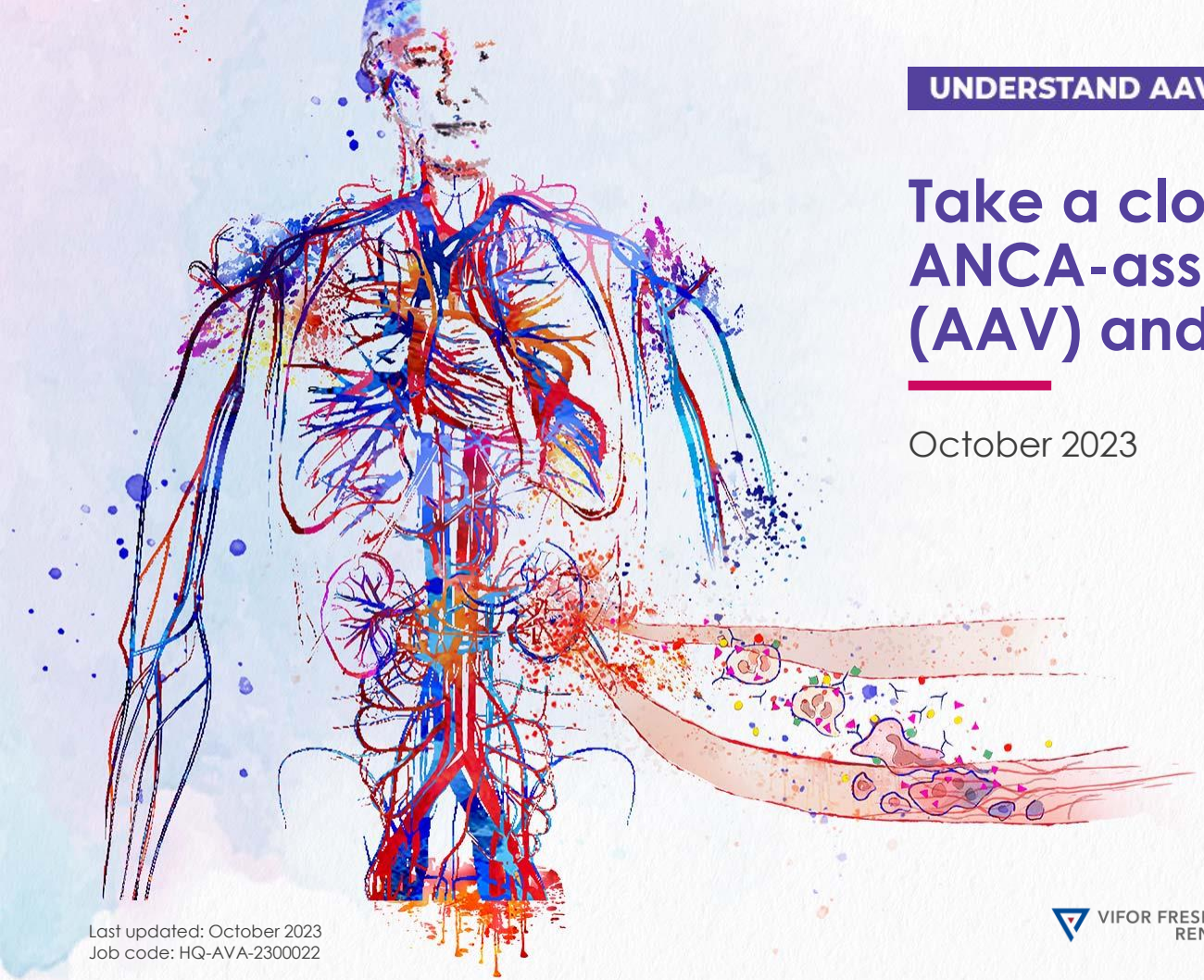

UNDERSTAND AAV

Take a closer look at ANCA-associated vasculitis (AAV) and avacopan

October 2023

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VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

CSL Vifor

AAV disease and treatment burden

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody.

AAV is a group of progressive, rare, severe autoimmune diseases[1,2]

Rare

Meets EMA definition of rare disease[3–5]

European incidence:

13–~20

per million per year[5]

Prevalence:

46–184

per million[5]

Incidence generally increases with age[4,5]

Autoimmune

Immune system mediated inflammation of small-medium blood vessels leads to organ damage [2,6,7]

AAV is a chronic condition with a relapsing course that can affect almost any organ – most commonly the respiratory tract and kidney[6-8]

Heterogeneous

Classification is based on antibody status or clinical phenotype and predicts the course of disease[6,7]

Antibody status:[2,6,7]

- PR3-ANCA+ (linked to GPA)
- MPO-ANCA+ (linked to MPA)

Two main clinical phenotypes:[6-8]

- Granulomatosis with polyangiitis (GPA)
- Microscopic polyangiitis (MPA)

Other phenotype:[6-8]

- Eosinophilic granulomatosis with polyangiitis (EGPA)

2022 ACR/EULAR classification criteria for GPA, MPA and EGPA **here**

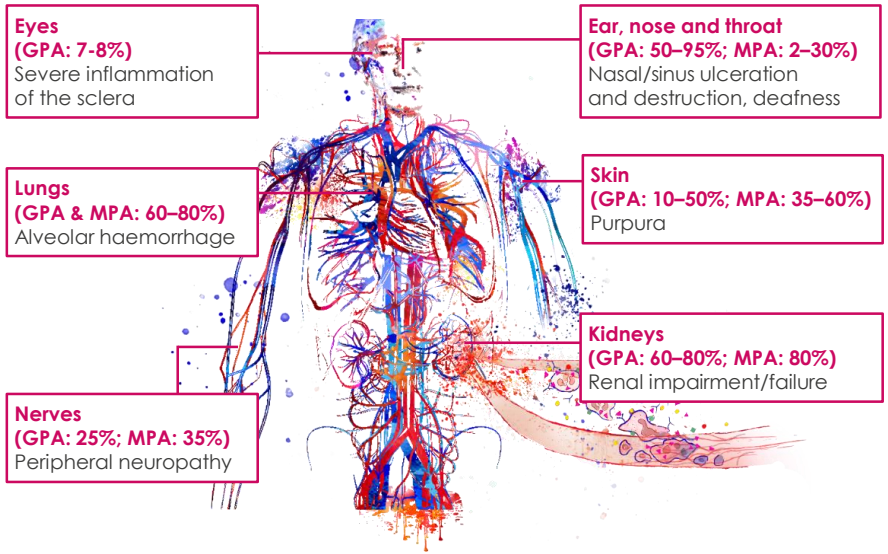
AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; EGPA, eosinophilic granulomatosis with polyangiitis; EMA, European Medicines Agency; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; MPO, myeloperoxidase; PR3, proteinase 3.

1. Hutton HL, et al. *Semin Nephrol* 2017;37(5):418–35. 2. Al-Hussain T, et al. *Adv Anat Pathol* 2017;24(4):226–34. 3. European Medicines Agency (2018). Development of medicines for rare diseases. Available at: https://www.ema.europa.eu/en/news/development-medicines-rare-diseases. Date accessed April 2021. 4. Watts RA, et al. *Arthritis Rheum* 2000;43(2):414–9. 5. Watts RA, et al. *Nephrol Dial Transplant* 2015;30(Suppl 1):i14–22. 6. Jennette JC, et al. *Arthritis Rheum* 2013;65(1):1–11. 7. Wallace ZS, Miloslavsky EM. *BMJ* 2020;368:m421. doi: 10.1136/bmj.m421. 8. Yates M, et al. *Ann Rheum Dis* 2016;75(9):1583–94.

GPA/MPA cause irreversible damage to critical organs and increase risk of morbidity and mortality[1–6]

Severe damage affects multiple organs[1–3,7]

Characteristics and frequency of manifestations in severe disease:[7]



High morbidity and mortality risk[4–6]

72% of patients are hospitalised or die over a 5 year period[4]

- GPA 5-year survival rates: **74–91%**[5]
- MPA 5-year survival rates: **45–76%**[5]

Common causes of hospitalisation:*[4]

- Renal involvement
- CV related
- Respiratory disease
- Infection

Information on clinical tools and scales used for the assessment of AAV patients, here

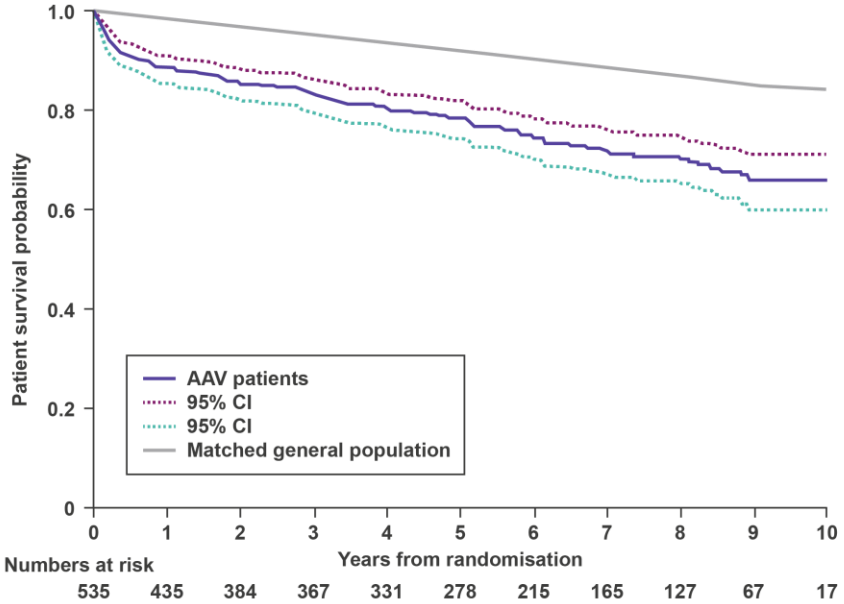
*Besides disease-related hospitalisation.

CV, cardiovascular; EUVAS, European Vasculitis Study Group; GI, gastrointestinal; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

1. Wallace ZS, Miloslavsky EM. *BMJ* 2020;368:m421. 2. Rutherford PA, Götte D. *EMJ Nephrol* 2020;8[Suppl 4]:2–16. 3. Robson J, et al. *Ann Rheum Dis* 2015;74(1):177–84. 4. Quartuccio L, et al. *Intern Emerg Med* 2020;16:581–89. 5. Yates et al. *Ann Rheum Dis* 2016;75(9):1583-94. 6. Flossmann O, et al. *Ann Rheum Dis* 2011;70(3):488–94. 7. Pagnoux C. *Eur J Rheumatol* 2016;3(3):122–33.

GPA/MPA lead to poorer survival and a higher mortality risk in both the short and long term[1–4]

EUVAS longitudinal study: overall GPA/MPA patient survival vs matched controls[3]



Graph adapted from Flossmann et al. 2011, EUVAS longitudinal study data (1995–2002): from four randomised trials with newly diagnosed GPA and MPA patients (n=535)

2.6x higher mortality rate vs general population over a median 5.2 years after diagnosis ($p<0.0001$)[3]

88% Year 1 GPA/MPA survival vs 98% in matched controls[3]

78% Year 5 GPA/MPA survival vs 92% in matched controls[3]

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; CI, confidence interval; EUVAS, European Vasculitis Study Group; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

1. Quartuccio L, et al. *Intern Emerg Med* 2020. doi: 10.1007/s11739-020-02431-y. 2. Yates et al. *Ann Rheum Dis* 2016;75(9):1583-94. 3. Flossmann O, et al. *Ann Rheum Dis* 2011;70(3):488–94. 4. Little MA, et al. *Ann Rheum Dis* 2010;69(6):1036–43.

Majority of AAV patients have renal involvement, which increases risk of ESKD and mortality[1–4]

Renal impairment is common in GPA/MPA[1]

Nearly 4 in 5 (78%) patients have renal impairment at diagnosis[2]

A substantial proportion of patients require renal replacement therapy (RRT)

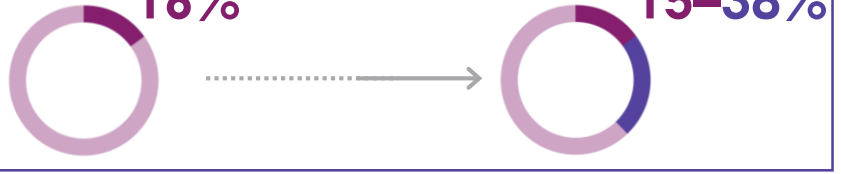
At remission induction[2]

16%

More patients need RRT as disease progresses

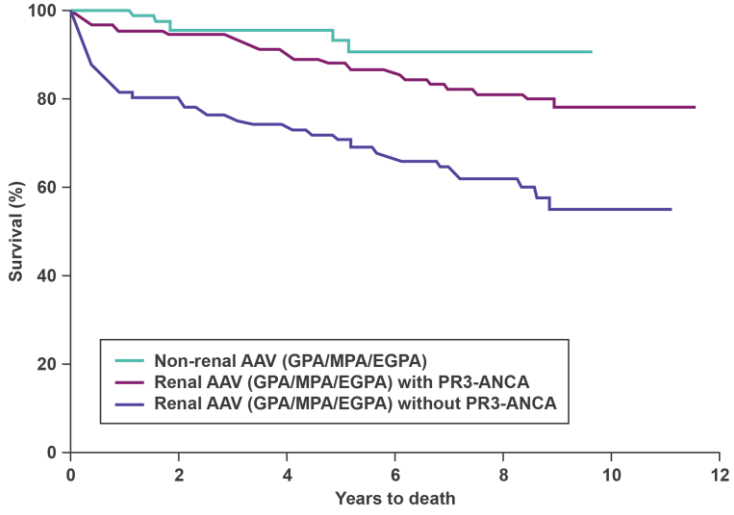
Within ~5 years of diagnosis:[3,4]

15–38%



EUVAS/FVSG longitudinal study

Mortality risk is 2x higher for renal AAV with PR3-ANCA and 6x higher for renal AAV without PR3-ANCA (vs non-renal AAV)[5,6]



Graph adapted from Mahr et al. 2013, EUVAS and FVSG longitudinal study data (1995–2003): from five clinical trials with newly diagnosed GPA, MPA and EGPA patients (n=673)

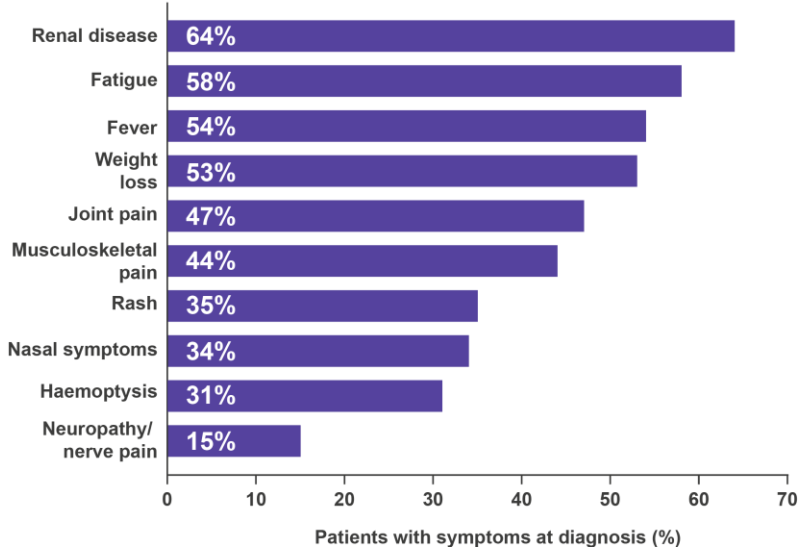
AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; EGPA, eosinophilic granulomatosis with polyangiitis; ESKD, end-stage kidney disease; EUVAS, European vasculitis study group, FVSG, French Vasculitis Study Group; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; PR3, proteinase 3; RRT, renal replacement therapy.

