Avacopan Vifor

Recommended for use by NICE*

Avacopan Vifor, a first-in-class therapy for GPA/MPA that selectively targets C5aR1 to achieve and sustain remission at 52 weeks[1–4]

*Avacopan Vifor, with a cyclophosphamide or rituximab regimen, is recommended by NICE, within its marketing authorisation, as an option for treating severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in adults[1,5]

UK formulary pack

This pack is provided to support healthcare professionals completing formulary applications for Avacopan Vifor

To access to the full UK Avacopan Vifor summary of product characteristics scan the QR code or click the link

https://emc.link/pi41644

VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

CSL Vifor

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Purpose of the formulary pack

This pack has been designed to assist healthcare professionals and other relevant decision-makers in producing formulary applications in their NHS institutions.

Once the document has been provided to a healthcare professional or another relevant decision-maker, CSL Vifor take no responsibility for how the document or parts thereof are used.

The information provided is not intended as a substitution for local data regarding patients and services but to provide additional background information to support cases for local implementation. Depending on local circumstances, the content of any given application may vary, and this document is designed to be used flexibly to suit local formulary application requirements.

Contents

List of abbreviations

AAV, ANCA-associated vasculitis

AE, adverse event

ALP, alkaline phosphatase

ALT, alanine aminotransferase

ANCA, anti-neutrophil cytoplasmic antibody

AST, aspartate aminotransferase

AUC, area under the plasma concentration time curve

AZA, azathioprine

BVAS, Birmingham Vasculitis Activity Score

BVAS/WG, Birmingham Vasculitis Activity Score for Wegener's Granulomatosis

C5a, complement component 5a

C5aR1, complement component 5a receptor 1

C5b, complement component 5b

C5L2, complement component 5a-like receptor 2

CD19, cluster of differentiation 19

CI, confidence interval

CKD, chronic kidney disease

CL/F, total apparent body clearance

C_{max}, maximum plasma concentration

CYC, cyclophosphamide

CYP3A4, cytochrome P450 family 3 subfamily A member 4

eGFR, estimated glomerular filtration rate

EGPA, eosinophilic granulomatosis with polyangiitis

EQ-5D-5L, EuroQol 5 dimension 5 level

ESRD, end-stage renal disease

EULAR, European Alliance of Associations for Rheumatology

EUVAS, European Vasculitis Society

GC, glucocorticoid

GFR, glomerular filtration rate

GPA, granulomatosis with polyangiitis

GTI-AIS, Glucocorticoid Toxicity Index Aggregate Improvement Score

GTI-CWS, Glucocorticoid Toxicity Index Cumulative Worsening Score

HIV, human immunodeficiency virus

HRQoL, health-related quality of life

IV, intravenous

KDIGO, Kidney Disease: Improving Global Outcomes

LSM, least squares mean

MAC, membrane attack complex

MCP-1, monocyte chemoattractant protein-1

MPA, microscopic polyangiitis

MPO, myeloperoxidase

NET, neutrophil extracellular trap

NHS, National Health Service

NICE, National Institute for Health and Care Excellence

P-gp, P-glycoprotein

PR3, proteinase 3

QoL, quality of life

RCAHR, retrospective clinical audit of healthcare records

ROS, reactive oxygen species

RPGN, rapidly progressive glomerulonephritis

RRT, renal replacement therapy

RTX, rituximab

SD, standard deviation

SEM, standard error of the mean

SF-36, 36-Item Short Form Health Survey

SoC, standard of care

T_{max}, time to maximum plasma concentration

UACR, urinary albumin:creatinine ratio

UK, United Kingdom

ULN, upper limit of normal

USA, United States of America

VAS, visual analogue scale

VBDS, vanishing bile duct syndrome

VDI, Vasculitis Damage Index

WBC, white blood cell

Executive summary

Executive summary

AAV and the problems associated with the current SoC as per 2022 EULAR and 2024 KDIGO guidelines[6,7]

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a rare,[8,9] progressive[10–12] and severe[11–14] autoimmune disease that is primarily characterised by:[15]

- Inflammation and necrosis of small- to medium-sized blood vessels
- Circulating ANCAs

The disease can affect patients of all ages, but the mean age at diagnosis is approximately 57 years.[16] Males are affected slightly more frequently than females are.[8,16] Most, but not all, AAV patients screen positive for the presence of ANCAs.[15] The ANCAs target the antimicrobial proteins myeloperoxidase (MPO) or proteinase 3 (PR3), which are normally located in the primary granules of neutrophils.[15,17]

Based on clinicopathology, the two most common types of AAV are granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA),[8] but AAV can also be classified based on serology (ANCA status and type).[15] Combining the two classification systems (for example, PR3-ANCA GPA, ANCA-negative MPA) can be useful for predicting a patient's prognosis and potential response to treatment.[18,19]

The aetiology of AAV is unclear.[17,20] For unknown reasons, ANCAs are developed in response to loss of immune tolerance to PR3 or MPO.[17] Neutrophils are primed by cytokines and start to express ANCA antigens (PR3 or MPO) on their cell surfaces.[20] ANCAs bind to the antigens, activating the neutrophils.[20]

ANCA-activated neutrophils:[17,20]

- Attack vascular endothelial cells
- Release factors that activate the complement cascade via the alternative pathway, resulting in the formation of complement component 5a (C5a)

C5a attracts more neutrophils and, upon binding to C5a receptor 1 (C5aR1), facilitates further neutrophil priming and activation.[17,20] Consequently, a vicious cycle is established that amplifies ANCA-induced vascular inflammation and necrosis.[17,20]

AAV can impact a range of organs[12,21] and cause irreversible organ damage.[11,12] The kidneys and respiratory tract are most commonly affected.[16,21] However, symptoms can vary greatly,[16] which can lead to a delay in diagnosis.[20]

The current standard of care (SoC) for the induction treatment of AAV is a combination of glucocorticoids (GCs) with either cyclophosphamide or rituximab, as per guidelines provided in 2022 by the European Alliance of Associations for Rheumatology (EULAR) and in 2024 by Kidney Disease: Improving Global Outcomes (KDIGO).[6,7] Without treatment, over 80% of patients may die within 1 year of diagnosis.[22] Treatment using the SoC improves survival, with 10.7% of GPA and MPA patients dying within 1 year.[13] However, the clinical response to the SoC is variable.[23] Relapses remain common,[24] increasing organ damage over time.[12]

Furthermore, long-term and/or high-dose GC use is associated with:

- Substantial adverse events (AEs), with infections accounting for 50% of deaths within the first year[13]
- Increased organ damage[12]
- Other negative effects, such as depression, anxiety and weight gain[25]

Another limitation of the current SoC is that it does not target a key mechanism of disease.[20,26,27]

