Remission, Glucocorticoid Toxicity, Health-Related Quality of Life, and Safety Outcomes in Patients With Renal Involvement in the Phase 3 Trial of Avacopan for the Treatment of ANCA-Associated Vasculitis

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INTRODUCTION

Most patients with ANCA-associated vasculitis have **renal involvement**,[1] and severe renal dysfunction is associated with poor patient survival and an increased risk of end-stage renal disease[2,3]

In the Phase 3 ADVOCATE trial,[4] 81% of patients with granulomatosis with polyangiitis **(GPA)** or microscopic polyangiitis **(MPA)** had renal involvement:

- Estimated glomerular filtration rate (eGFR) improved at 52 weeks by 7.3 mL/min/1.73 m^2 with **avacopan** compared with 4.1 mL/min/1.73 m^2 with a prednisone taper
- Urinary albumin:creatinine ratio (UACR) decreased at 4 weeks by 40% with avacopan compared with 0% with a prednisone taper in those with UACR ≥10 mg/g

OBJECTIVE

To evaluate efficacy and safety outcomes beyond eGFR and UACR for patients with GPA or MPA with baseline renal involvement

References: 1. Binda V, et al. *J Nephrol.* 2018;31:197–208; 2. Day CJ, et al. *Am J Kidney Dis.* 2010;55:250–8; 3. Flossmann O, et al. *Ann Rheum Dis.* 2011;70:488–94; 4. Jayne DRW, et al. *N Engl J Med.* 2021;384:599–609.

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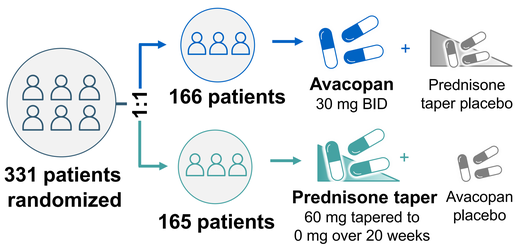
METHODS

ADVOCATE trial

52-week study (NCT02994927)

Eligible patients

- Newly diagnosed or relapsing GPA or MPA
- Anti-proteinase-3 (PR3)+ or anti-myeloperoxidase+ ANCA
- eGFR ≥15 mL/min/1.73 m^2
- Birmingham Vasculitis Activity Score (BVAS): ≥1 major item, or 3 non-major items, or ≥2 renal items of hematuria and proteinuria



All patients:

- Background therapy with cyclophosphamide/azathioprine or cyclophosphamide/mycophenolate mofetil or rituximab
- Non-study supplied glucocorticoids (GCs) were allowed under certain protocol-specified conditions

Post hoc subgroup analysis in 268 patients with renal involvement at baseline (based on presence of any BVAS renal item)

Efficacy outcomes

- Remission at Week 26, Sustained remission at Week 52
- Glucocorticoid Toxicity Index (GTI) at Week 26
- Health-Related Quality of Life (HRQoL, Short Form-36 [SF-36] Health Survey v2)

Safety outcomes

- Adverse events (AEs), Serious Adverse Events (SAEs)

RENAL SUBGROUP RESULTS

Avacopan (N=134)

63% Male; Mean age: 61 years; 52% MPA
73% Newly diagnosed; 40% PR3-ANCA
60% Background rituximab therapy;
Mean eGFR: 44.6 mL/min/1.73 m^2

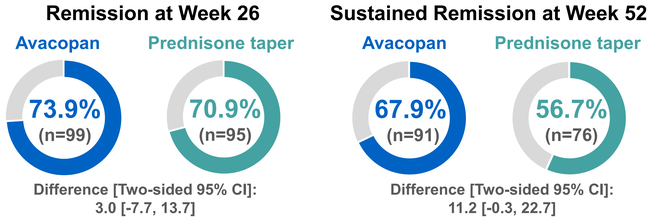
Baseline Characteristics

57% Male; Mean age: 62 years; 53% MPA
75% Newly diagnosed; 35% PR3-ANCA
61% Background rituximab therapy;
Mean eGFR: 45.6 mL/min/1.73 m^2

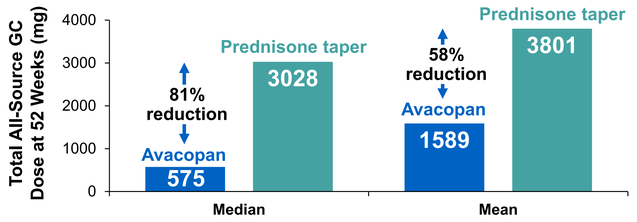
Prednisone taper (N=134)

Key Efficacy Outcomes

Sustained remission rates of this subgroup favored avacopan and were consistent with the results of the overall ADVOCATE trial



The avacopan group received a lower total GC dose than the prednisone taper group

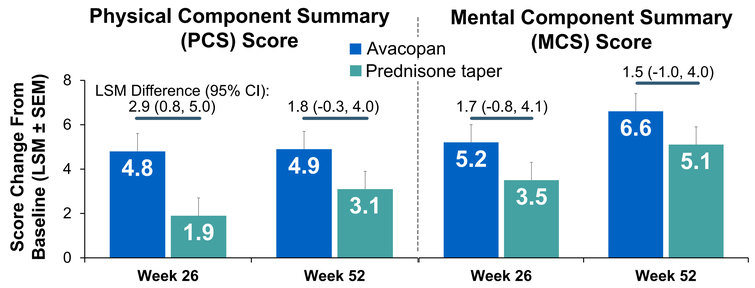


GTI-Cumulative Worsening Score (CWS) and GTI-Aggregate Improvement Score (AIS) were lower (more favorable) in the avacopan group than in the prednisone taper group

Lower values are optimal, demonstrating less toxicity	Avacopan	Prednisone taper	Avacopan vs Prednisone taper
GTI-CWS at Week 26 Ranges from 0 to 410	38.9	58.5	1.5× Difference [95% CI] -19.6 [-29.6, -9.6]
GTI-AIS at Week 26 Ranges from -317 to 410	11.2	24.3	2.2× Difference [95% CI] -13.1 [-23.2, -3.0]

Data are Least Squares Means (LSMs)

The avacopan group reported a greater improvement in SF-36 PCS scores at Week 26 and numerical improvements in PCS scores at Week 52 and MCS scores at Weeks 26 and 52



Key Safety Outcomes

Safety profile was comparable between the two groups

	Avacopan (N=134)	Prednisone taper (N=134)
AEs, n (%) [n events]	132 (98.5) 1465 events	133 (99.3) 1777 events
SAEs, n (%) [n events]	61 (45.5) 104 events	65 (48.5) 148 events
Deaths, n (%)	2 (1.5)	3 (2.2)

CONCLUSIONS

- **This post hoc subgroup analysis of the ADVOCATE trial showed that patients with GPA or MPA with baseline renal involvement treated with avacopan versus a prednisone taper:**
  - ✓ **achieved higher sustained remission rates at Week 52**
  - ✓ **received lower GC doses**
  - ✓ **experienced less GC-related toxicity**
  - ✓ **reported numerically greater improvements in HRQoL**
- **The safety profile was comparable between the two groups**

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