1. Walllace et al. *BMJ* 2020;368:m421. 2. Rutherford PA, Götte D. *EMJ Nephrol* 2020;8[Suppl 4]:2–16. 3. Mohammed AJ, Segelmark M. *J Rheumatol* 2014;14(5):1366-73. 4. Takala JH, et al. *Scand J Rheumatol* 2011;40(4):283–8.
5. Heijl C, et al. RMD Open 2017 Jul 13;3(1):e000435.. 6. Mahr A, et al. Ann Rheum Dis 2013;72(6):1003–10.

AAV symptoms have a substantial impact on QoL[1–4]

Real-world data

Symptoms at GPA/MPA patient diagnosis[1]



Graph adapted from Rutherford et al. 2018, real world research (2014–2017): retrospective clinical audit of healthcare records from newly diagnosed GPA and MPA patients (n=929). Sponsored by Vifor Pharma

Meta-analysis data

QoL is already significantly impaired at the time of diagnosis in GPA/MPA/EGPA (vs. general population)[2,3]

Poor physical QoL (OR 7.0, 95% CI 4.4, 11.1)

Contributory factors:[2]

- Fatigue
- Sleep disturbance
- Pain
- Current use of high-dose GCs

Poor mental QoL (OR 2.5, 95% CI 1.7, 3.6)

Contributory factors:[2]

- Fatigue
- Hypoalbuminanemia
- Anxiety
- Depression
- Unemployment

Basu et al, 2014, Clinical trial data: case-control study of GPA, MPA and EGPA patients (n=410)

Fatigue is independently associated with unemployment (OR 7.1, 95% CI 1.5–33.1)[4]

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; ASN, American Society of Nephrology; CI, confidence interval, EGPA, eosinophilic granulomatosis with polyangiitis; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; OR, odds ratio; QoL, quality of life.

1. Rutherford PA, et al. Poster SA-PO403 presented at the American Society of Nephrology, October 2018, San Diego USA. 2. Basu N, et al. *Ann Rheum Dis* 2014;73(1):207–11. 3. Walsh M, et al. *Arthritis Care Res (Hoboken)* 2011;63(7):1055–61. 4. Basu N, et al. *Rheumatology (Oxford)* 2014;53(5):953–6.

Many patients do not achieve or sustain remission and risk of relapse persists when receiving standard of care AAV treatment[1-5]

Clinical trial data

1 in 3 patients fail to achieve remission at 6 months without use of GCs[1,2]

- **64%** of RTX patients achieved remission (n=63/99)
- **53%** of CYC patients achieved remission (n=52/98)

1 in 2 patients are unable to sustain remission at 12 months without GCs[3]

- **48%** of RTX patients sustained remission (n=47/99)
- **39%** of CYC patients sustained remission (n=38/98)

RAVE clinical trial data (2010): non-inferiority trial comparing RTX with CYC remission regimens in GPA and MPA patients (N=197). Remission defined as BVAS=0 and stopped use of GCs.

Real-world data

<60% of patients achieve remission (no AAV activity and glucocorticoid taper on track) at 12 months[4]

>50% of patients continue to use GCs at 12 months[4]

Rutherford et al. 2018, real world research (2014–2017): retrospective clinical audit of healthcare records from newly diagnosed GPA and MPA patients (n=929). Sponsored by Vifor Pharma

45% of GPA/MPA patients still receive GCs nearly 5 years after initiation of RTX to sustain remission[5]

Charles et al 2020, Clinical trial data: evaluating relapse rates in GPA and MPA patients already in remission.

Standard of care AAV therapies, here

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; AZA, azathioprine; BVAS, Birmingham Vasculitis Activity Score; CYC, cyclophosphamide; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RTX, rituximab.

1. Stone JH, et al. N Engl J Med 2010;363(3):221–32. 2. Stone JH, et al. N Engl J Med 2010;363(3)[Suppl]2–16. 3. Specks U, et al. N Engl J Med 2013;369(5):417–27. 4. Rutherford P, et al. Arthritis Rheumatol 2018;70(Suppl 1. 10):Abstract 2724.
5. Charles P, et al. Ann Int Med 2020;10.7326/M19-3827.

Relapses lead to more long-term complications including organ and tissue damage in GPA/MPA patients[1–3]

Real-world data

Up to 8% of GPA/MPA patients experience relapses of varying severity each year[1]

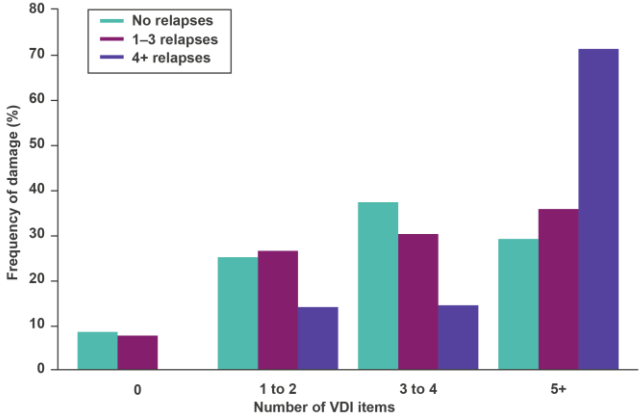
Up to 12% of GPA/MPA patients had a relapse within 4 years of diagnosis[1]

Spearpoint et al. 2019, real world research (2011–2016): German retrospective InGef database audit from newly diagnosed GPA and MPA patients. Poster presented at: ERA-EDTA 2019. Sponsored by Vifor Pharma

Non-severe relapse is an under-recognised clinical problem leading to high GC exposure[2]

EUVAS longitudinal study

Relapse increases frequency of damage at long-term follow-up[3]



Graph adapted from Robson J, et al. Rheumatology 2015. Robson et al. 2015, EUVAS longitudinal study data (1995–2004): from four clinical trials with LTFU of newly diagnosed GPA and MPA patients (n=296)

Organ damage accumulates over time in GPA/MPA and is independently associated with increasing relapse number[3]

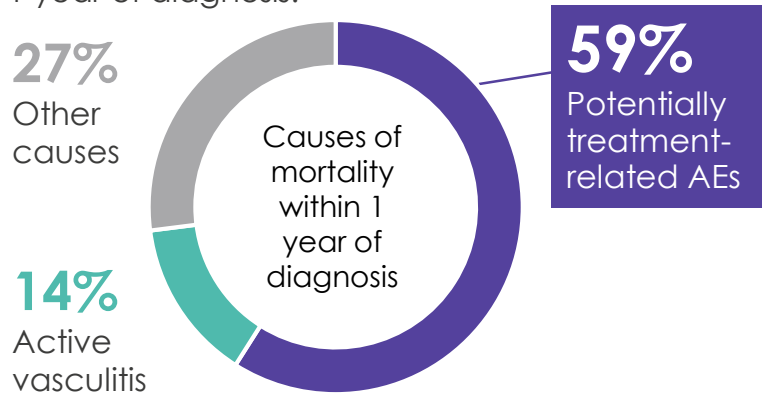
ERA–EDTA, European Renal Association–European Dialysis and Transplant Association; EUVAS, European Vasculitis Study Group; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; LTFU; long-term follow-up, MPA, microscopic polyangiitis; VDI, Vasculitis Damage Index.

1. Spearpoint P, et al. Nephrol Dial Transplant 2019;34(Suppl 1). 2. Miloslavsky EM, et al. Arthritis Rheum 2015;67(6):1629–36. 3. Robson J, et al. Rheumatology 2015;54(3):471–81.

Treatment-related events are the main cause of short-term mortality and remain a prevalent cause long term[1-3]

EUVAS longitudinal study

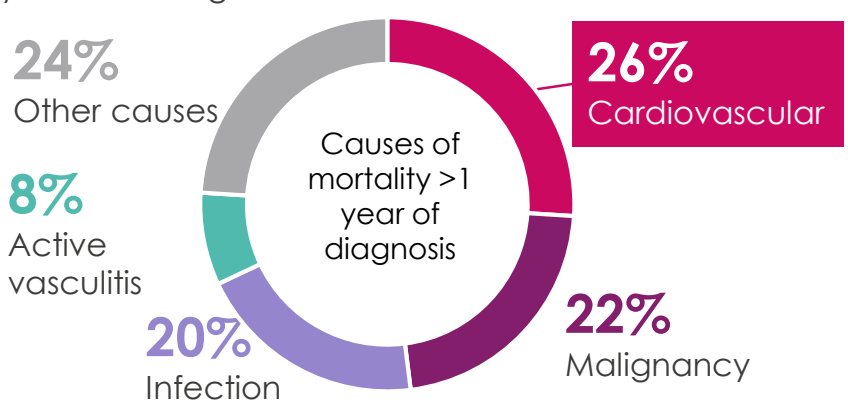
Of 10.7% (n=56 of 524) of GPA/MPA patients who died within 1 year of diagnosis:[1]



Adapted from Little et al. 2010, EUVAS longitudinal study data (1995–2005): from four randomised trials with newly diagnosed GPA and MPA patients (N=524)

GC-related infection is the leading cause of early mortality in GPA/MPA patients[2,3]

Cardiovascular disease is the primary cause of mortality >1 year after diagnosis[4]



Adapted from Flossmann et al. 2011, EUVAS longitudinal study data (1995–2002): from four randomised trials with newly diagnosed GPA and MPA patients (n=535)

Long-term GC use is associated with increased risk of infection and CV risk factors (diabetes) vs patients not receiving GCs[5]

AE, adverse event; ANCA, anti-neutrophil cytoplasmic antibody; EUVAS, European Vasculitis Study Group; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

1. Little MA, et al. Ann Rheum Dis 2010;69(6):1036–43. 2. Rutherford PA, et al. Poster SA-PO405 presented at the American Society of Nephrology, October 2018, San Diego USA. 3. Rutherford PA, Götte D. EMJ Nephrol 2020;8[Suppl 4]:2–16. 4. Flossmann et al. Ann Rheum Dis. 2011;70:488-94. 5. McGregor JG, et al. Clin J Am Nephrol 2012;7(2):240–7.

Avacopan mechanism of action

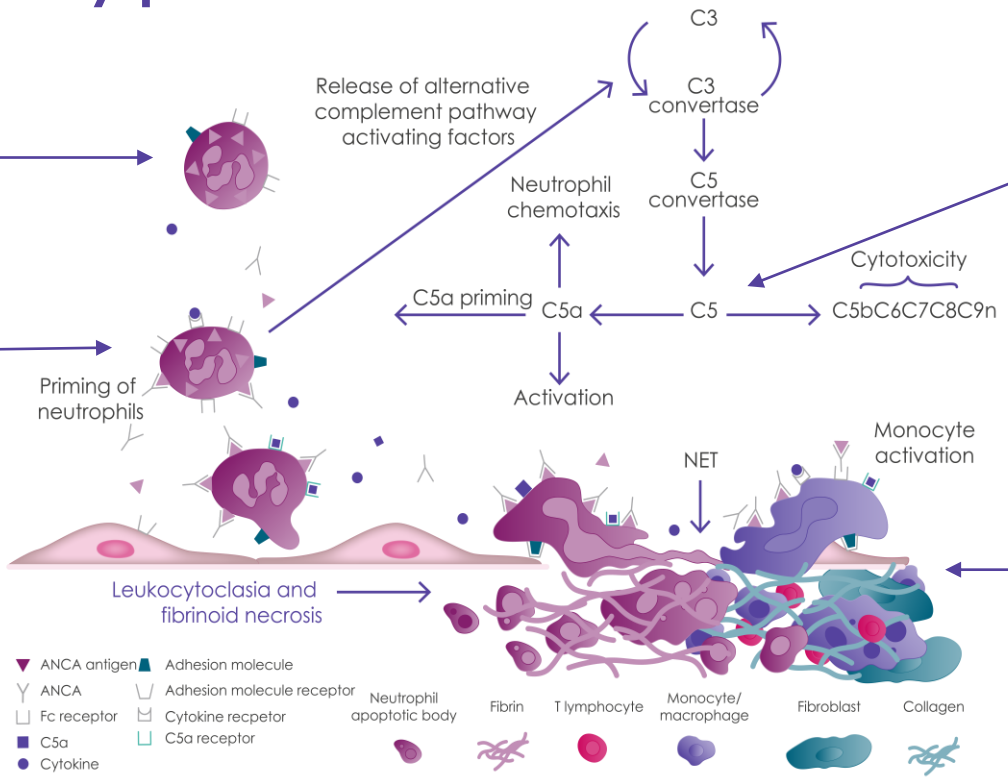
Note: avacopan has only been studied in patients with GPA/MPA

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

Interaction between neutrophils and C5a drives the inflammatory process in AAV[1–3]

1 **Loss of immune tolerance to ANCA antigens** and the development of ANCA[2,4]

2 Neutrophils are primed and **start to express ANCA antigens** (e.g. MPO and PR3) on their cell surface that bind to ANCA, resulting in neutrophil activation[1–4]



3 Activated neutrophils release a variety of inflammatory mediators, which damage tissues and also **activate the alternative complement pathway**, resulting in the formation of **C5a**[1,2]

4 Binding of **C5a to C5aR1 leads to the inflammatory cycle driving the disease**, creating a self-fuelling inflammatory amplification loop[5,6]

Diagram adapted from Jennette JC, Nachman PH. *Clin J Am Soc Nephrol* 2017

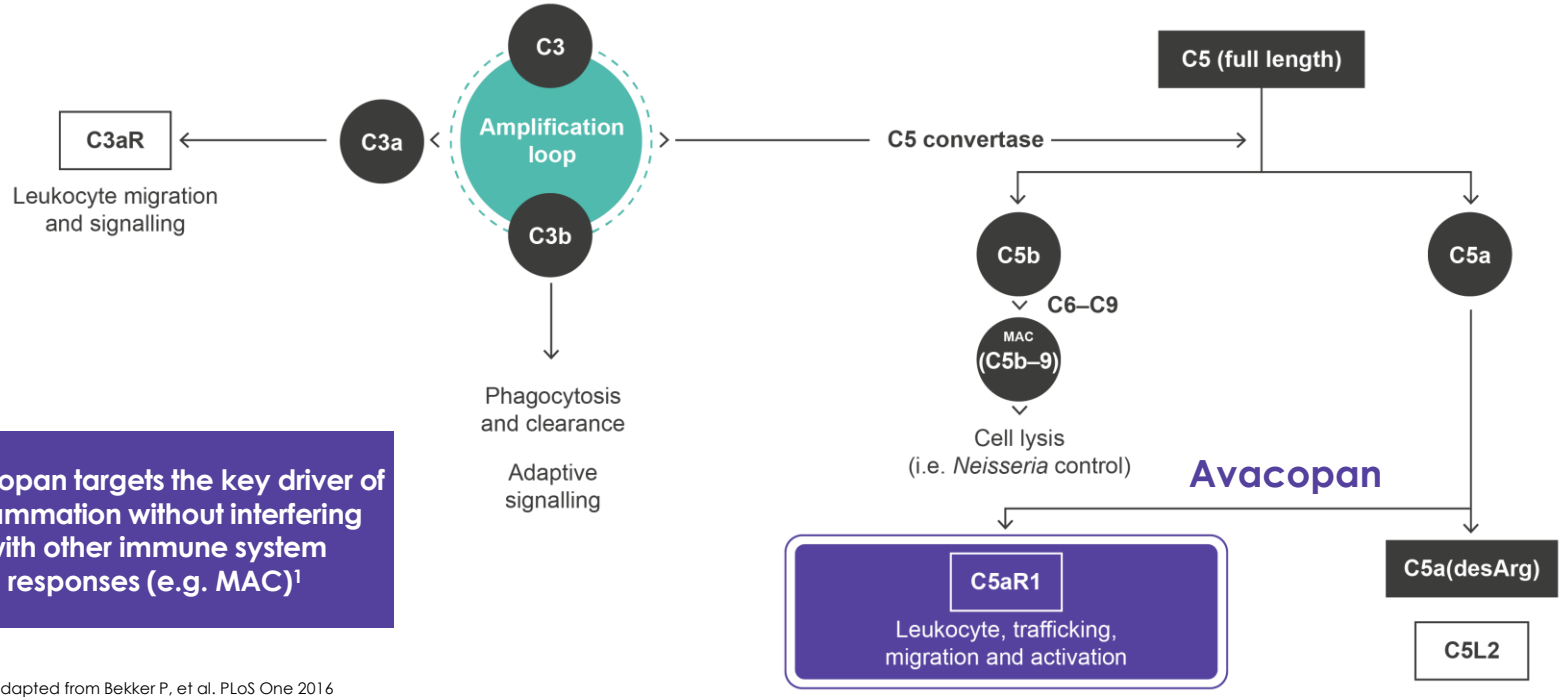
Complement system in AAV, here

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; C5a, complement component 5a; C5aR1, C5a receptor 1; MPO, myeloperoxidase; NET, neutrophil extracellular trap; PR3, proteinase 3.