AAV also imposes a economic burden,[28–31] with high healthcare costs being driven by hospitalisations,[30–33] relapses[28,34] and severe concomitant morbidities, especially end-stage renal disease (ESRD).[30,34]

The Avacopan Vifor-based regimen and how it achieved and sustained remission for 52 weeks, while reducing GC use[2]

Avacopan Vifor is a selective small-molecule antagonist of C5aR1 and a first-in-class therapy for GPA and MPA.[1,3] In combination with a rituximab or cyclophosphamide regimen, it is indicated for the treatment of adult patients with severe, active GPA or MPA.[1]

The Avacopan Vifor-based regimen can sustain remission of AAV for 52 weeks[2] and reduce the use of GCs.[2] This is achieved by blockage of C5aR1 by Avacopan Vifor, which interrupts the vicious cycle that amplifies inflammation.[3] Avacopan Vifor is not expected to affect other aspects of complement system activation.[3]

The efficacy and tolerability of Avacopan Vifor were evaluated in a clinical trial programme that consisted of two phase 2 (CLEAR and CLASSIC) and one phase 3 (ADVOCATE) studies.[2,35,36] In CLEAR, Avacopan Vifor was found to be effective at replacing high-dose oral GCs in the treatment of adults with newly diagnosed/relapsing GPA or MPA.[35] The conclusion from CLASSIC was that Avacopan Vifor + SoC is well tolerated in the treatment of the same population.[36]

In ADVOCATE, compared with a GC-based regimen, the Avacopan Vifor-based regimen demonstrated:

- A non-inferior clinical remission rate at 26 weeks and superiority at sustaining remission at 52 weeks[2]
- A lower absolute risk of relapse over 52 weeks[2]
- A reduction in the use of GCs[2,37]
- A larger reduction in GC toxicity[2]
- A larger numerical increase in estimated glomerular filtration rate (eGFR) at weeks 26 and 52[2]
- A larger numerical increase in physical domains of health-related quality of life (HRQoL)[2,37]
- Association with fewer AEs of any kind, including potentially GC-related AEs, serious AEs, deaths and infections[2]

Treatment with Avacopan Vifor should be initiated and monitored by healthcare professionals who are experienced in the diagnosis and treatment of GPA or MPA.[1]

The list price of Avacopan Vifor is £5,547.95 per pack of 180 x 10 mg capsules.[5] CSL Vifor has a commercial arrangement with the NHS (simple discount patient access scheme).[5] This makes Avacopan Vifor available to the NHS at a discount.[5] Orders can be made through Alloga UK via email (allogauk.orders@alloga.co.uk) or telephone (+44 [0] 01773 441702).

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ANCA-associated vasculitis (AAV) – GPA/MPA

ANCA-associated vasculitis (AAV) – GPA/MPA

Key points

- AAV is a rare,[1,2] progressive[3–5] and severe[4–7] autoimmune disease characterised by necrotic inflammation of small–medium blood vessels and circulating anti-neutrophil cytoplasmic antibodies (ANCAs)[8]
- The two most common phenotypes are granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)[1]
- AAV can cause irreversible damage to a range of organs,[4,9–11] with the kidneys and respiratory tract being most commonly affected[10,11]
- Patients of all ages can be affected, but the incidence of AAV increases with age[10]
- In the pathogenesis of AAV, neutrophils attack vascular endothelial cells both directly and indirectly, with indirect damage being caused by activation of the alternative complement pathway, which initiates a vicious inflammatory amplification cycle[12]
- Treatment with the current standard of care (SoC), as per 2022 EULAR and 2024 KDIGO guidelines,[13,14] improves survival, but mortality is still elevated compared with the general population, with 10.7% of patients dying within 1 year of diagnosis, mostly (59%) due to adverse events (AEs)[6]
- Renal involvement is the most common severe manifestation of AAV, increasing the risk of mortality compared with AAV patients without renal involvement[9,10]
- AAV may have a substantial impact on quality of life (QoL)[15] and is associated with a economic burden[16–19]

Definition of AAV

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a rare,[1,2] progressive[3–5] and severe[4–7] autoimmune disease that is characterised by:[8]

1. Inflammation and destruction of small- and medium-sized blood vessels
2. Few or no immunoglobulin deposits in vessel walls
3. Circulating ANCAs (though not in all cases)

ANCAs are autoantibodies that target antimicrobial proteins that are normally located in the primary granules of neutrophils.[20] In the case of AAV, the antimicrobial proteins being targeted are myeloperoxidase (MPO) and proteinase 3 (PR3).[20]

Classification of AAV

AAV can be classified based on clinical characteristics (clinicopathology), serology (ANCA status and type), or both.[8,12] The clinicopathologic classification system (Table 1) divides AAV into three main phenotypes:[8]

1. Granulomatosis with polyangiitis (GPA)
2. Microscopic polyangiitis (MPA)
3. Eosinophilic granulomatosis with polyangiitis (EGPA)

Avacopan Vifor is indicated for the treatment of GPA and MPA but not EGPA.[21]

Table 1. Clinicopathologic classification of AAV[8]

PHENOTYPE	CHARACTERISTICS
Granulomatosis with polyangiitis (GPA), previously known as Wegener's granulomatosis	• Necrotising granulomatous (granuloma-rich) inflammation usually involving the respiratory tract • Necrotising vasculitis predominantly affecting small–medium vessels • Necrotising glomerulonephritis (inflammation of glomeruli) is common
Microscopic polyangiitis (MPA)	• Necrotising vasculitis predominantly affecting small vessels • Necrotising glomerulonephritis and pulmonary capillaritis are common • Necrotising arteritis involving small–medium arteries may be present • Granulomatous inflammation is absent
Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg–Strauss syndrome	• Necrotising granulomatous inflammation often involving the respiratory tract • Necrotising vasculitis predominantly affecting small–medium vessels • Presence of eosinophilia and asthma • ANCAs are more frequent when glomerulonephritis is present

The serologic classification system divides AAV into three serotypes based on ANCA status and type:[8]

