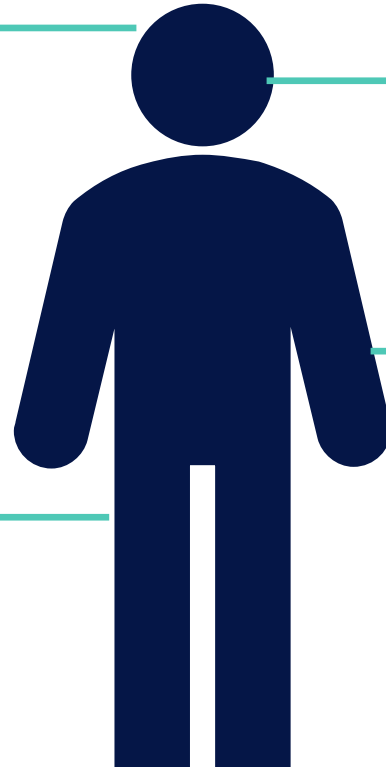
- Avacopan as an alternative to glucocorticoids:
 - Combined with another agent, such as RTX

Glucocorticoid-related toxicity

Active glomerulonephritis + rapidly deteriorating kidney function who had better recovery with avacopan

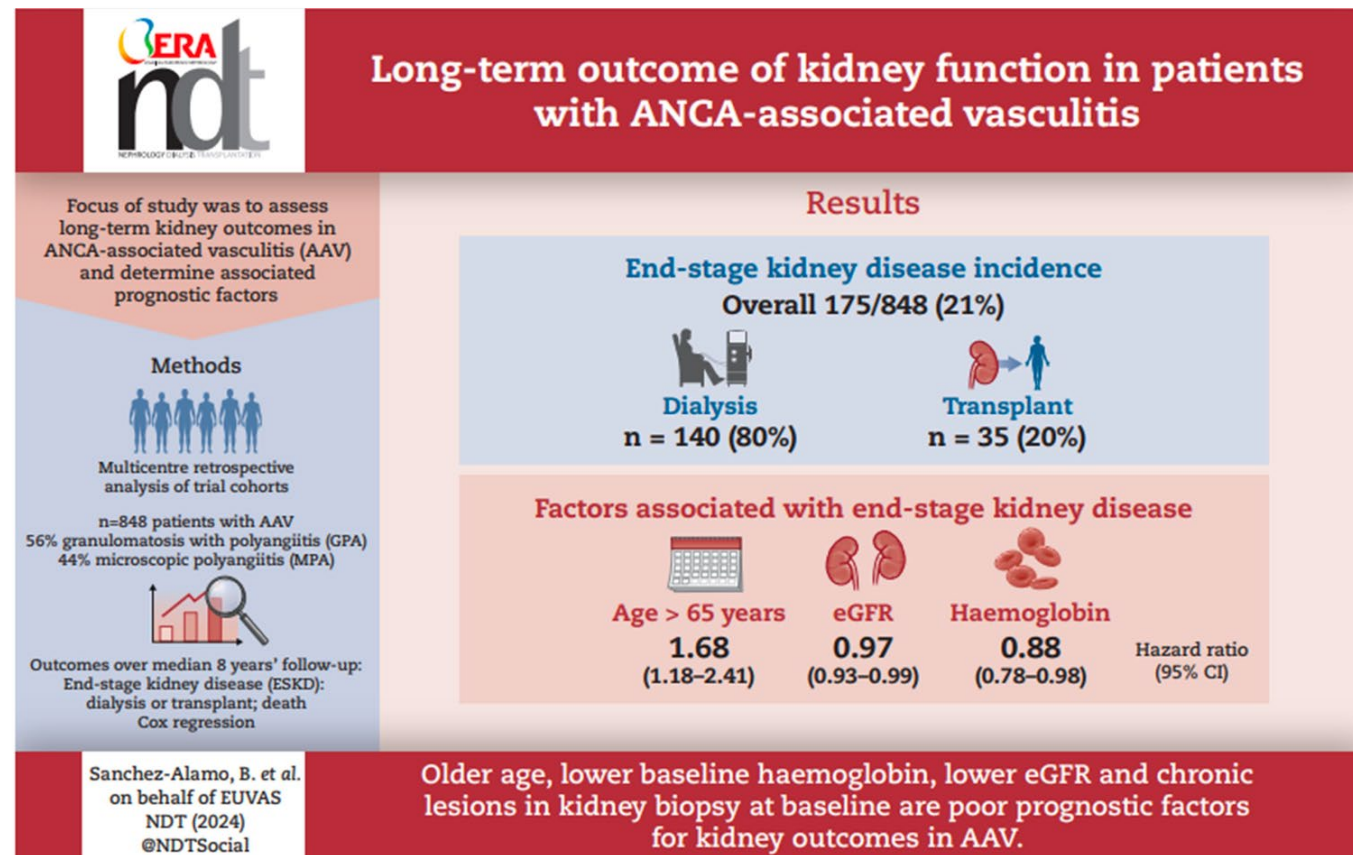
Glucocorticoid complications

No response to a standard of care treatment



ESKD Frequency Depends on eGFR!

- 644 (of 848) had ANCA-GN, median eGFR of 42.1 mL/min/1.73 m²
- Patients with ESKD had a median baseline eGFR of 13.2 mL/min/1.73 m²



Avacopan: Relapsing Patients

- In ADVOCATE, lower rate of relapses in patients treated with avacopan
- Over 12 months' follow-up, relapse rate in patients treated with a standard regimen was 20%
- Relapse rate was cut in half to about **10%** in patients treated with **avacopan**



Quote by Stephen McAdoo, MD

"I think we can sometimes really underestimate the impact of that glucocorticoid toxicity in our patient population. So this is an exciting time to have a new option to glucocorticoids for the treatment of vasculitis."