1. Jennette JC, Nachman PH. Clin J Am Soc Nephrol 2017;12(10):1680–91. 2. Hutton HL, et al. Semin Nephrol 2017;37(5):418–35. 3. Al-Hussain T, et al. Adv Anat Pathol 2017;24(4):226–34. 4. von Borstel A, et al. Autoimmun Rev 2018;17(4):413–21. 5. Bekker P, et al. PLoS One 2016;11(10):e0164646. 6. Jennette JC, et al. Semin Nephrol 2013;33(6):557–64.

Avacopan selectively targets C5aR1 – the component of the immune system that drives vascular inflammation[1,2]

ALTERNATIVE COMPLEMENT PATHWAY



Avacopan targets the key driver of inflammation without interfering with other immune system responses (e.g. MAC)[1]

Diagram adapted from Bekker P, et al. PLoS One 2016

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; C5a, complement component 5a; C5aR1, C5a receptor 1; MAC, membrane attack complex.
1. Bekker P, et al. PLoS One 2016;11(10):e0164646. 2. Thurman JM, Holers VM. J Immunol 2006;176(3):1305–10.

Avacopan selectively blocks C5aR1 to inhibit the inflammatory amplification loop[1–5]

Avacopan reduces the pro-inflammatory effects of C5a including:[1-5]

- Neutrophil activation and migration
- Neutrophil adherence to sites of small blood vessel inflammation
- Vascular endothelial cell retraction and increased permeability

In a mouse model, avacopan was able to reduce C5a-mediated depletion of blood leukocytes[1]

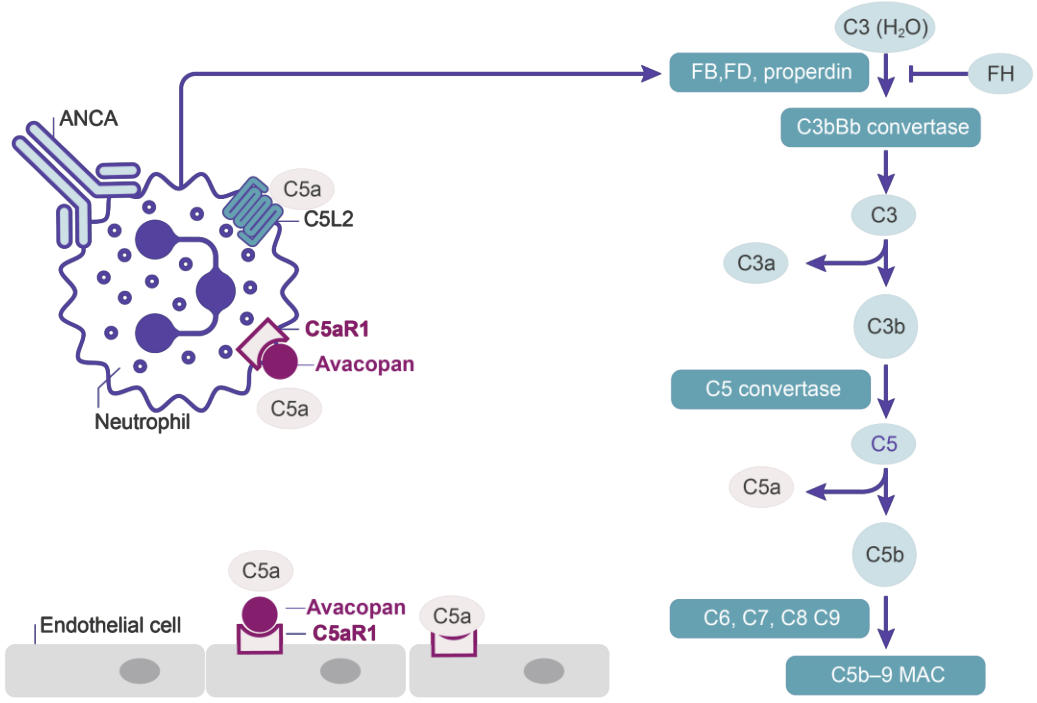
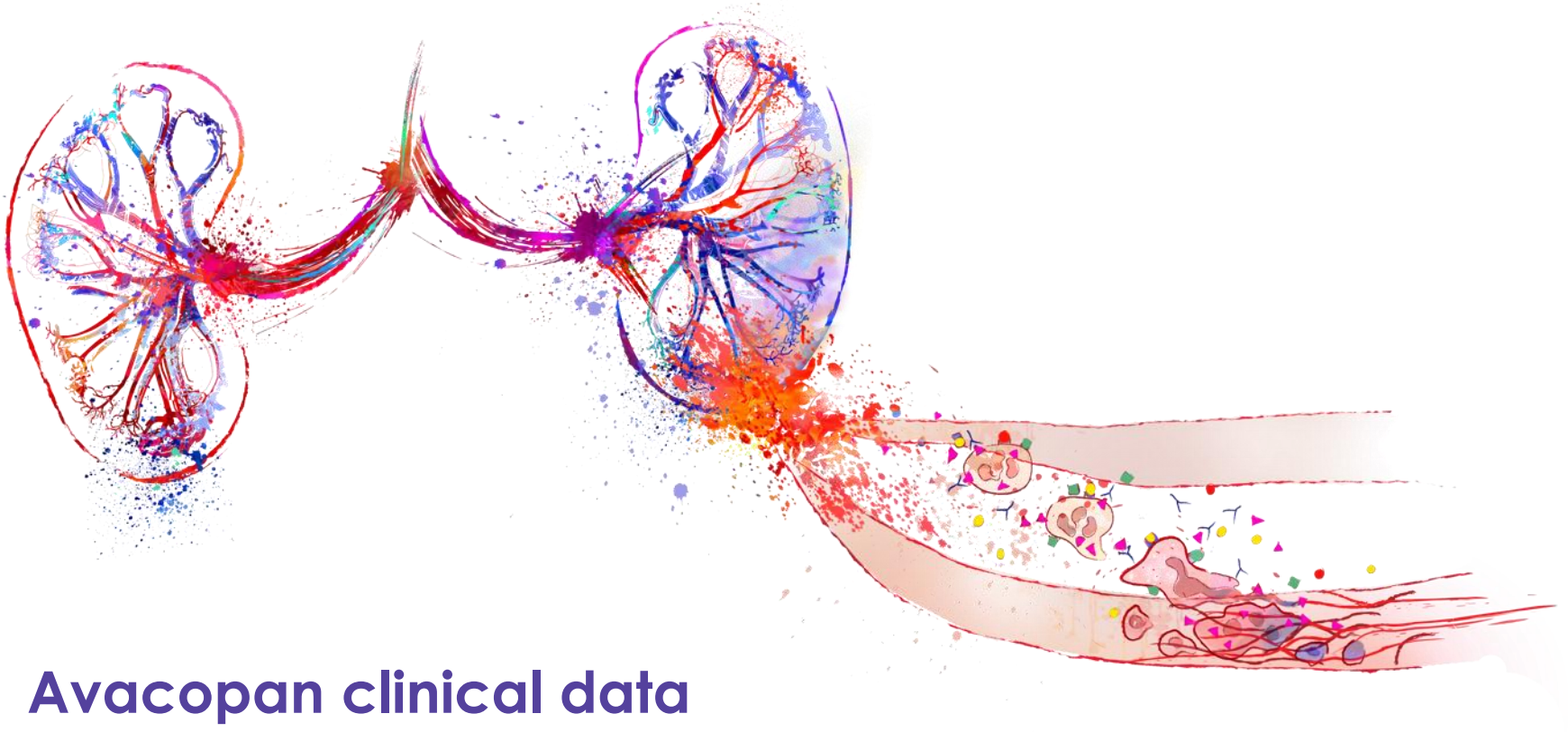


Diagram adapted from Kettritz E. *Nat Rev Nephrol* 2017.

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; C5a, complement component 5a; C5aR1, C5a receptor 1; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

1. Bekker P, et al. *PLoS One* 2016;11(10):e0164646. 2. Thurman JM, Holers VM. *J Immunol* 2006;176(3):1305–10. 3. Kettritz E. *Nat Rev Nephrol* 2017;13(8):448–50. 4. Nakano H, et al. *J Immunol* 2015;194(8):3808–19.
5. Vifor 2022. Tavneos (avacopan) SmPC. Available at https://www.ema.europa.eu/en/documents/product-information/tavneos-epar-product-information_en.pdf (accessed February 2023).

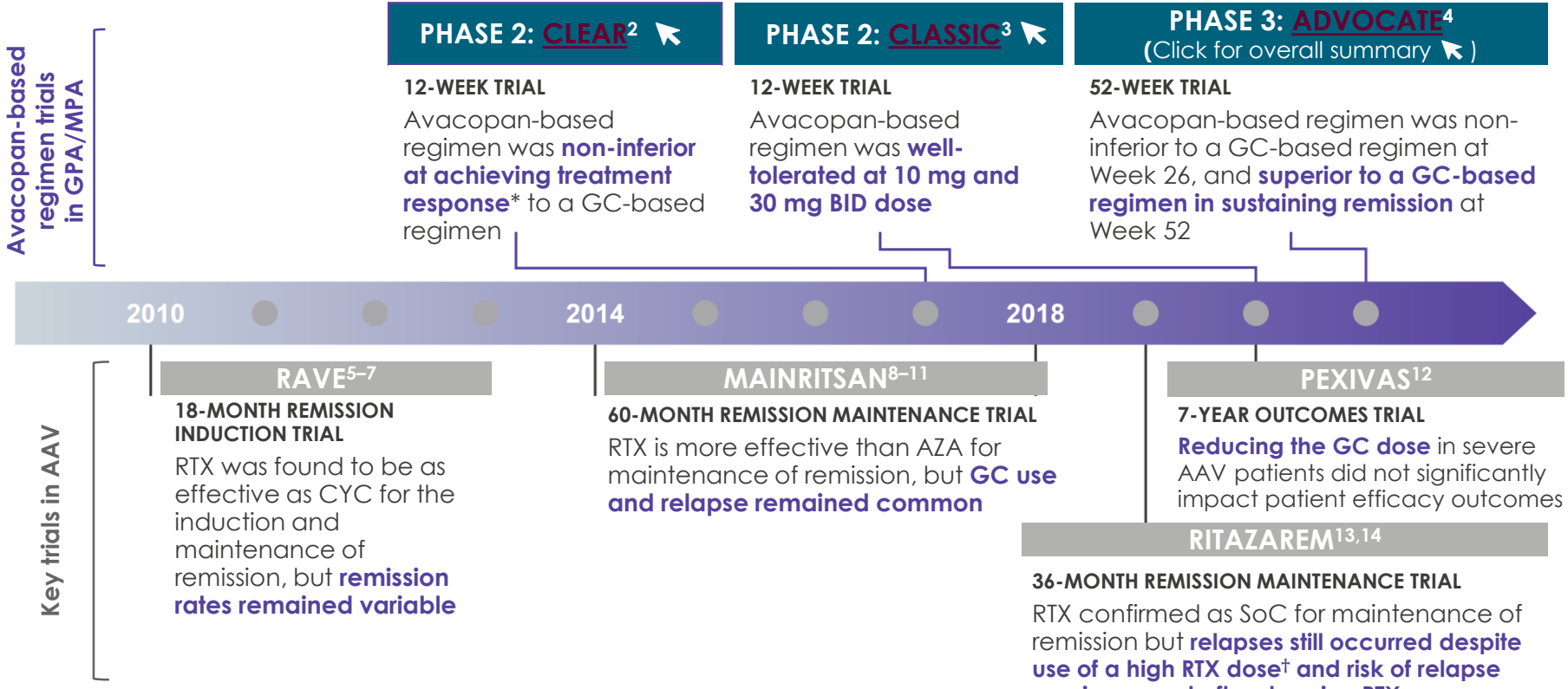


Avacopan clinical data

Note: avacopan has only been studied in patients with GPA/MPA

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

Key studies for AAV management showed an avacopan-based regimen has potential to meet the unmet need in AAV[1–14]



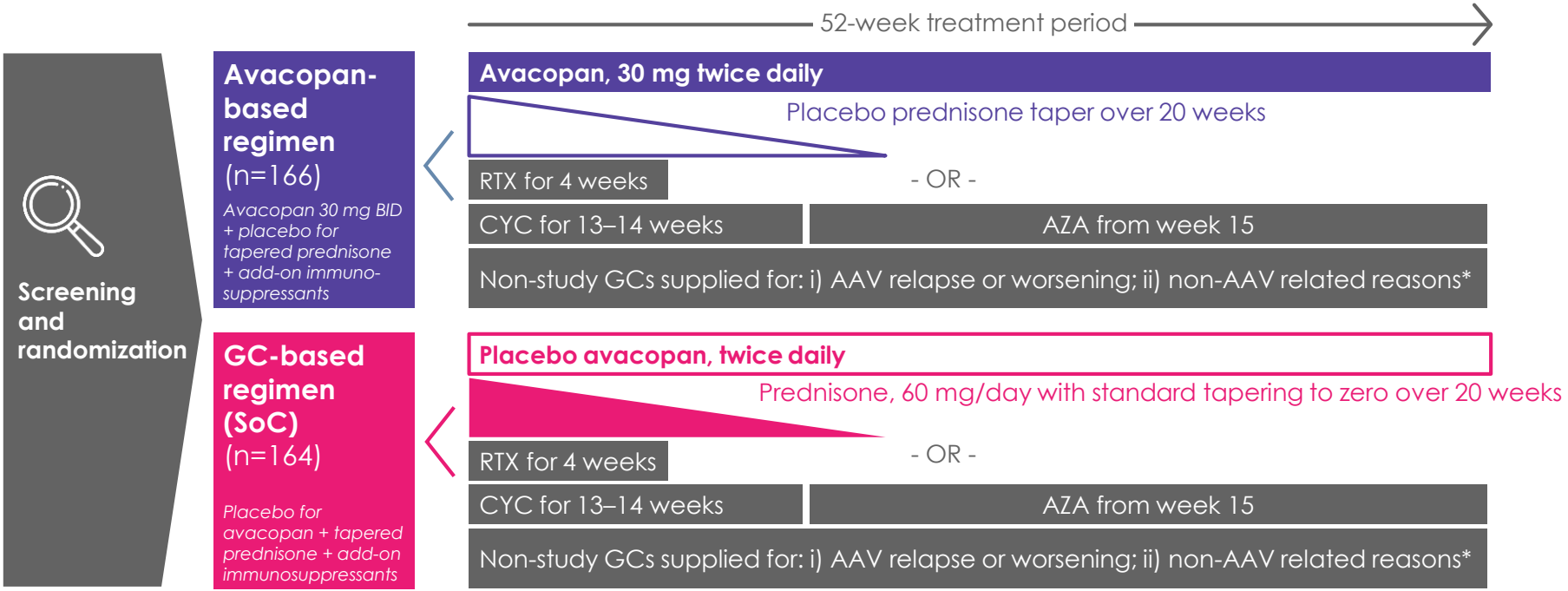
*BVAS decrease of at least 50% from baseline and no worsening in any body system. †IV RTX dose higher than previously studied: 1000 mg every 4 months for 5 doses through month 20.