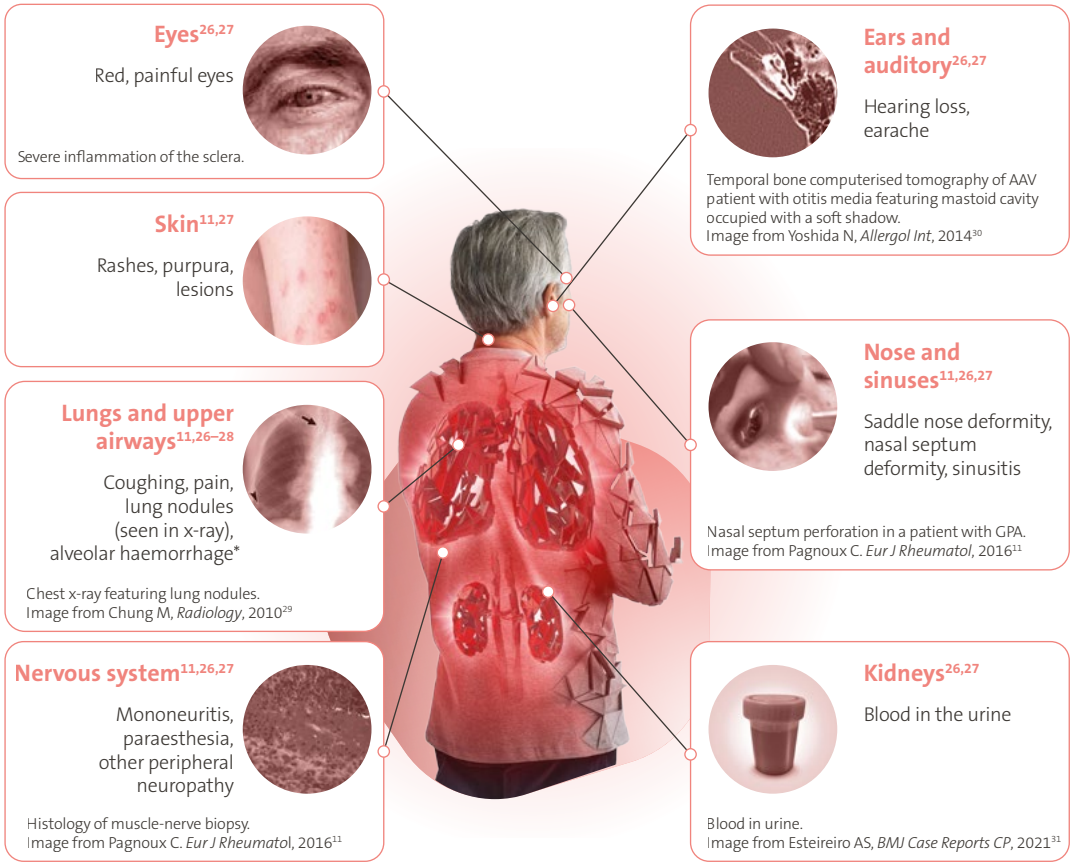
1. PR3-ANCA
2. MPO-ANCA
3. ANCA-negative

Combining the clinicopathologic and serologic classification systems (for example, PR3-ANCA GPA, MPO-ANCA MPA, ANCA-negative MPA) is useful for characterising the nature of the disease in a given patient, as well as predicting the prognosis and potential response to treatment.[22,23] The presence of both PR3 and MPO ANCAs in a single patient is rare, occurring in 4% of GPA and 2% of MPA patients.[7]

Signs and symptoms

AAV can impact a range of organs and have a high disease burden on patients (Figure 1).[4,9–11] The kidneys and respiratory tract are most commonly affected.[10,11] However, symptoms of AAV can vary greatly from one patient to the next.[10] Many AAV patients have general, non-specific symptoms, such as fatigue, fever, weight loss, joint pain and a rash,[10] which can lead to a delay in diagnosis.[24]

Figure 1. Systemic disease with organ involvement and other disease manifestations[9,11,25–31]



*GPA: 7–45%; MPA: 10–30%. Adapted from Wallace ZS and Miloslavsky EM 2020,[9] Pagnoux C 2016,[11] Al Hussain T et al. 2017,[25] Hunter R et al. 2020,[26] Kitching A et al. 2020,[27] Quartuccio L et al. 2020,[28] Chung MP et al. 2010,[29] Yoshida N and Iino Y 2014[30] and Esteireiro AS et al. 2021.[31]

Disease severity

Based on data from a retrospective clinical audit of the healthcare records (RCAHR) of 929 newly diagnosed AAV patients from France, Germany, Italy and the UK, the severity of AAV at the start of therapy ranges from:[10]

- Mild localised disease, 12%
- Moderate systemic disease, 54%
- Severe, rapidly progressive systemic disease, 34%

The clinical tool used to assess disease activity is the Birmingham Vasculitis Activity Score (BVAS),[32] whilst a common tool used to measure the extent of organ damage is the Vasculitis Damage Index (VDI).[33]

Incidence and prevalence

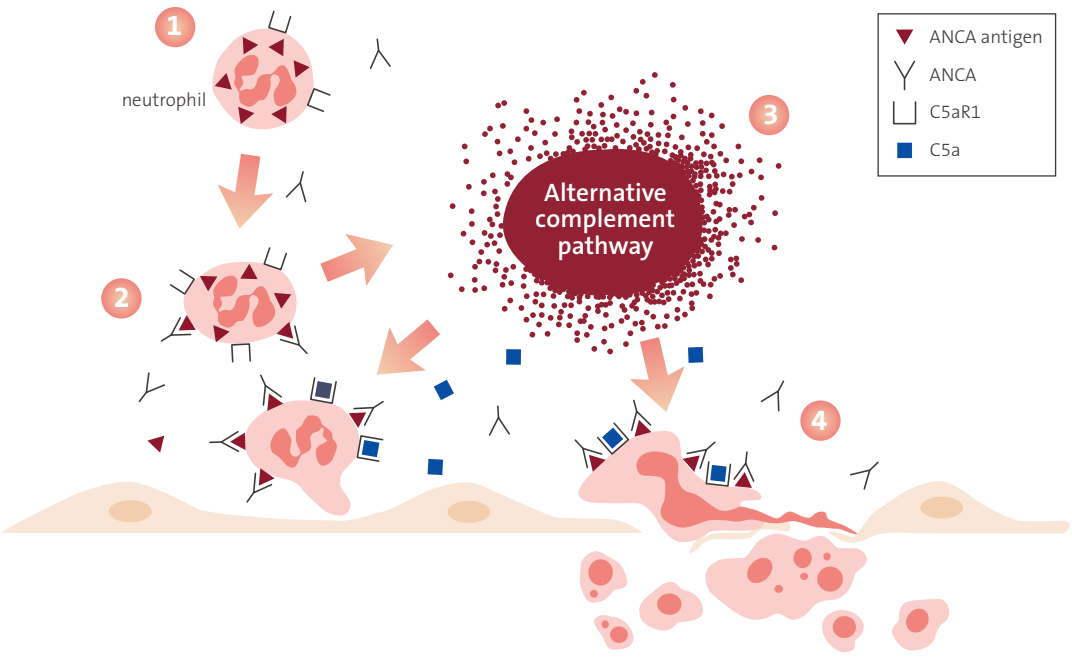
AAV meets the European Medicines Agency's definition of a rare disease (fewer than five cases per 10,000 people[2]).[1] It can affect patients of all ages, but its incidence increases with age, with the mean age at diagnosis being approximately 57 years.[10] Males are affected slightly more than females are.[1,10]

In Europe, the overall incidence rate of AAV (GPA/MPA/EGPA) is approximately 13 to 20 patients per million people per year.[1] There have been relatively few prevalence studies,[1] with global estimates ranging from 30 to 218 patients per million people.[3,4] The most common clinical phenotypes in Europe are GPA (approximately 23.7 to 160 patients per million people) and MPA (approximately 25.1 to 94 patients per million people).[1]

Pathogenesis of AAV

The pathogenesis of AAV can be divided into four stages (Figure 2).