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; AZA, azathioprine; BID, bis in die (twice a day); CYC, cyclophosphamide; GC, glucocorticoid; RTX, rituximab; SoC, standard of care.

1. Bekker P, et al. *PLoS One* 2016;11(10):e0164646. 2. Jayne DRW, et al. *J Am Soc Nephrol* 2017;28(9):2756–67. 3. Merkel PA, et al. *ACR Open Rheumatol* 2020;2(11):662–7. 4. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 5. Stone JH, et al. *N Engl J Med* 2010;363(3):221–32. 6. Specks U, et al. *N Engl J Med* 2013;369(5):417–27. 7. Miloslavsky EM, et al. *Arthritis Rheum* 2015;67(6):1629–36. 8. Guillevin L, et al. *N Engl J Med* 2014;371(19):1771–80. 9. Terrier B, et al. *Ann Rheum Dis* 2018;77(8):1150–6. 10. Terrier B, et al. *Ann Rheum Dis* 2018;77(8): 1150–6. [Supplementary appendix]. 11. Guillevin L, et al. *N Engl J Med* 2014;371(19):1771–80. [Supplementary appendix].12. Walsh M, et al. *N Eng J Med* 2020;382(7):622-31. 13. Smith RM, et al. *Ann Rheum Dis* 2020;79(9):1243–96.14. Smith RM, et al. *Ann Rheum Dis* 2023;82(7):937–44.

ADVOCATE study design: evaluating the ability of an avacopan-based regimen to achieve and sustain remission[1,2]

Landmark ADVOCATE trial compared the ability of an avacopan-based regimen to induce and sustain remission in AAV (GPA/MPA) patients against a GC-based regimen, while assessing its GC-sparing benefits and impact upon organ preservation



*Such as replacement of GCs for adrenal insufficiency.
AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; AZA, azathioprine; CYC, cyclophosphamide; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RTX, rituximab; SoC, standard of care.

1. Merkel PA, et al. *JMIR Res Protoc* 2020;9(4):e16664. doi: 10.2196/16664. 2 Jayne D, et al. *N Engl J Med* 2021;384(7):599–609.

Reduced dose regimen used in ADVOCATE GC-based arm, here

ADVOCATE: comparing the ability of an avacopan-based regimen to achieve remission in AAV (GPA/MPA) vs a GC-based regimen[1,2]

PATIENT POPULATION

Randomisation:[2]

- Avacopan-based regimen **(n=166)**
- GC-based regimen **(n=164)**

Major inclusion criteria:[1]

- Age ≥12 years
- Newly diagnosed or relapsing GPA/MPA
- PR3+ or MPO+
- Active disease assessed by BVAS
- eGFR ≥15 mL/min/1.73 m^2

81% of patients had renal vasculitis[2]

Conducted in **198 study locations across 20 countries**[3]

TRIAL ENDPOINTS[1,2]

PRIMARY

- **Achievement of remission** at Week 26 (BVAS 0 and no GC use in prior 4 weeks)
- **Sustained remission** at both Week 26 and Week 52 (BVAS 0 and no GC use in the 4 weeks before Week 52)

SECONDARY

- **Safety:** adverse events, physical exam, vital signs, serum chemistry, haematology, urinalysis, and electrocardiogram
- **Change in GC-related toxicity** during first 26 weeks according to the GTI
- **Rapidity of response** as measured by BVAS at Week 4
- **Change in damage** over 52 weeks as measured by VDI
- **Change in HR-QoL scores** over 52 weeks as measured by SF-36v2 and EuroQoL-5D-5L
- In patients with renal disease at baseline, **change over 52 weeks in eGFR, UACR, and MCP-1:creatinine ratio**
- **Proportion of patients and time to relapse** from previous BVAS=0 at Week 26

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; BVAS, Birmingham Vasculitis Activity Score; eGFR, estimated glomerular filtration rate; EuroQoL-5D-5L, EuroQol 5-dimension 5-level; GTI, Glucocorticoid Toxicity Index; HR-QoL, health-related quality of life; MCP-1, monocyte chemoattractant protein-1; SF-36, The Short Form 36 Health Survey Questionnaire; UACR, urine albumin-to-creatinine ratio; VDI, Vasculitis Damage Index.

1. Merkel PA, et al. *JMIR Res Protoc* 2020;9(4):e16664. doi: 10.2196/16664. 2 Jayne D, et al. *N Engl J Med* 2021;384(7):599–609.
3. U.S. National Library of Medicine (NIH). NCT02994927 (ADVOCATE). Available at: https://clinicaltrials.gov/ct2/show/NCT02994927. Date accessed November 2021.

ADVOCATE: Demographic and clinical characteristics of patients at baseline were similar in both treatment groups (1/2)[1]

Characteristic	Avacopan-based regimen (n=166)	GC-based regimen (n=164)
Age – years	61.2±14.6	60.5±14.5
Sex – no. (%)		
Male	98 (59.0)	88 (53.7)
Female	68 (41.0)	76 (46.3)
Race – no. (%)		
White	138 (83.1)	140 (85.4)
Asian	17 (10.2)	15 (9.1)
Black	3 (1.8)	2 (1.2)
Other	8 (4.8)	7 (4.3)
Body-mass index	26.7±6.0	26.8±5.2
Median duration of AAV (range) – months	0.23 (0–362.3)	0.25 (0–212.5)
Vasculitis disease status – no. (%)		
Newly diagnosed	115 (69.3)	114 (69.5)
Relapsed	51 (30.7)	50 (30.5)
ANCA status – no. (%)		
PR3+	72 (43.4)	70 (42.7)
MPO+	94 (56.6)	94 (57.3)

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; GC, glucocorticoid; MPO, antimyeloperoxidase; no., number; PR3, antiproteinase 3.

1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609.

ADVOCATE: Demographic and clinical characteristics of patients at baseline were similar in both treatment groups (2/2)[1]

Characteristic	Avacopan-based regimen (n=166)	GC-based regimen (n=164)
Type of vasculitis – no. (%)[1]		
GPA	91 (54.8)	90 (54.9)
MPA	75 (45.2)	74 (45.1)
BVAS score[1]	16.3±5.9	16.2±5.7
VDI[1]	0.7±1.5	0.7±1.4
Immunosuppressant induction treatment – no. (%)[1]		
Intravenous rituximab	107 (64.5)	107 (65.2)
Intravenous cyclophosphamide	51 (30.7)	51 (31.1)
Oral cyclophosphamide	8 (4.8)	6 (3.7)
Renal involvement – no. (%)*[1]	134 (80.7)	134 (81.7)
Glucocorticoid use during screening period		
Use of any glucocorticoids – no. (%)[1]	125 (75.3)	135 (82.3)
Total prednisone-equivalent dose, mg – mean±SD†[2]	907.3±1145.9	978.0±1157.5
Previous immunosuppressant use – no. (%)‡[1]		
Cyclophosphamide	4 (2.4)	2 (1.2)
Rituximab	1 (0.6)	4 (2.4)

*Organ involvement based on BVAS. †The prednisone-equivalent dose includes both intravenous and oral use of GCs. ‡Shown are patients who used immunosuppressants within the previous 12 months.
BVAS, Birmingham Vasculitis Activity Score; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; no., number; VDI, Vasculitis Damage Index.
1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Vifor data on file 2023.

Avacopan-based regimen was non inferior to GC-based regimen at 26 weeks in achieving remission and superior at 52 weeks in sustaining remission[1]

WEEK 26

Avacopan-based regimen (n=166)

GC-based regimen (n=164)

p<0.001 for non-inferiority

Graph adapted from Jayne D, et al. *N Engl J Med* 2021

WEEK 52

Avacopan-based regimen (n=166)

GC-based regimen (n=164)

p=0.007 for superiority

Graph adapted from Jayne D, et al. *N Engl J Med* 2021

Remission and relapse with low-dose GC and avacopan regimens, here

Remission rates across prespecified subgroups, here

Outcomes in patients with non-major AAV manifestations at baseline, here

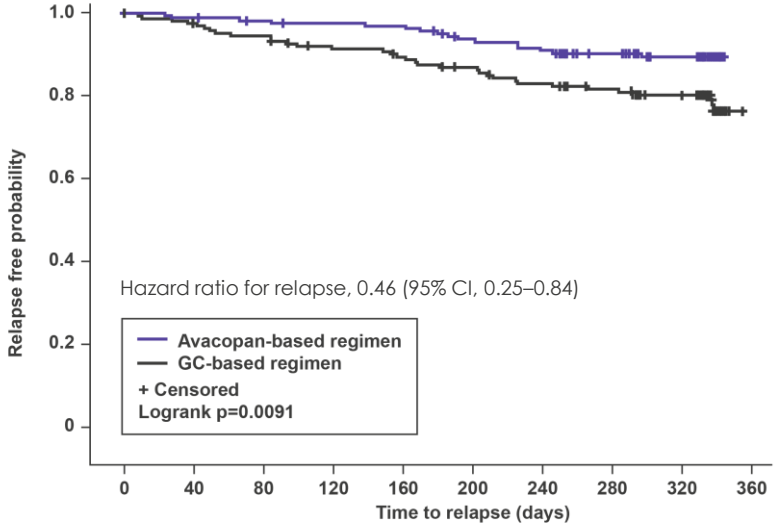
Outcomes in patients receiving background rituximab, here

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody.

1. Jayne D, et al. N Engl J Med 2021;384(7):599–609.

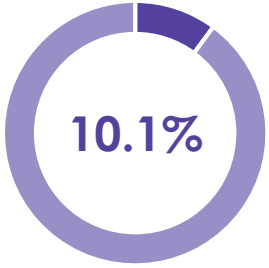
Patients treated with an avacopan-based regimen experienced fewer relapses vs GC-based regimen[1]

54% RELATIVE REDUCTION IN RELAPSE RISK OVER 52 WEEKS[1,2]



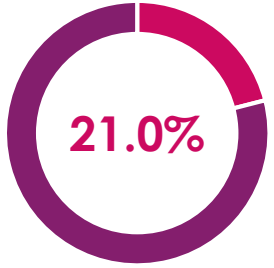
Graph adapted from Jayne D, et al. *N Engl J Med* 2021

Absolute **risk of relapse** over 52 weeks of treatment:[1]



Avacopan-based regimen
(n/N=16/158)

VS



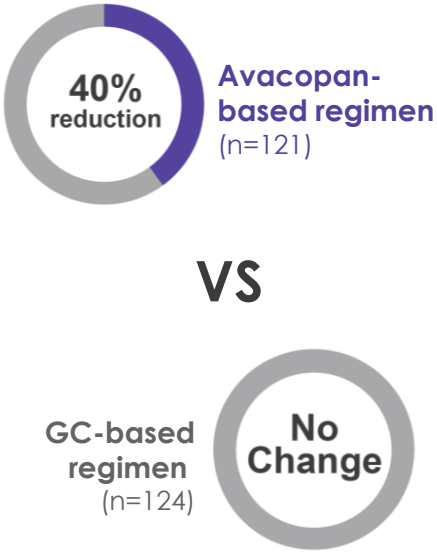
GC-based regimen
(n/N=33/157)

Relapse rates during the 8 weeks following avacopan-based regimen cessation in ADVOCATE, here

GC, glucocorticoid.
1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Vifor Pharma (2020). Data on file.

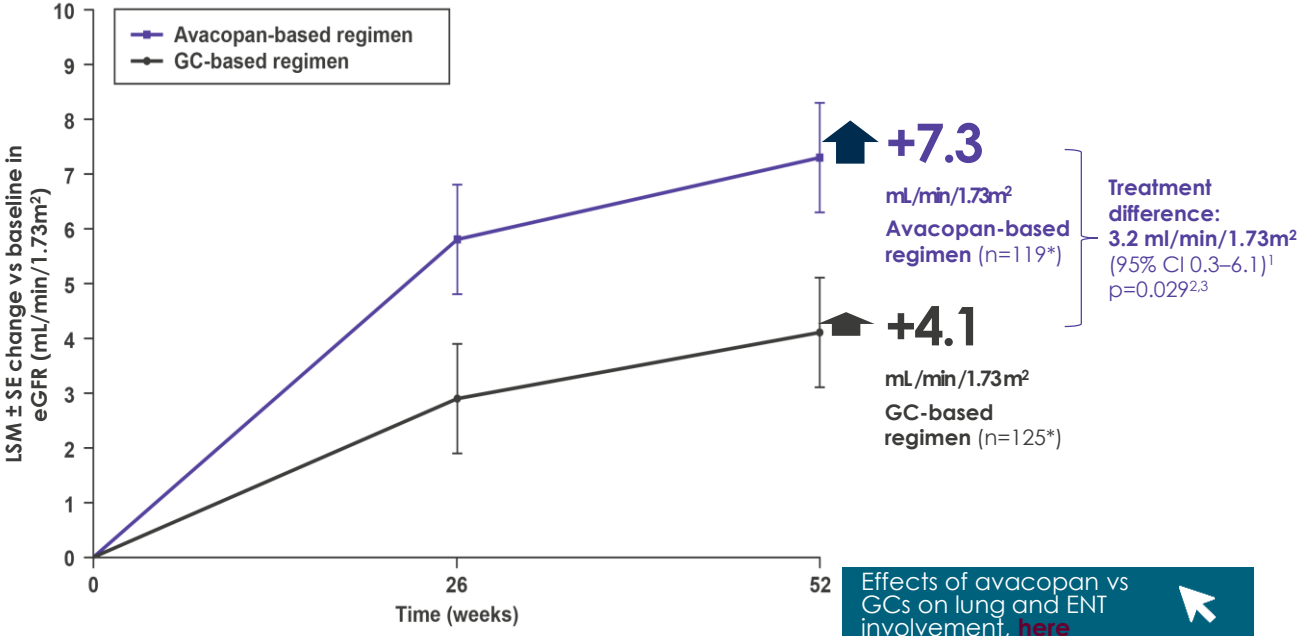
Avacopan-based regimen resulted in greater improvements in renal function VS GC-based regimen[1–3]

DECREASED UACR AT WEEK 4[1]



Baseline to Week 4 (p<0.0001)
No difference in UACR was observed across the treatment groups at Week 52

IMPROVEMENTS IN eGFR TO WEEK 52[1]



Mean eGFR at baseline: 44.6 and 45.6 mL/min/1.73 m² in avacopan-based and GC-based regimen groups, respectively[1]

Effects of avacopan vs GCs on lung and ENT involvement, here

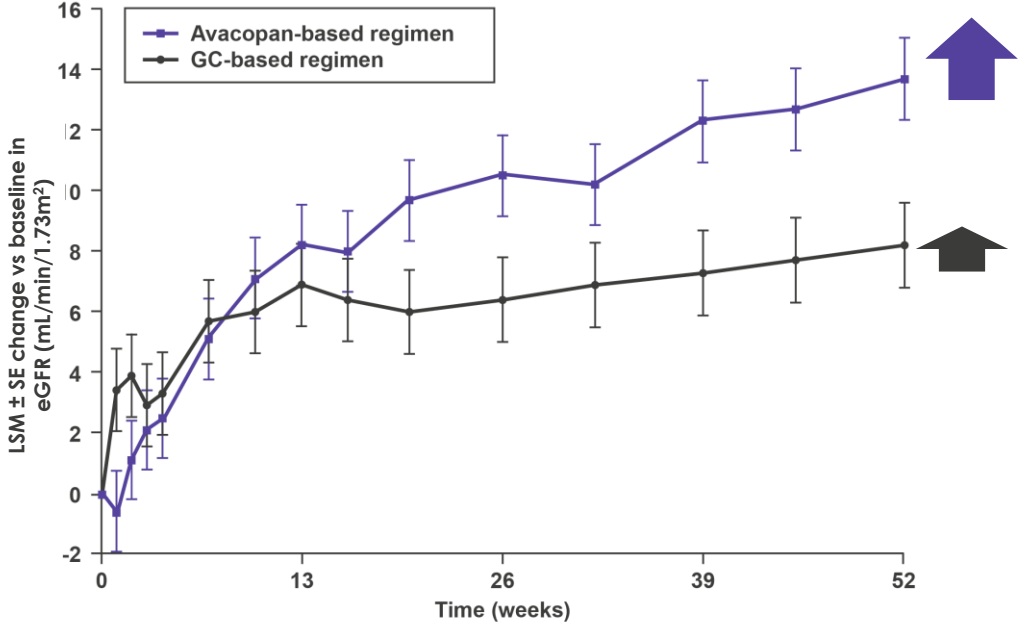
Post hoc analysis of UACR, here

*Patient numbers shown are for Week 52 only; patient numbers in avacopan-based and GC-based regimens at baseline were 131 and 134, respectively, and at week 24 were 121 and 127, respectively.
eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio.

1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Jayne D, et al. *Nephrol Dial Transplant* 2020;35(Suppl 3 [LB003]). 3. Cortazar FB, et al. *Kidney Int Rep* 2023;8(4):860–70.

Greatest improvement in eGFR observed in patients with lowest renal function at baseline[1,2]

IMPROVED eGFR IN STAGE 4* CKD PATIENTS AT WEEK 52



+13.7 mL/min/1.73m²
Avacopan-based regimen

+8.2 mL /min /1.73 m²
GC-based regimen

Treatment difference:
5.6 ml/min/1.73m²
(95% CI 1.7–9.5)[1]
p=0.005[3]

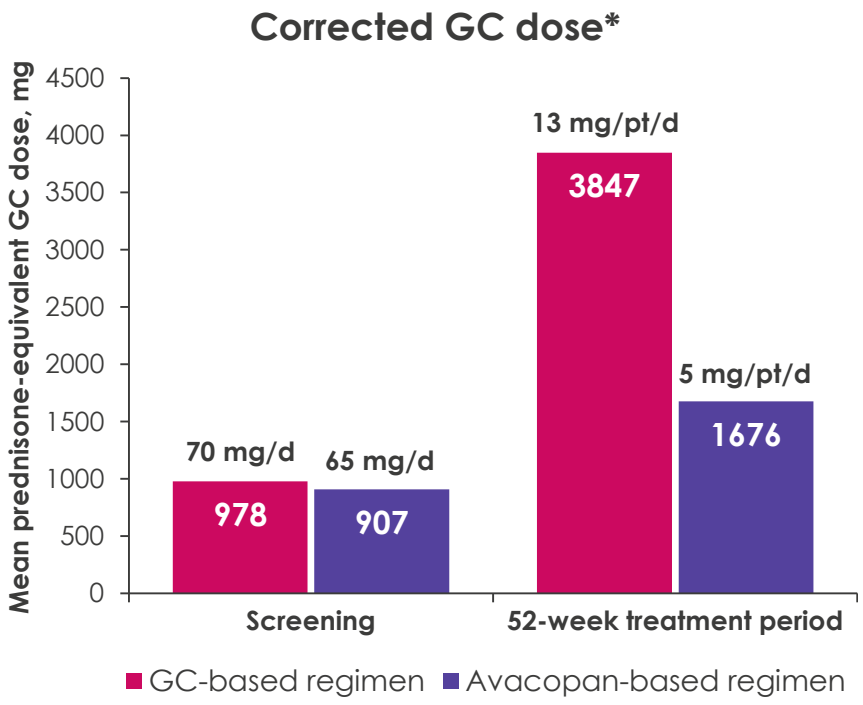
LSM eGFR improvement for patients with stage 4 kidney disease (<30 mL/min/1.73 m²)

Graph adapted from Jayne D, et al. *N Engl J Med* 2021 [Suppl Appendix].

*eGFR <30 mL/min/1.73m².
Mean baseline eGFR was 21.6 ± 0.6 and 21.1 mL/min/1.73 m2 for the GC-basaed and avacopan –basded regimens, respectively
CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; LSM, least square mean; SE, standard error.
1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. [Suppl Appendix]. 3. Cortazar FB, et al. *Kidney Int Rep* 2023;8(4):860–70.

Renal recovery in ADVOCATE patients with low eGFR, here

Avacopan-based regimen lowered overall GC dose vs GC-based regimen in the ADVOCATE trial



≈ GC doses during screening were similar in the two treatment groups

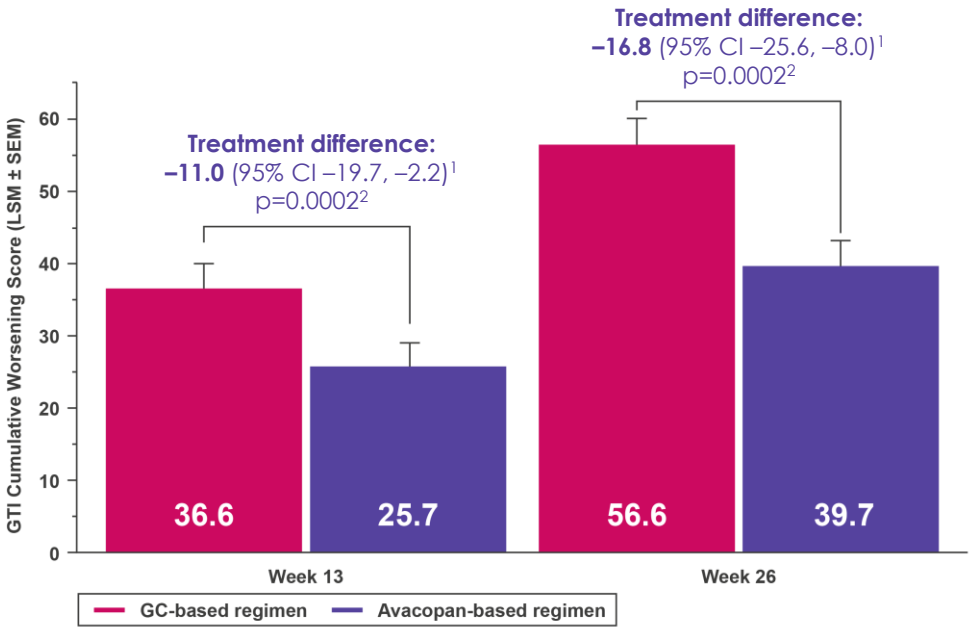
56% lower overall GC dose with avacopan-based regimen than GC-based regimen in the 52-week treatment period

Non-study supplied GC use and data correction, here

*Prednisone-equivalent dose includes both intravenous and oral use of GCs.
d, day; GC, glucocorticoid; pt, patient.
CSL Vifor data on file, 2023 (*corrigendum to Jayne DRW, et al. N Engl J Med 2021;384:599–609 pending as of 22 June 2023*); Tavneos SmPC July 2023.

Significant reduction in GC toxicity with avacopan-based regimen compared with GC-based regimen (1/2)[1]

REDUCED GTI CUMULATIVE WORSENING SCORE (CWS)[1]



- **16.8 reduction** in GTI-CWS (cumulative toxicity from baseline) with avacopan-based regimen vs GC-based regimen at Week 26 (95% CI –25.6 to –8.0)[1]

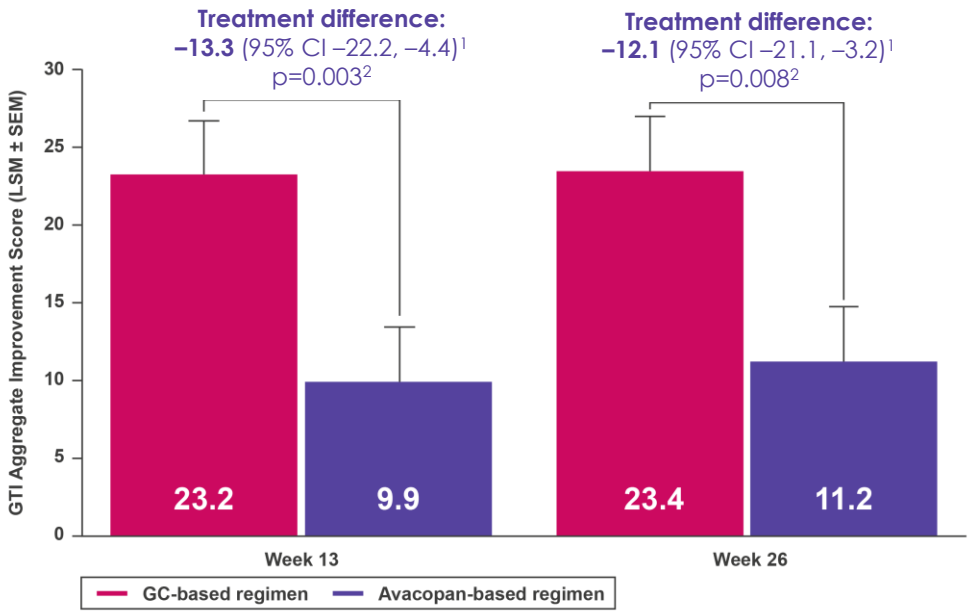
Changes in GTI score of >10 points have been estimated to represent a clinically meaningful change in GC toxicity*[3]

Reduced GTI CWS demonstrated reduction in GC-toxicity with avacopan- vs GC-based regimen[1]

*Smallest change likely to reflect a true difference as opposed to a measurement error of the effect.
CI, confidence interval; GC, glucocorticoid; GTI, glucocorticoid toxicity index; LSM, least-squares mean; SEM, standard error of the mean.
1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Vifor Pharma (2020). Data on file. 3. Stone JH, et al. *Semin Arthritis Rheum* 2022;55:152010.

Significant reduction in GC toxicity with avacopan-based regimen compared with GC-based regimen (2/2)[1]

REDUCED GTI AGGREGATE IMPROVEMENT SCORE (AIS)



- **12.1 reduction** in GTI AIS (present toxicity vs baseline) with avacopan-based regimen vs GC-based regimen at Week 26 (95% CI, –21.1 to –3.2)[1]

Changes in GTI score of >10 points have been estimated to represent a clinically meaningful change in GC toxicity[3]*

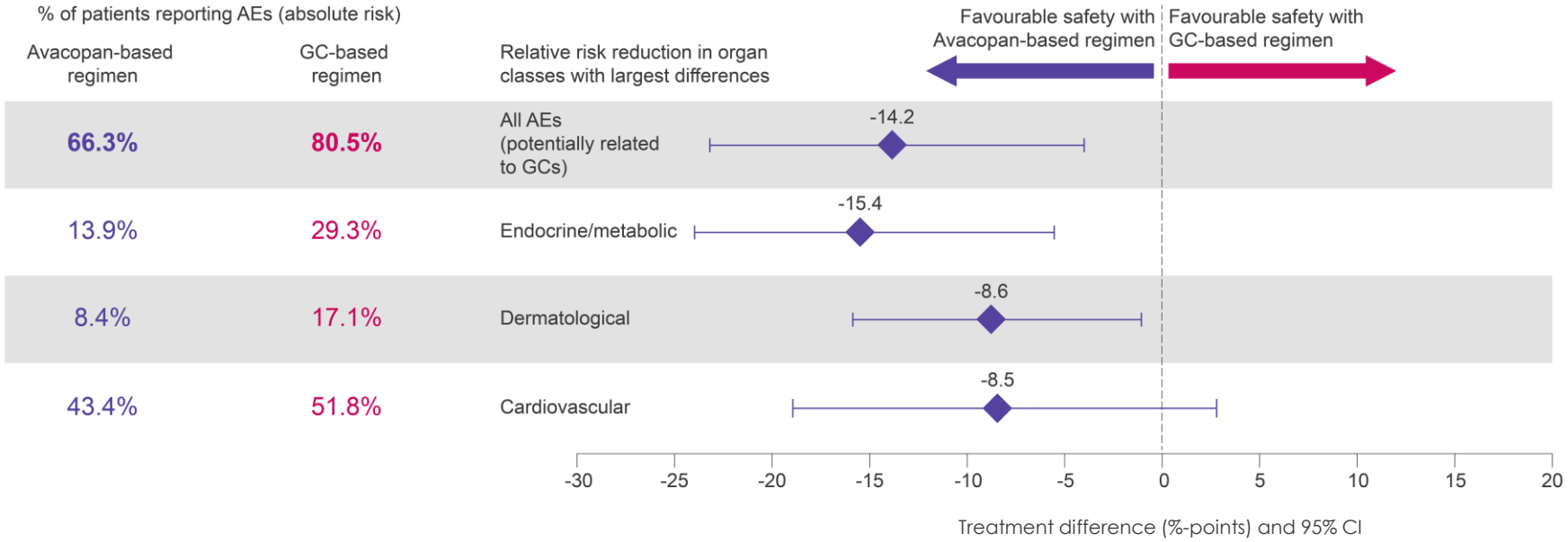
GTI subdomain results in ADVOCATE, here

Reduced GTI AIS demonstrated reduction in GC-toxicity with avacopan- vs GC-based regimen[1]

*Smallest change likely to reflect a true difference as opposed to a measurement error of the effect.
CI, confidence interval; GC, glucocorticoid; GTI, glucocorticoid toxicity index; LSM, least-squares mean; SEM, standard error of the mean.
1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Vifor Pharma (2020). Data on file. 3. Stone JH, et al. *Semin Arthritis Rheum* 2022;55:152010.