Figure 2. The four stages of AAV pathogenesis[12,20]



For unclear reasons, immune tolerance to PR3 or MPO is lost, and ANCAs are developed (1). Neutrophils are primed by cytokines and then activated when ANCAs bind to ANCA (PR3 or MPO) antigens expressed on the surfaces of neutrophils (2). ANCA-activated neutrophils attack endothelial cells, as well as amplify the alternative complement pathway, resulting in the formation of complement component 5a (C5a; 3). C5a attracts more neutrophils and, upon binding to C5a receptors (C5aR1), facilitates further neutrophil priming, thus amplifying inflammation and vascular damage (4). Adapted from Jennette JC and Nachman PH 2017[12] and Geetha D and Jefferson JA 2019.[20]

Stage 1

ANCAs are developed in response to loss of immune tolerance to PR3 or MPO, which are normally safely stored in the primary granules of neutrophils.[20] The reason for the loss of immunity is currently unclear,[12,20] but potential risk factors include infections, genetics, environmental agents and therapeutic drugs.[35,36]

Stage 2

Neutrophils are primed by cytokines and other factors and start to express ANCA antigens (PR3 or MPO) on their cell surfaces.[12] Priming makes ANCA antigens more accessible to ANCAs, which bind to the antigens, resulting in robust neutrophil activation.[12]

Stage 3

Activated neutrophils attack and damage vascular endothelial cells through:[12,20]

1. Oxidative bursts (release of highly reactive chemicals formed of oxygen, known as reactive oxygen species [ROS])
2. Degranulation (secretion of granules that contain lytic and pro-inflammatory enzymes, including MPO and PR3)
3. NETosis (a process whereby the neutrophils eject a framework of chromatin and lytic enzymes, including MPO and PR3. The framework is known as a neutrophil extracellular trap [NET], and the process results in the death of the neutrophil)

Crucially, activated neutrophils also release factors such as properdin that amplify the alternative complement pathway, resulting in the formation of C5a and membrane attack complexes (MACs).[12,20] MACs are important effectors of the immune system that form pores on the surfaces of microbes, leading to cell lysis.[37]

Stage 4

Whilst MACs play a limited role in the pathogenesis of AAV, C5a attracts more neutrophils.[20] Upon binding to C5aR1 on the surfaces of neutrophils, C5a also facilitates further neutrophil priming and activation.[12,20]

As a result of stages 1 to 4, not only are vascular endothelial cells damaged and destroyed, but a vicious cycle is established that amplifies ANCA-induced inflammation and vascular necrosis,[12,20] potentially leading to severe and irreversible damage of critical organs.[4,10]

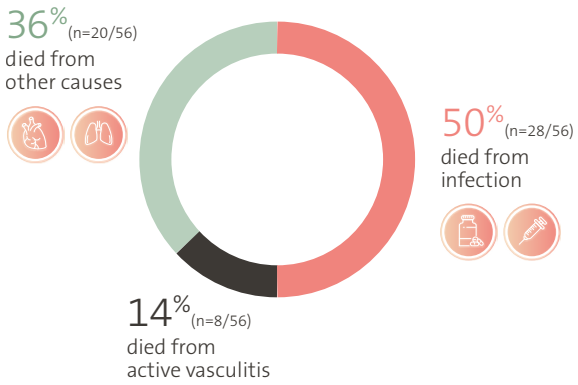
Risk of mortality

Without treatment, over 80% of AAV patients may die within 1 year of diagnosis.[24] Treatment using the current standard of care (SoC) improves survival, but mortality is still higher than it is for the general population, both in the short and long terms.[6,7] The current SoC for induction treatment is glucocorticoids (GCs) in combination with immunosuppressive therapy (either cyclophosphamide or rituximab), as per the 2022 EULAR and 2024 KDIGO guidelines.[13,14]

Short-term mortality risk

Data collected from 524 newly diagnosed AAV patients from four European Vasculitis Society (EUVAS) trials were used to compare the burden of AAV with the burden of AEs caused by SoC over 1 year.[6] A total of 10.7% of the patients died within 1 year of their GPA or MPA diagnosis.[6] AEs and active AAV accounted for 59% and 14% of deaths, respectively, indicating that the greatest threat to GPA/MPA patients in the first year is posed by AEs rather than active disease.[6] Infections were responsible for 50% of the deaths (Figure 3).[6]

Figure 3. Causes of death of GPA and MPA patients within 1 year of diagnosis[6]

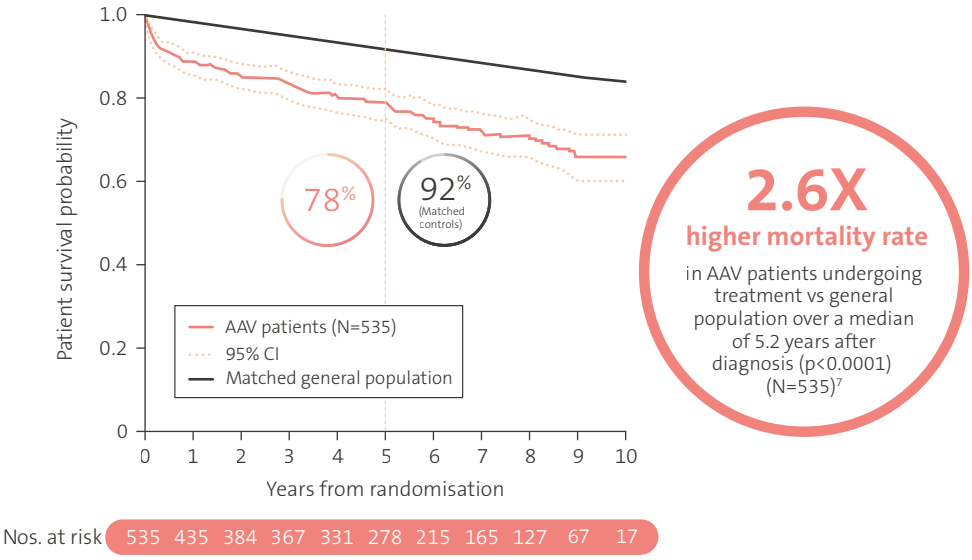


Adapted from Little MA et al. 2010.[6]