Reduction in GC-related adverse events with avacopan-based regimen compared with GC-based regimen[1]

LOWER FREQUENCY OF GC-RELATED AEs IN AVACOPAN-BASED REGIMEN[1,2]



AE, adverse events; CI, confidence interval; GC, glucocorticoid.

1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609.
2. De Gomma E et al. Glucocorticoid Use and Related Adverse Events in ADVOCATE Trial of Avacopan in ANCA-Associated Vasculitis. Abstract 1078, presented at: ACR 2022, 10–14 November 2022, Philadelphia, PA, USA.

Overall safety profile of an avacopan-based regimen appeared favourable in patients with GPA/MPA at 52 weeks

Overall subject incidence of SAEs was consistent with previous AAV trials (45.1% GC-based regimen; 42.2% avacopan-based regimen)

	Avacopan-based regimen (n=166)	GC-based regimen (n=164)
Treatment-emergent adverse events (TEAEs)		
Number of any TEAEs	1779	2139
Subject incidence (%) of TEAEs	164 (98.8)	161 (98.2)
Serious adverse events (SAEs)		
Number of SAEs	116	166
Subject incidence (%) of SAEs	70 (42.2)	74 (45.1)
Subjects with any life-threatening adverse event	8 (4.8)	14 (8.5)
Deaths		
Total number of deaths	2 (1.2)	4 (2.4)
Infection		
Number of serious infection events	25	31
Subjects with any adverse event potentially related to glucocorticoids		
Investigators blinded assessment	110 (66.3)	132 (80.5)

Table adapted from Jayne D, et al. *N Engl J Med* 2021

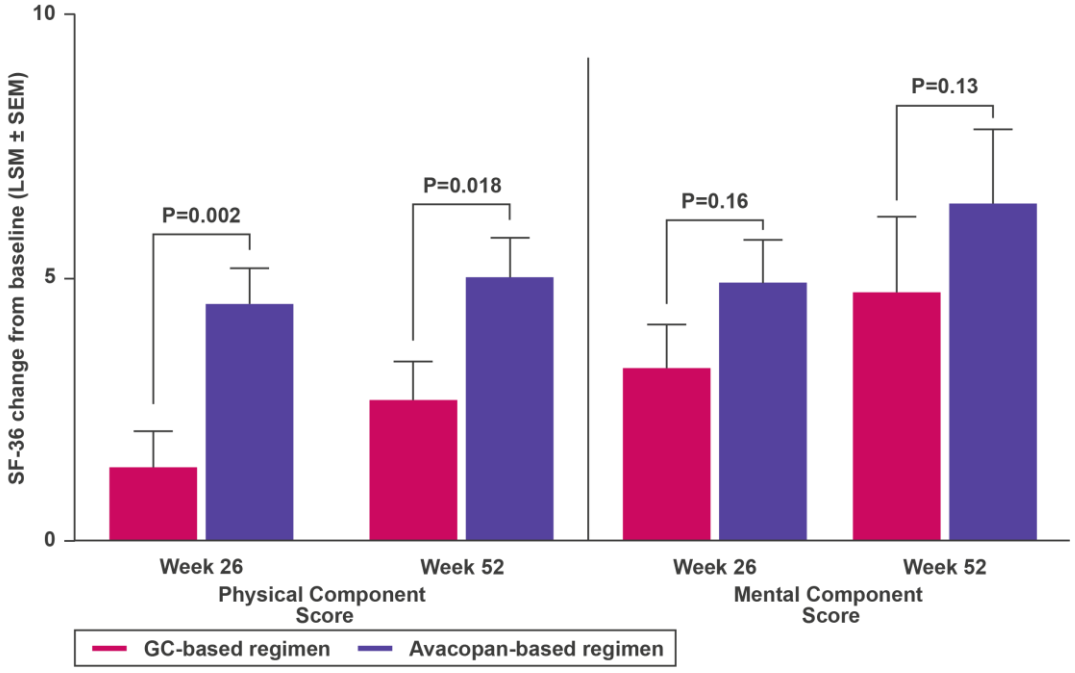
AAV, ANCA-associated vasculitis; AE, adverse events; ANCA, anti-neutrophil cytoplasmic antibody; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; SAEs, serious averse events; TEAEs, treatment-emergent adverse events.

1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609.

Avacopan safety data, here

Avacopan-based regimen improved all domains of quality of life[1–3]

IMPROVED PHYSICAL AND MENTAL HEALTH



Graph adapted from Jayne D, et al. *N Engl J Med* 2021

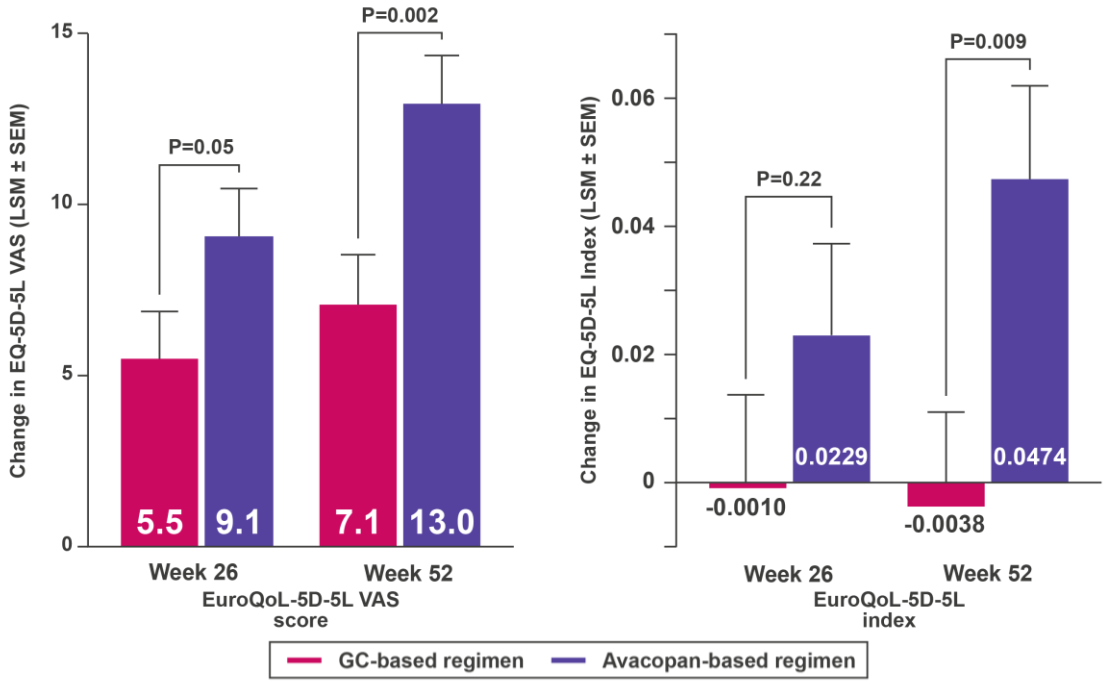
- Greater improvement shown in physical component score and in mental SF-36 domain scores in Avacopan-based regimen vs GC-based regimen at Week 52[1,2]
- Emotional and vitality domains drove the higher mental component score with the Avacopan-based regimen[2]

EQ-5D-5L, EuroQol 5-dimension 5-level; GCs, glucocorticoids; LSM, least-squares method; SEM, standard error of the mean; SF, social functioning; SF-36, Medical Outcomes Survey Short-Form 36; QoL, quality of life; VAS, visual analog scale.

1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. [Suppl Appendix]; 3. Strand V, et al. *Lancet Rheumatol* 2023;5(8):e451–60.

Avacopan-based regimen improved all domains of quality of life[1]

IMPROVED HEALTH-RELATED QoL[1–3]

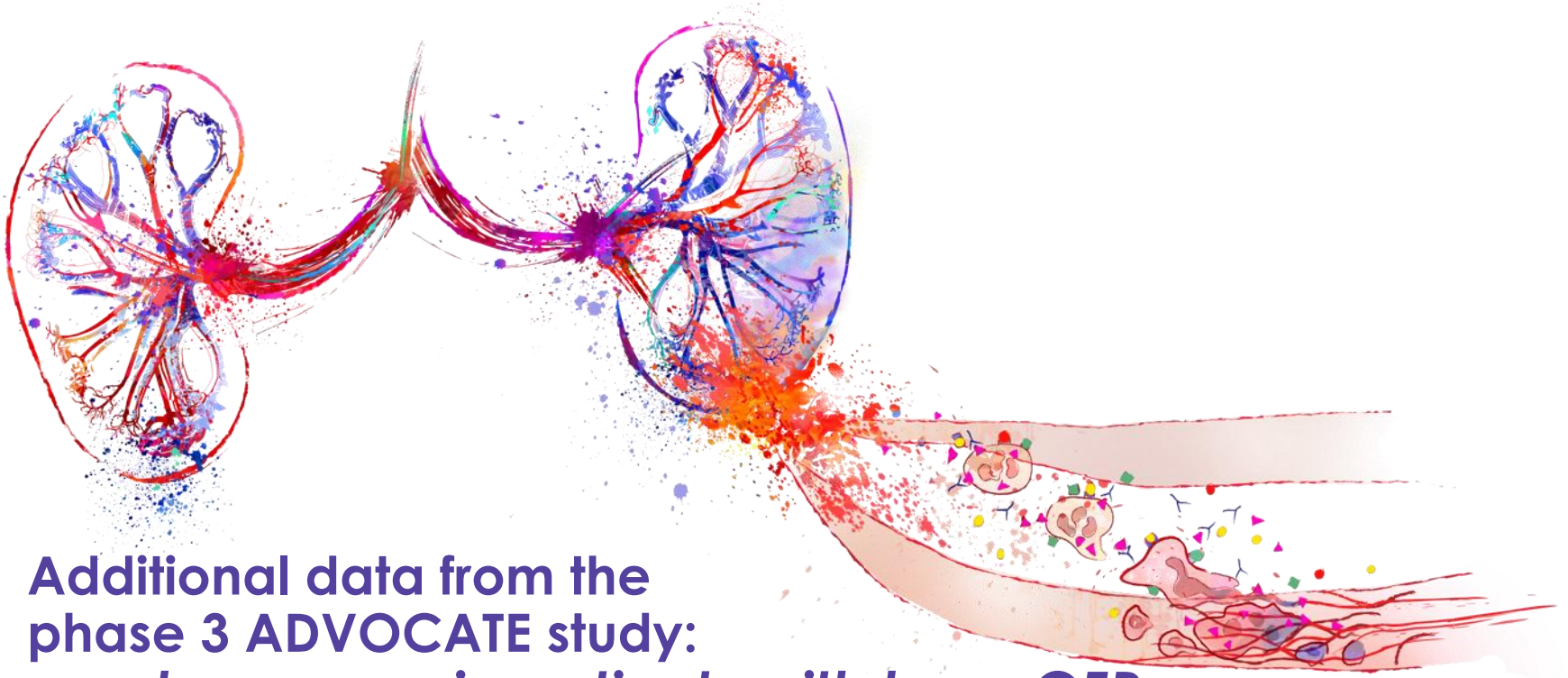


- Greater improvements demonstrated in health-related QoL (EuroQoL-5D-5L)[1,2]
- EuroQoL-5D-5L index measures health using five levels of severity to describe the patient's health state[4]
- Visual analog scale (VAS) rates patient's overall health that day on a scale of 0 –100 (with higher number indicating greater severity)[4]

Graph adapted from Jayne D, et al. *N Engl J Med* 2021

EQ-5D-5L, EuroQol 5-dimension 5-level; GCs, glucocorticoids; LSM, least-squares method; SEM, standard error of the mean; SF, social functioning; SF-36, Medical Outcomes Survey Short-Form 36; QoL, quality of life; VAS, visual analog scale.

1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. [Suppl Appendix]. 3. Vifor Pharma (2020). Data on file. 4. Herdman M, et al. *Qual Life Res* 2011;20(10):1727–36.



Additional data from the phase 3 ADVOCATE study: *renal recovery in patients with low eGFR*

Note: Avacopan has only been studied in GPA/MPA patients

Exploratory analyses suggest greater renal recovery with avacopan vs prednisone if baseline eGFR ≤20 mL/min/1.73 m²

ADVOCATE *post hoc* analyses of patients with baseline eGFR ≤20 mL/min/1.73 m²

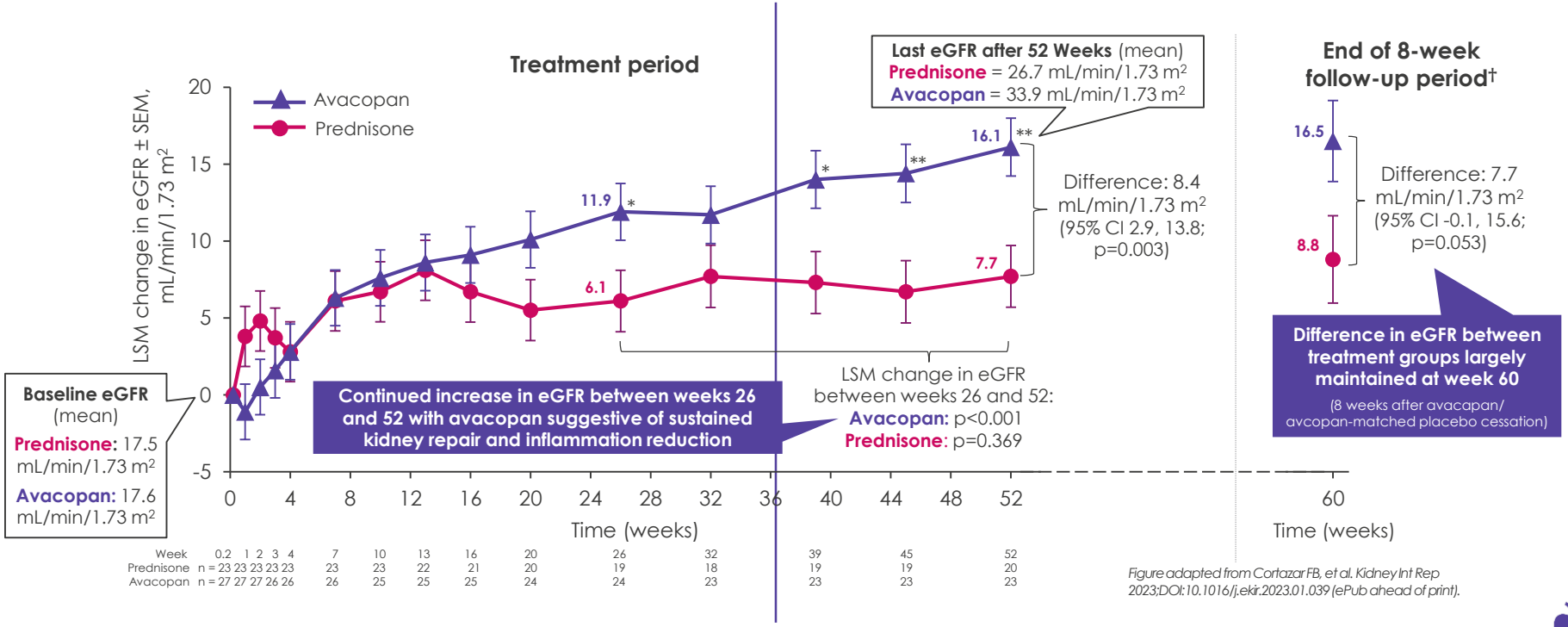
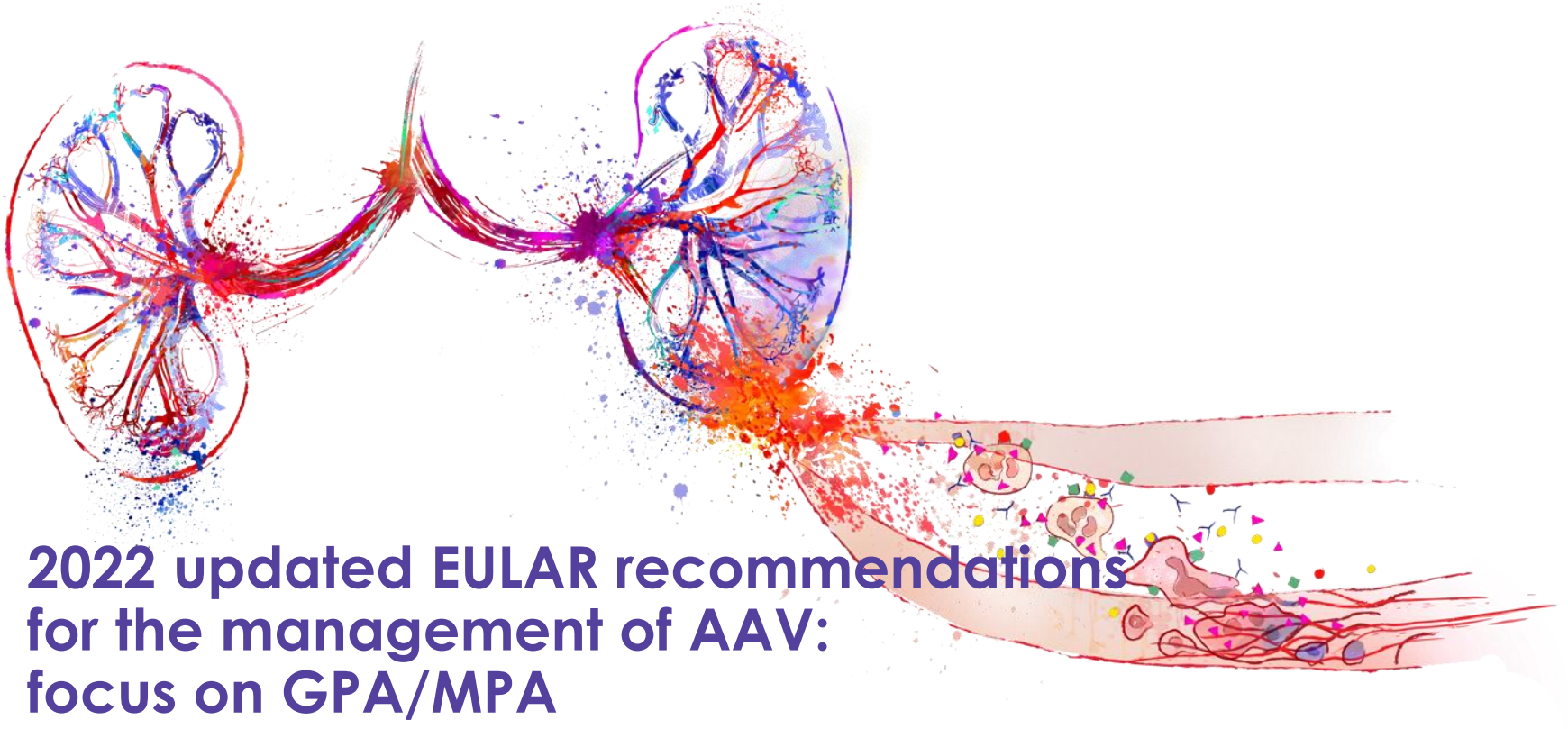


Figure adapted from Cortazar FB, et al. Kidney Int Rep 2023;DOI:10.1016/j.ekir.2023.01.039 (ePub ahead of print).

*p<0.05, **p<0.01 by mixed effects models for repeated measures with treatment group, study visit, and treatment-by-visit interaction as factors and baseline as covariate.
†Patients did not receive any avacopan or avacopan-matched placebo during this period.
eGFR, estimated glomerular filtration rate; GC, glucocorticoid; LSM, least squares mean; SEM, standard error of the mean.
Cortazar FB, et al. *Kidney Int Rep 2023;DOI:10.1016/j.ekir.2023.01.039 (ePub ahead of print).*

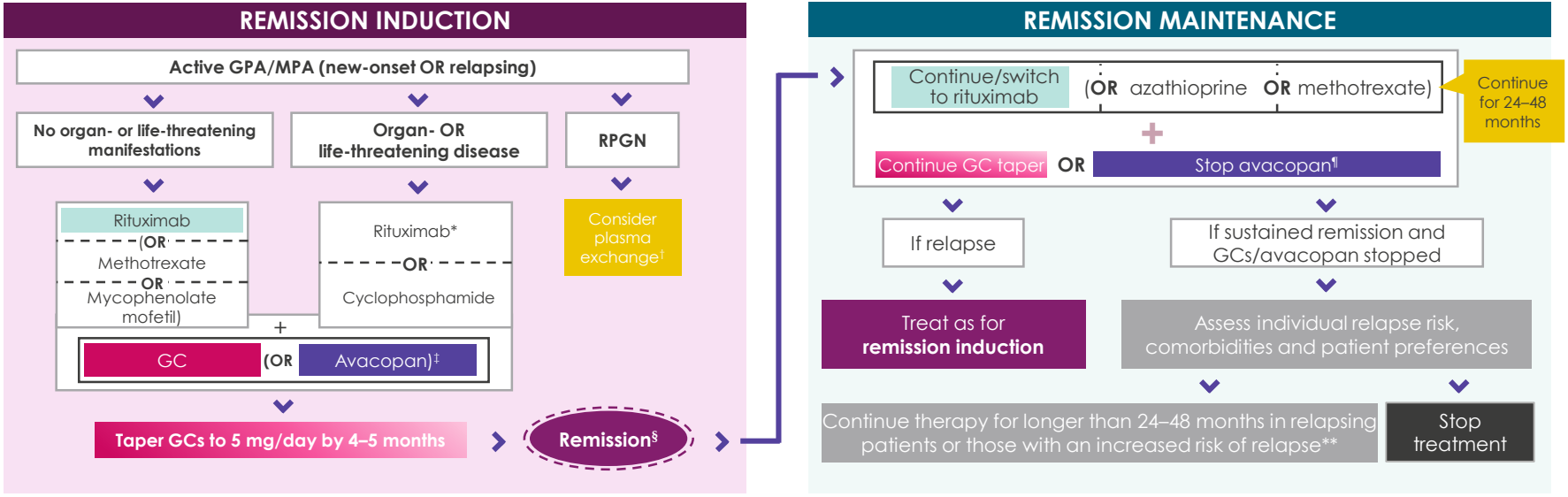
Return to core slides, here



2022 updated EULAR recommendations for the management of AAV: focus on GPA/MPA

Note: Avacopan has only been studied in patients with GPA/MPA

Overview of the 2022 updated EULAR recommendations for the management of GPA/MPA



Diagrams adapted from reference. Always refer to the product SmPCs for approved indications before prescribing.

*Rituximab preferred in relapsing disease. †In patients with serum creatinine >300 µmol/L due to active glomerulonephritis. ‡As part of a strategy to substantially reduce exposure to GCs. §If remission not achieved, consult an expert centre; if remission achieved, proceed to maintenance phase. ¶Stop avacopan after duration of treatment of 6–12 months (there are no data on use of avacopan beyond 1 year, so longer-term use cannot be recommended); in ADVOCATE, remission sustained until Week 52 (the second primary endpoint) was reached at a higher rate in the avacopan (65.7%) than GC (54.9%) treatment groups, suggesting that avacopan may have efficacy for maintenance of remission. **Longer duration of treatment should be balanced against patient preferences and risks of continuing immunosuppression.
EULAR, European League Against Rheumatism; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RPGN, rapidly progressive glomerular nephropathy.

1. Hellmich B, et al. Ann Rheum Dis 2023. doi: 10.1136/ard-2022-223764 [Epub ahead of print].

2022 addendum to the CanVasc Consensus Recommendations

Use of avacopan in patients with newly diagnosed/relapsing GPA/MPA treated with CYC or RTX

Consider tapering GCs

Aim to discontinue by end of week 4

For full CanVasc Consensus Recommendations, please refer to:
Mendel A, et al. J Rheumatol 2021;48:555–566

- **Category 1B, Strength B recommendations** based on evidence including the ADVOCATE clinical trial
- **Note:** avacopan should be used with caution in patients severe end organ manifestations (e.g. eGFR <15 ml/min/1.73 m^2) and alveolar hemorrhage requiring mechanical ventilation†

*Guidelines state that data informing on the benefits and safety of avacopan past 52 weeks is limited and further long-term, real-world data would be valuable.
†These patients were excluded from the CLEAR, CLASSIC and ADVOCATE clinical trials.
AAV, ANCA-associated vasculitis; CanVasc, Canadian Vasculitis Research Network; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RTX, rituximab.
Turgeon D, et al. Rheumatology 2023;kead087.

To return to core deck, click here

Avacopan administration

Note: avacopan has only been studied in patients with GPA/MPA

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

Avacopan: oral administration with no dose adjustment[1,2]

AVACOPAN FIXED-DOSE REGIMEN

The oral avacopan regimen does not require dose adjustment:[1,3]

30 mg avacopan

Taken twice-daily

With food

Treatment regimen in conjunction with immunosuppressants (RTX or CYC/AZA)[1]

30 mg BID oral dose of avacopan provides 24-hour C5aR1 coverage[2]

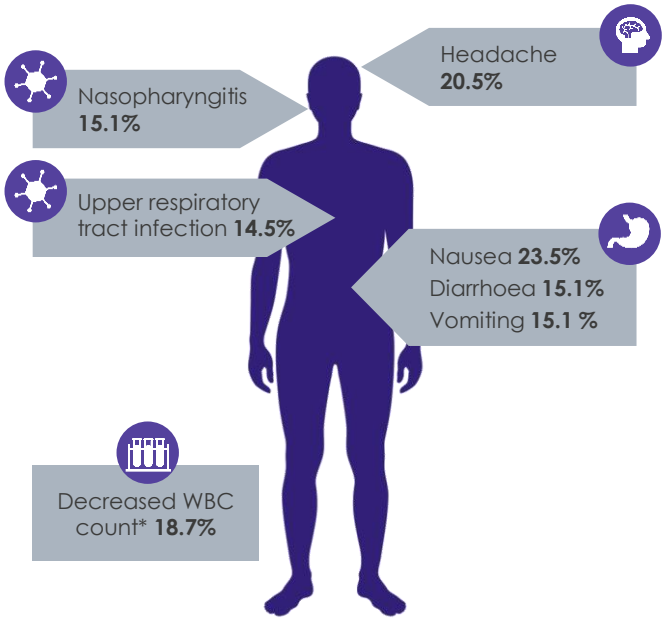
Avacopan pharmacokinetics and dose management, here

AZA, azathioprine; BID, bis in die (twice a day); CYC, cyclophosphamide; C5a, complement component 5a; C5aR1, C5a receptor 1; GC, glucocorticoid; RTX, rituximab.

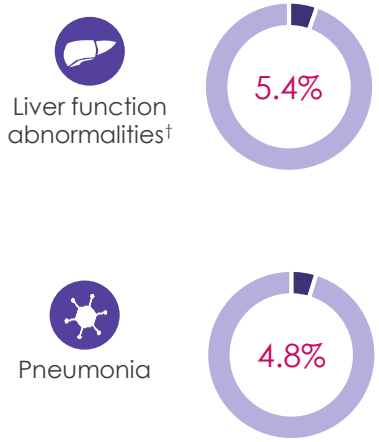
1. Jayne D, et al. *N Engl J Med* 2021;384(7):599–609. 2. Bekker P, et al. *PLoS One* 2016;11(10):e0164646. 3. Vifor (2020). Tavneos 10 mg hard capsules (Avacopan). SmPC.

SmPC identifies nausea and headache as the most common reported adverse reactions in patients treated with avacopan

MOST FREQUENT ADVERSE REACTIONS



MOST FREQUENT SARs



RECOMMENDED TESTING

Prior to avacopan initiation

Obtain **WBC counts‡**, **hepatic transaminases** and **total bilirubin§**

Following avacopan initiation

Continue to monitor WBC counts, hepatic transaminases and **total bilirubin** as clinically indicated and as part of routine follow-up

Ask patients to immediately **report any manifestations of bone marrow failure**, such as infection, unexpected bruising or bleeding

*Includes leukopenia. †Increased alanine aminotransferase, total blood bilirubin, gamma glutamyl transferase, hepatic enzyme or transaminase or abnormal hepatic function. ‡Avacopan should not be initiated if WBC count <3500/µl, neutrophil count <1500/µl, or lymphocyte count <500/µL. §Avacopan should not be initiated in patients with signs of liver disease, such as elevated aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase or total bilirubin >3 times upper limit of normal. MI, myocardial infarction; SAE, serious adverse event; WBC, white blood cell.
Tavneos 10 mg hard capsules (Avacopan); Summary of product characteristics.

Avacopan: dose management recommendations from SmPC

CLINICALLY REASSESS AND TEMPORARILY STOP TREATMENT IF…

- **ALT or AST >3 × ULN**

TEMPORARILY STOP TREATMENT IF…

- **ALT or AST >5 × ULN**
- Patient **develops:**
  - **Leukopenia** (WBC count <2 × 10^9/L) OR
  - **Neutropenia** (neutrophils <1 × 10^9/L) OR
  - **Lymphopenia** (lymphocytes <0.2 × 10^9/L)
- Patient has **active, serious infection** (i.e. requiring hospitalisation or prolonged hospitalisation)

CONSIDER PERMANENTLY DISCONTINUING TREATMENT IF…

- **ALT or AST >8 × ULN**
- **ALT or AST >5 × ULN for >2 weeks**
- **ALT or AST >3 × ULN** and **total bilirubin >2 × ULN or INR >1.5**
- **ALT or AST >3 × ULN** with the appearance of **fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia** (>5%)
- An **association between avacopan and hepatic dysfunction** has been established

RESUME TREATMENT…

- **Upon normalisation of values** AND
- Based on an **individual benefit/risk assessment**

If resuming treatment, **monitor hepatic transaminases** and **total bilirubin** closely

ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalised ratio; ULN, upper limit of normal; WBC, white blood cell.

Vifor. Tavneos 10 mg hard capsules (Avacopan). Summary of product characteristics. 2022.