Long-term mortality risk

In a separate study (N=535) of the data from the same four EUVAS trials, this time exploring long-term survival, the AAV patients were found to be 2.6 times more likely to die over a median follow-up of 5.2 years compared with matched controls (Figure 4).[7] In the AAV and matched control populations, survival at 1 year and 5 years was 88% versus 98% and 78% versus 92%, respectively.[7]

Figure 4. Overall AAV patient survival versus matched controls over 10 years[7]



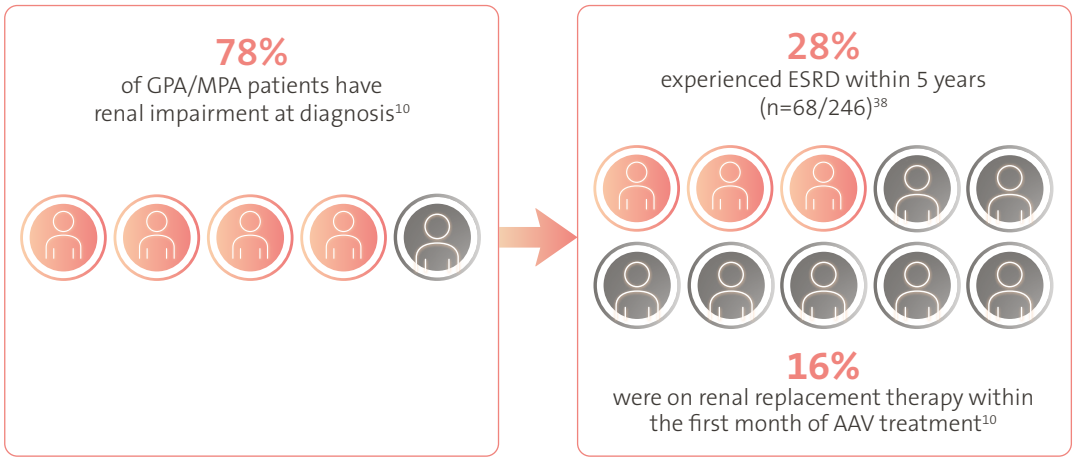
Reproduced from Flossmann O et al. 2011.[7]

Renal involvement

Renal involvement is the most common severe manifestation of AAV,[9,10] the histopathological hallmark of which is pauci-immune necrotising and crescentic glomerulonephritis.[12] A total of 78% of GPA and MPA patients may have renal impairment at diagnosis, which increases the risk of end-stage renal disease (ESRD).[10]

Renal replacement therapy (RRT) may be required by 16% of patients in the first month of AAV treatment.[10] Within 5 years of AAV diagnosis, ESRD may develop in up to 28% of patients (Figure 5).[38]

Figure 5. The increase in RRT requirement with AAV progression[10,38]



Adapted from Rutherford and Götte. 2020[10] and Booth AD et al. 2003.[38]

In a cluster analysis designed to identify novel subgroupings of AAV, compared with non-renal AAV, the risk of mortality was found to be two times higher for renal AAV with PR3-ANCA and six times higher for renal AAV without PR3-ANCA (Figure 6).[39] The data came from five clinical trials involving newly diagnosed GPA and MPA patients (cumulative N=673).[39]

Figure 6. Comparison of mortality rate in non-renal AAV versus renal AAV with and without PR3-ANCA[39]

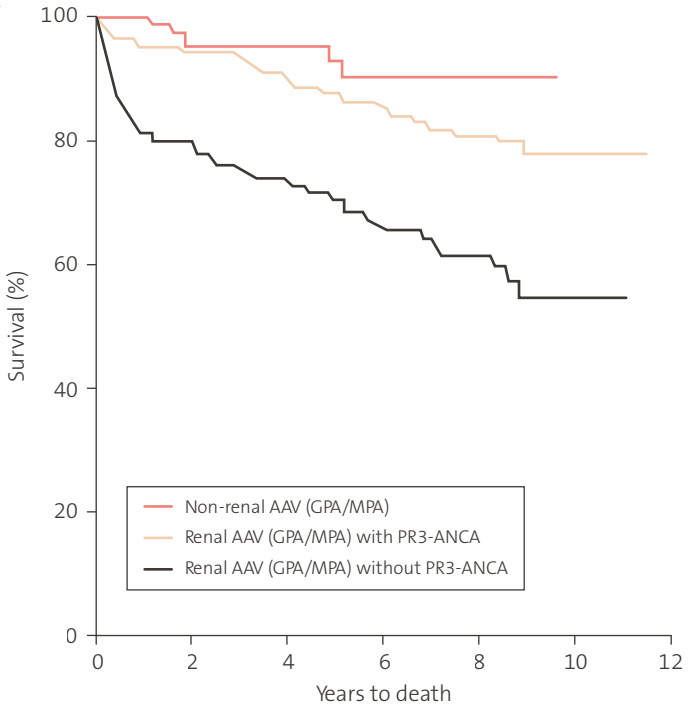
EUVAS/FVSG LONGITUDINAL STUDY

2x HIGHER MORTALITY RISK

for renal AAV with PR3-ANCA
(vs non-renal AAV)
over 12 years[39]

6x HIGHER MORTALITY RISK

for renal AAV without PR3-ANCA*
(vs non-renal AAV)
over 12 years[39]



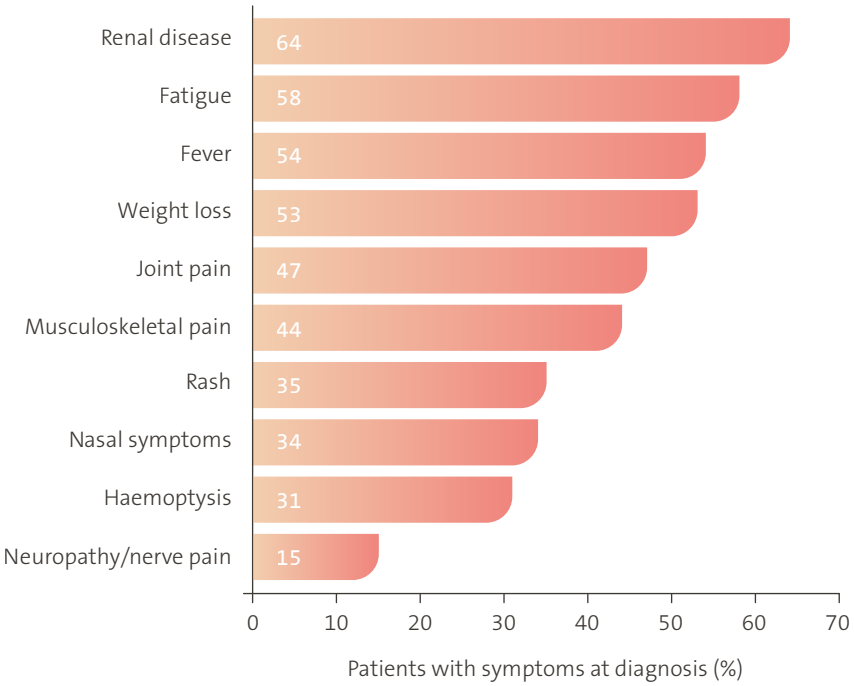
*Mainly MPO-ANCA and ANCA-negative patients. Adapted from Mahr A et al. 2013.[39]