Return to core slides, here

Avacopan real-world experience

Note: avacopan has only been studied in patients with GPA/MPA

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

First real-world experience with avacopan in the Netherlands: treatment before and after avacopan initiation[1]

Eight adult AAV patients treated with avacopan as part of the compassionate use program[1]

n=6 with generalized disease

n=2 with limited ENT disease

n=5 with renal involvement

n=4 with pulmonary involvement

MPO+

n=4 with MPO+ ANCA serology

PR3+

n=4 with PR3+ ANCA serology

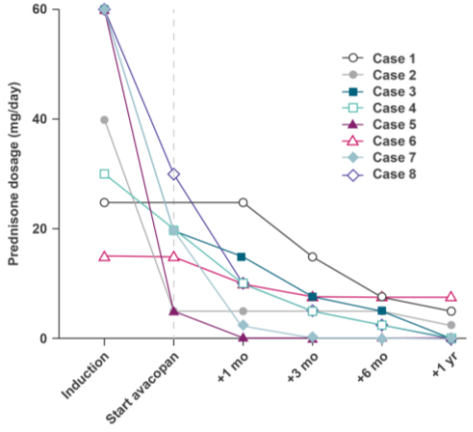
Patients* received multiple remission induction therapies prior to avacopan[1]

	Therapy before start of avacopan	Therapy after start of avacopan	
	Immunosuppressive medication	Concomitant maintenance treatment	Extra induction therapies
Case 1	-1 month: CYC -6 months: MP, RTX	Prednisone (5 mg/day)	
Case 2	-4 months: MP, PE, obinutuzumab -5 months: MP, PE, obinutuzumab -1 year: RTX, MP, CYC -11/9/7 years: MMF	Prednisone (2.5 mg/day)	
Case 3	-3 months: MP, RTX -2 years: MP, RTX	+2 months: RTX (1000 mg) +8 months: RTX (500 mg)	
Case 4	-2 months: MP, RTX, AZA -7 months: RTX -1 year: MP, CYC		
Case 5	-1 month: MP, CYC -4 months: RTX -1 year: CYC	+14 months: RTX (1000 mg)	+8 months: RTX (2000 mg)
Case 6	-2 months: RTX -6 months: RTX, MMF -8 months: AZA -1 year: RTX -2–3 years: RTX, MTX	Prednisone (7.5 mg/day) +1 year: RTX (1000 mg)	
Case 7	-1 month: RTX† -3 years: MP, RTX, AZA	+1 year: RTX (500 mg)	
Case 8	-1 month: MP, RTX -8 years: CYC		

Median time between start of latest induction therapy and start of avacopan: 7.7 weeks

GC tapering was successful in all patients[1]

Prednisone dosage (mg/day) per patient at different time points



†RTX not given as induction, but tailored treatment before start of avacopan.

Avacopan, in combination with a rituximab or cyclophosphamide regimen, is indicated for the treatment of adult patients with severe, active GPA or MPA and should be initiated and monitored by healthcare professionals experienced in the diagnosis and treatment of GPA or MPA.[2] Avacopan should be administered in combination with a rituximab or cyclophosphamide regimen as follows: rituximab for 4 weekly intravenous doses or, intravenous or oral cyclophosphamide for 13 or 14 weeks, followed by oral azathioprine or mycophenolate mofetil and, glucocorticoids as clinically indicated.[2] AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; AZA, azathioprine; CYC, cyclophosphamide; ENT, ears nose throat; GPA, granulomatosis with polyangiitis; MMF, mycophenolate mofetil; MP, methylprednisolone; MPA microscopic polyangiitis; MP, methylprednisolone; MPO, myeloperoxidase; PE, plasma exchange; PR3; proteinase 3; RTX, rituximab.

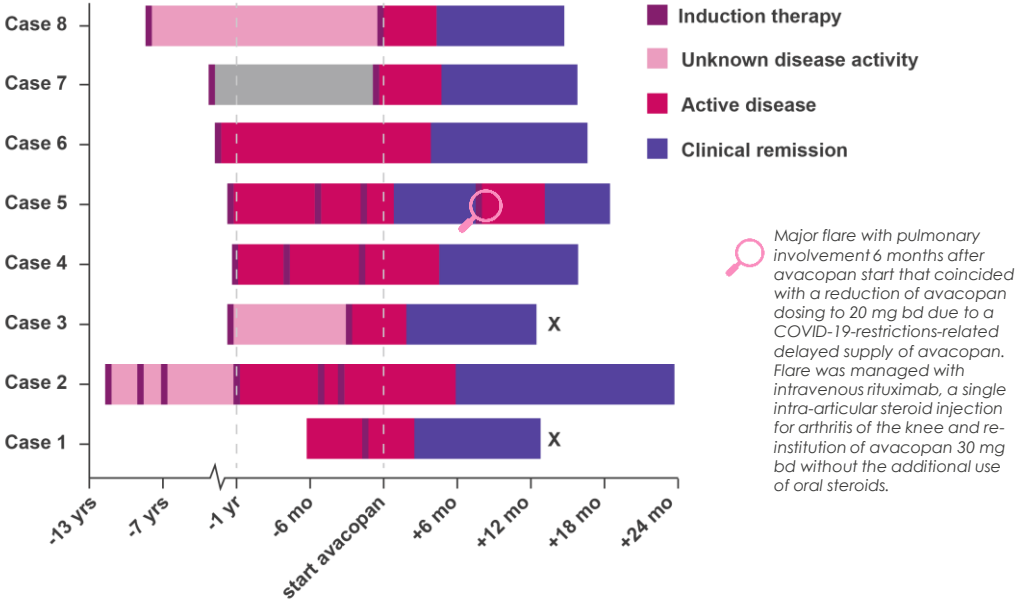
1. van Leeuwen J, et al. *Kidney Int Rep* 2022;7:624–628. 2. Tavneos SmPC Jan 2022

First real-world experience with avacopan in the Netherlands: demonstrated added value of avacopan in AAV treatment[1]

Treatment outcomes[1]

- All patients achieved **clinical remission (BVAS=0) within 6 months**
- **eGFR improved** in **4 patients** (+5 to + 9 ml/min), decreased in none
- After one year of avacopan use the **GTI improved in 4**, remained **stable in 3**, **worsened in 1** (weight gain despite improved glucose intolerance)
- **No side effects or infections** related to avacopan were reported*

Disease course per patient shown in relation to start of avacopan[1]



Major flare with pulmonary involvement 6 months after avacopan start that coincided with a reduction of avacopan dosing to 20 mg bd due to a COVID-19-restrictions-related delayed supply of avacopan. Flare was managed with intravenous rituximab, a single intra-articular steroid injection for arthritis of the knee and re-institution of avacopan 30 mg bd without the additional use of oral steroids.

*Adverse events were not systematically registered.

Avacopan, in combination with a rituximab or cyclophosphamide regimen, is indicated for the treatment of adult patients with severe, active GPA or MPA and should be initiated and monitored by healthcare professionals experienced in the diagnosis and treatment of GPA or MPA.[2] Avacopan should be administered in combination with a rituximab or cyclophosphamide regimen as follows: rituximab for 4 weekly intravenous doses or, intravenous or oral cyclophosphamide for 13 or 14 weeks, followed by oral azathioprine or mycophenolate mofetil and, glucocorticoids as clinically indicated.[2]

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; BVAS; Birmingham Vascultis Activity Score; eGFR, estimated glomerular filtration rate; GTI, glucocorticoid toxicity index.

1. van Leeuwen J, et al. *Kidney Int Rep 2022;7:624–628.* 2. Tavneos SmPC Jan 2022.

Real-world experience with avacopan in France: Patient characteristics[1]

Nine adult AAV patients treated with avacopan as part of the compassionate use program, with a minimum of 12 months of follow-up[1]*

	Age (years)	AAV		Clinical characteristics at inclusion		Kidney biopsy	Immunosuppressive regimen				Adverse events	Outcomes at Month 12	
		De novo vs relapse	ANCA type	BVAS	eGFR (mL/min)	Glomeruli with crescents, n (%)	Induction treatment		Cumulative GC dose during first month (g)	Overlap between avacopan and GC (days)		BVAS	eGFR (mL/min)
Case 1	54	Relapse	MPO	17	11	2 (25%)	Rituximab	GC	0.8 (0.8)	0	No	0	23‡
Case 2	86	De novo	MPO	12	26	7 (37%)	Rituximab	GC	0.78 (0.78)	0	No	0	49
Case 3	34	De novo	Both	29	49	8 (61%)	Rituximab	GC + pulse†	4.02 (4.36)	7	No	0	93
Case 4	61	De novo	MPO	18	34	11 (50%)	Rituximab	GC	1.04 (1.2)	21	No	0	28
Case 5	83	De novo	MPO	23	15	1 (17%)	Rituximab	GC	1.14 (1.26)	16	Urinary infection	0	11
Case 6	76	Relapse	PR3	24	30	N/A	Rituximab	GC	1.56 (1.56)	0	No	0	34
Case 7	40	Relapse	MPO	12	40	6 (32%)	Obinituzumab	GC	1.58 (1.73)	21	No	0	50
Case 8	85	De novo	MPO	21	35	1 (20%)	Rituximab	-	-	N/A	No	1	45
Case 9	75	Relapse	MPO	12	26	N/A	Rituximab	-	-	N/A	No	0	23

Table adapted from Gabilan C, et al. *Kidney Int Rep* 2022

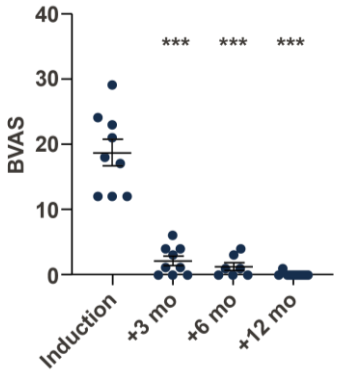
*Two patients were excluded because of early withdrawal of Avacopan related to swallowing disorders (n=1), or too short follow-up (< 3 months).[1] †1 g/day for 3 days.[1] ‡This patient required dialysis from month 1 to month 6.[1]
Avacopan, in combination with a rituximab or cyclophosphamide regimen, is indicated for the treatment of adult patients with severe, active GPA or MPA and should be initiated and monitored by healthcare professionals experienced in the diagnosis and treatment of GPA or MPA.[2] Avacopan should be administered in combination with a rituximab or cyclophosphamide regimen as follows: rituximab for 4 weekly intravenous doses or, intravenous or oral cyclophosphamide for 13 or 14 weeks, followed by oral azathioprine or mycophenolate mofetil and, glucocorticoids as clinically indicated.[2]
AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; BVAS, Birmingham Vasculitis Activity Score; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; MPO, myeloperoxidase; N/A, not applicable; PR3; proteinase 3.
1. Gabilan C, et al. *Kidney Int Rep* 2022. DOI: https://doi.org/10.1016/j.ekir.2022.01.1065. 2. Tavneos SmPC Jan 2022.

Real-world experience with avacopan in France: demonstrated high rate of AAV remission and GC sparing [1]

Treatment outcomes[1]

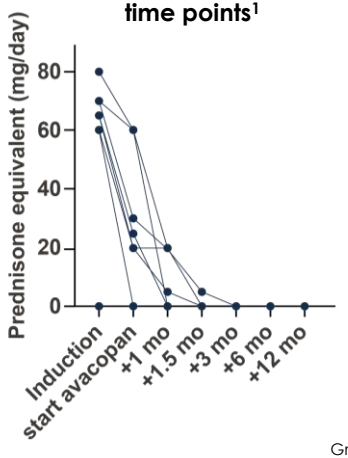
- **Month 3**: median **BVAS** of 1 (range 0–6) was **significantly decreased compared to baseline (p<0.001)**
- **Month 12: 8 out of 9 of patients** had achieved **complete remission** (BVAS=0)
- **No relapse** occurred during follow-up
- **Kidney function**: median eGFR was 34 ml/min/1.73m^2 (range 11–93) at month 12 (p=0.14 vs baseline)*
- **Safety**: one report of urinary infection and one report of progressive visual acuity loss in a patient with a history of age-related macular degeneration

BVAS at different time points[1]

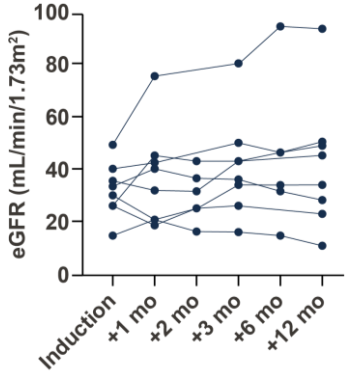


***p<0.001 with paired t-test

Prednisone dosage (mg/day/patient) at different time points[1]



eGFR at different time points[1]



Graphs adapted from Gabilan C, et al. *Kidney Int Rep* 2022

*One patient required kidney replacement therapy from months 1 to 6 and then recovered stable kidney function (eGFR 23 mL/min/1.73m²).[1] According to the information on the graph, only 4 patients are presented: seven patients received GCs before avacopan, with 3 possible schemes: 1. GCs were stopped 13 days before Avacopan (patient 1); 2. GCs were stopped on the day corresponding to the first dose of avacopan (patients 2 and 6); and 3. GCs were tapered, overlapping with avacopan for a median period of 19 days (ranges: 7–21; patients 3, 4, 5, and 7).

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; BVAS, Birmingham Vasculitis Activity Score; eGFR, estimated glomerular filtration rate; GC, glucocorticoid.

1. Gabilan C, et al. *Kidney Int Rep* 2022. DOI: https://doi.org/10.1016/j.ekir.2022.01.1065.

Real-world experience with avacopan in Italy: added value as a GC-sparing strategy in the early stages of treatment

Study overview

- **Aim:** assess avacopan efficacy and safety, and describe QoL changes
- **Design:** prospective multicentre study at nine centres in Italy
- **Inclusion criteria:** GPA or MPA treated with avacopan from May 2022, with ≥3 months' follow-up
- Avacopan initiated on a **background of GCs and RTX***

12 adult AAV patients treated with avacopan as part of the compassionate use programme

- Male: **n=5**
- Median age: **64** years
- Median BVAS: **12**
- New onset disease: **n=4**
- Relapsing disease: **n=8**
  - Median disease duration: **12 years**
  - Prior treatment: RTX: **n=5**, CYC: **n=5**, AZA: **n=3**, MTX: **n=2**, MMF: **n=1**
- **GPA** n=9
- **MPA** n=3
- Median VDI: **3**
- Renal involvement: **n=9**

Results

	Baseline	After Month 3
Median **GC dose**†	**50 mg** [IQR 7–50 mg])	**5 mg** (IQR 2–11 mg)
Patients in **clinical remission**	**0**/12	**10**/12
Median 24-hour **urine protein** value	**681** (IQR 408–2300) mg/day	**254** (IQR 170–488) mg/day
% patients reporting one of the **three highest severity/ impact levels across all AAV-PRO_ita domains**	**57%**	**32%**
Grade 1/2 **AEs**		**1 UTI;‡** **1 HSV infection;§** **1 self-limiting dyspnoea/fatigue§**

The added value of avacopan as a GC-sparing strategy can be observed at early stages of therapy

*RTX 1 g every 2 weeks (75%) or 375 mg/m² weekly (25%); 2 patients also received 1 g CYC before RTX; †Prednisone equivalent. ‡Grade 2; temporary suspension of avacopan. §Grade 1.
AAV, ANCA-associated vasculitis; AAV-PRO_ita; Italian version of anti-neutrophil cytoplasm antibody-associated vasculitis patient-reported outcome questionnaire; AE, adverse event; AZA, azathioprine; BVAS, Birmingham Vasculitis Activity Score; CYC, cyclophosphamide; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; HSV, herpes simplex virus; IQR, interquartile range; MMF, mycophenolate mofetil; MPA, microscopic polyangiitis; MTX, methotrexate; QoL, quality of life; RPGN, rapidly progressive glomerulonephropathy; RTX, rituximab; UTI, urinary track infection; VDI, Vasculitis Damage Index.
Treppo E, et al. EULAR 2023. Abstract AB0789.

More real-world experience with avacopan and CD163, here