Impact on QoL

AAV may have a substantial impact on QoL.[15,40] Compared with the general population, QoL is already significantly impaired at the time of AAV diagnosis.[40]

Based on data from the RCAHR cohort introduced earlier (n=929), the most common symptom at diagnosis is fatigue, experienced by 58% of patients (Figure 7).[10] Other common symptoms at diagnosis include fever, weight loss, musculoskeletal pain and a rash.[10]

Figure 7. Symptoms at diagnosis of GPA and MPA patients[10]



Adapted from Rutherford and Götte. 2020.[10]

In a multicentre case-control study of AAV patients (n=410) that was designed to identify and contextualise the determinants of poor QoL, AAV patients reported impairment of QoL similar to that of patients with chronic diseases whose substantial needs are already recognised.[15] Fatigue was the most common factor contributing to both poor physical and mental QoL (Table 2).[15]

Table 2. Most common factors contributing to poor physical and mental QoL[15]

PHYSICAL QoL (n=277)	MENTAL QoL (n=289)
• High fatigue • High sleep disturbance • Pain • High-dose AAV treatment	• High fatigue • Self-distraction • Hypoalbuminaemia • Anxiety • Depression

Economic burden

Burden on working-age patients

AAV is associated with a economic burden.[16–19] As the mean age at diagnosis of a GPA/MPA patient is approximately 57,[10] much of the economic burden is due to loss of work-related productivity.[41,42]

In a cross-sectional analysis of the employment statuses, disabilities and QoL of working-age (<60 years) AAV (GPA/MPA/EGPA) patients in a hospital in France (N=189), 40% had a work disability and 19% were unemployed due to their disease (Figure 8).[41]

Figure 8. Impact of AAV on working-age patients[41]

40% Have work disability (N=88)

19% Are unemployed due to their disease (N=94)

43% Felt AAV limited their work capacity (N=94)

50% Felt AAV hindered their careers (N=94)

43% Suggested AAV led to a salary reduction (N=94)

Adapted from Benarous L et al. 2017.[41]

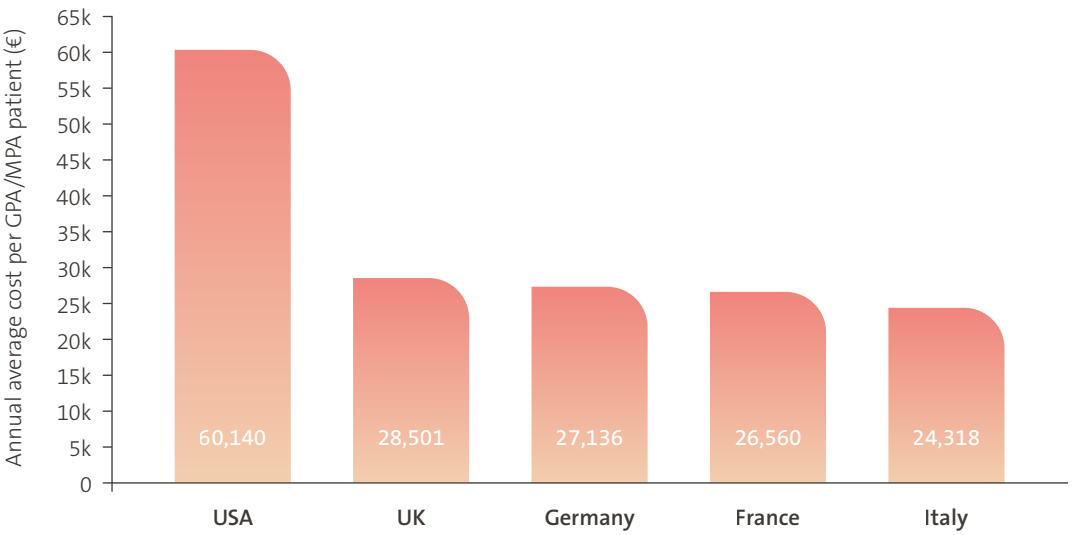
Burden on elderly patients

In elderly patients (>65 years), the economic burden is driven by healthcare costs associated with morbidities.[43,44] ESRD is a key driver, increasing the length of hospitalisations and the cumulative cost of care.[43,45]

Burden on healthcare systems

The total cost of illness in working-age and elderly AAV patients imposes a major burden on healthcare systems.[16,19,46–48] Findings from independent investigations from different countries around the world reveal that, at €60,140 per year, the USA has the highest annual average cost per GPA and MPA patient, followed by the UK, Germany, France and Italy (Figure 9).[16,19,46–48]

Figure 9. Annual average healthcare cost (€) of AAV per GPA/MPA patient in the USA and European countries[16,19,46–48]



Adapted from Kong AM et al. 2018,[16] de Arellano Serna R et al. 2020,[19] Genreau M et al. 2020,[46] Hellmich B et al. 2021[47] and Perrone V et al. 2022.[48]

The high healthcare costs are driven by hospitalisation,[18,19,46,47] relapse[16,49] and severe concomitant morbidities, especially ESRD.[18,49] GPA and MPA patients can be hospitalised for 6 to 13 days per quarter depending on the presence of comorbidities.[17] In-patient healthcare costs make the biggest contribution to the total cost (Table 3).[19,46,50]

Table 3. Total in-patient costs per AAV patient per year in Canada, the UK and France

CANADA	€49,339 (GPA only)[50]
UK	€17,597[19]
FRANCE	€16,201 (GPA/MPA only)[46]

The healthcare cost associated with relapsing patients is four times greater than the cost associated with patients who do not relapse (€50,541 versus €12,913, respectively).[49] As to ESRD, up to 28% of AAV patients with renal involvement may progress to ESRD.[38] The average annual cost to the NHS in England per patient who develops ESRD and requires dialysis is £23,426 (based on 2009/2010 data).[51]

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The unmet needs in the treatment of AAV (GPA/MPA)

The unmet needs in the treatment of AAV (GPA/MPA)

Key points

- The rarity and non-specific nature of AAV leads to a delay in diagnosis of more than 6 months in one-third of patients[1]
- The current SoC (GCs + immunosuppressants[2]) is associated with substantial AEs, especially infections and organ damage[3–6]
- The leading cause of mortality in GPA and MPA patients within the first year is treatment-related infection[3,4]
- One in three (36%) patients fails to achieve complete remission by 6 months without GCs[7]
- Even if remission is achieved, relapses are common and increase organ damage over time[5]
- The current SoC does not target a key mechanism of disease in GPA/MPA[8–10]

Diagnosis of AAV is often delayed[1,11]

Given that AAV can cause irreversible damage to critical organs and increase the risk of mortality,[3,4,12] early diagnosis and treatment are important goals.[13] However, the relative rarity and non-specific presentation of AAV (GPA/MPA/EGPA) lead to a delay in diagnosis of more than 6 months in one-third of patients.[1]

In a retrospective study of AAV (GPA/MPA/EGPA) patients (N=171) looking at the outcomes of those with uncommon presentations (n=8), the mean delay in diagnosis from time of symptom development was 12 months.[11] If the clinical onset of AAV is manifested mainly in the kidneys, a quick diagnosis may be delayed due to the often-silent nature of kidney disease.[4]

The current SoC is associated with substantial AEs[3–6]

Guidelines for managing AAV were provided in 2022 by the European Alliance of Associations for Rheumatology (EULAR),[2] and in 2024 by Kidney Disease: Improving Global Outcomes (KDIGO).[14]

The SoC for AAV recommended by EULAR and KDIGO includes treatment with non-specific immunosuppressants in combination with GCs.[2,14] EULAR recommends treatment with a combination of GCs and either rituximab or cyclophosphamide in patients with new-onset or relapsing GPA/MPA with organ-threatening or life-threatening disease.[2] Similarly, the KDIGO guidelines also recommend using GCs in combination with rituximab or cyclophosphamide for the initial treatment of new-onset AAV.[14]

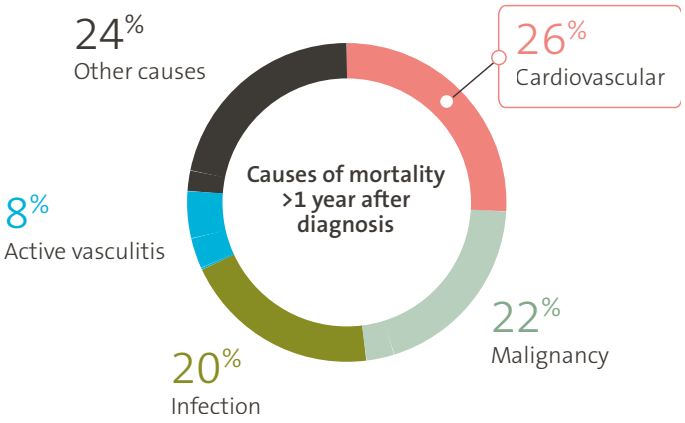
As mentioned in the previous section, the greatest threat to GPA and MPA patients in the first year of therapy is posed by AEs rather than active disease.[3] The most common AEs are infections (especially of the urinary and respiratory tracts), anaemia, hypertension and leukopenia.[6] Organ damage due to GC use is another major issue.[5]

Data from 535 patients from four EUVAS trials of newly diagnosed GPA and MPA patients were analysed to determine the factors associated with long-term organ damage, as assessed using the VDI.[5] A total of 296 patients had GC use and VDI data available at long-term follow-up (approximately 7 years after trial entry).[5] Long-term GC use was found to be independently associated with high levels of organ damage.[5] GPA and MPA patients with long-term GC use were more likely to have a VDI score ≥5 compared with patients with short-term GC use.[5]

The current SoC increases the risk of mortality[3,4]

SoC-related toxicity and AEs are also linked with mortality, both in the short and long terms.[3,4] The leading cause of mortality in GPA and MPA patients within the first year is infection.[3,4] After 1 year, the primary cause of mortality is cardiovascular disease, followed by malignancy and infection (Figure 10).[4]

Figure 10. Major causes of death after the first year of AAV diagnosis[4]



Adapted from Flossmann O et al. 2011.[4]

Many AAV patients do not achieve or sustain remission with or without SoC[7,15]

Achieving and sustaining remission without prolonged use of GCs can be challenging.[7,15] This was highlighted by a multicentre, randomised, double-blind trial (N=197) that investigated whether rituximab + GCs was inferior to cyclophosphamide + GCs at inducing remission by 6 months, with the GCs being tapered off.[7] The primary endpoint was remission of disease (BVAS/WG of 0) and successful completion of the GC (prednisone) taper at 6 months.[7] By 6 months, a substantial proportion of the patients in both groups failed to achieve complete remission (Table 4).[7]

Table 4. Patients (%) who failed to achieve/maintain remission at 6 and 12 months after completion of GC taper at 6 months[7,15]

	RITUXIMAB GROUP (n=99)	CYCLOPHOSPHAMIDE GROUP (n=98)
Patients (%) who failed to achieve complete remission by 6 months[7]	36	47
Patients (%) who failed to maintain complete remission at 12 months[14]	52	61

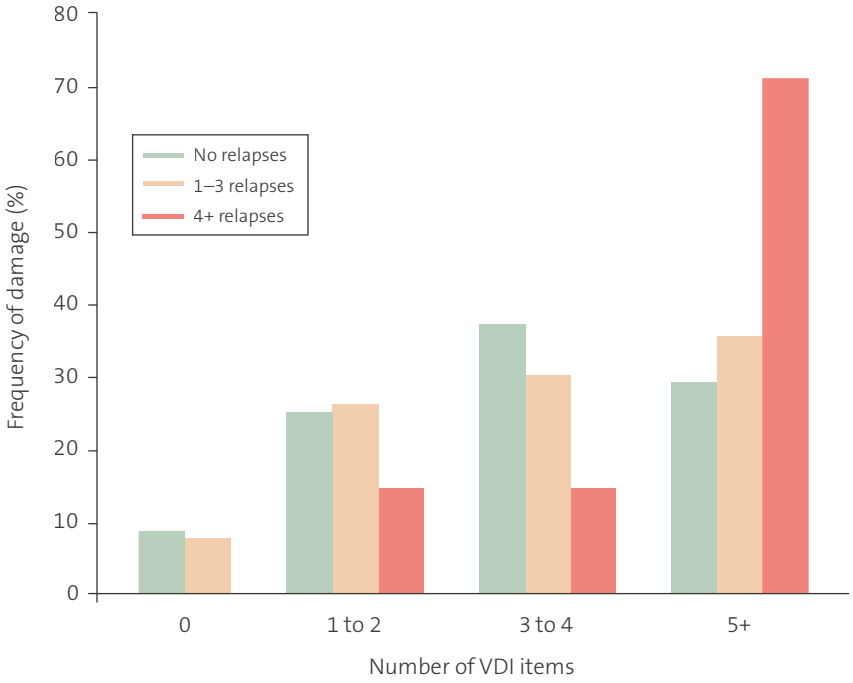
If complete remission is not achieved, either as a result of refractory disease or cessation of therapy due to fear of further GC toxicity, the disease can 'smoulder' and continue to exacerbate organ damage.[16]

Frequent relapses remain a common problem and result in greater organ damage over time[5]

Even if remission is achieved, with or without GCs, relapses are common, leading to an increase in organ damage over time.[5] According to data from the EUVAS study introduced above, the accumulation of organ damage over time is independently associated not only with long-term GC use but also:[5]

- Older age at baseline
- Lower glomerular filtration rate (GFR)
- Higher BVAS
- Increasing number of relapses (Figure 11)

Figure 11. Frequency of organ damage by number of relapses[5]



Reproduced from Robson J et al. 2015.[5]

The current SoC does not target a key mechanism of disease in GPA/MPA[8–10]

A key element of the pathogenesis of AAV is activation of the alternative complement pathway, resulting in the formation of C5a and the establishment of a vicious cycle that amplifies ANCA-induced inflammation and vascular necrosis (Figure 2; page 11).[8] One of the major drawbacks of the current SoC is that it's not designed to selectively target C5a and its downstream effects.[8–10] Targeting the underlying inflammatory process in AAV (GPA/MPA) is vital to:[8,17]

1. Improve remission rates
2. Reduce relapse rates
3. Reduce GC toxicity

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Avacopan Vifor introduction and mechanism of action

Avacopan Vifor introduction and mechanism of action

Key points

- Avacopan Vifor is a small-molecule antagonist of C5aR1 and a first-in-class therapy for adults suffering from severe, active GPA or MPA,[1,2] the most common forms of AAV[3,4]
- Avacopan Vifor selectively targets a key driver of vascular inflammation in GPA/MPA.[1] As such, it is not expected to interfere with other important aspects of complement system activation, such as the formation of MACs[1]
- Avacopan Vifor is the first targeted treatment for GPA/MPA recognised by EULAR and KDIGO[1,4–6]

Avacopan Vifor is a first-in-class orally administered therapy that inhibits a key driver of vascular inflammation in GPA and MPA.[1,4] Each hard capsule contains 10 mg of avacopan, the active substance.[2]

Avacopan Vifor, in combination with a rituximab or cyclophosphamide regimen, is indicated for the treatment of adult patients with severe, active GPA or MPA.[2] It is not indicated for the treatment of EGPA.[2]

Mechanism of action

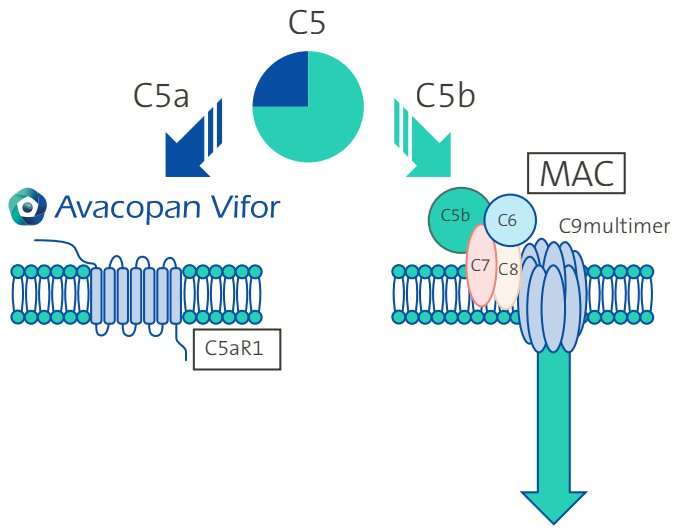
Avacopan Vifor is a small-molecule selective antagonist of the human C5aR1.[1,2] It works by inhibiting the pro-inflammatory effects of C5a by blocking C5aR1 in neutrophils and vascular endothelial cells (Figure 12).[1,2,7] In so doing, Avacopan Vifor prevents:[1,2]

1. Adherence of neutrophils to vascular endothelial cells
2. An increase in the permeability of vascular endothelial cells, which would further mediate inflammation
3. Migration, priming and activation of additional neutrophils and thus establishment of the vicious loop that amplifies inflammation and vascular necrosis

Avacopan Vifor is not expected to block other important aspects of complement system activation, such as:[1]

- The formation of MACs, which are important for defence against infection
- The functions of complement component 5a-like receptor 2 (C5L2)

Figure 12. Selective blockage by Avacopan Vifor of C5aR1 without impact on formation of MACs[1]



Avacopan Vifor reduces the pro-inflammatory effects of C5a[1]

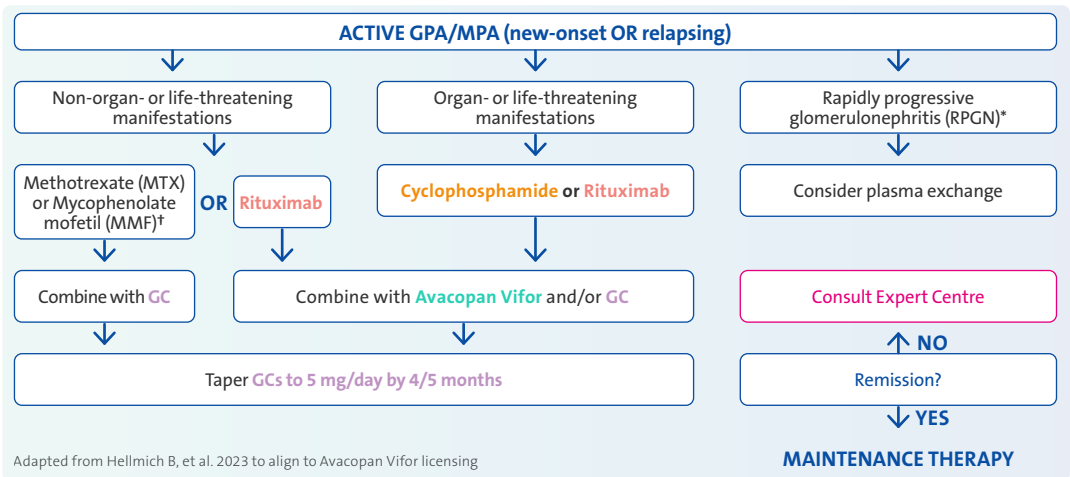
Avacopan Vifor is not expected to interfere with other aspects of complement system activation[1]

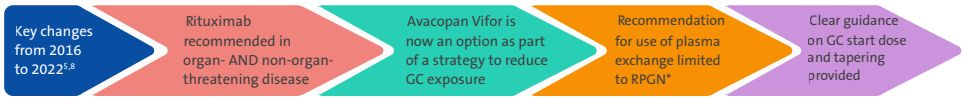
Adapted from Bekker P et al. 2016.[1]

Recognised by EULAR and KDIGO[5,6]

The EULAR recommendations for the management of ANCA-associated vasculitis update in 2022 are based on the phase 3 ADVOCATE study. The EULAR 2022 recommendation level of evidence 1b states that Avacopan Vifor, in combination with rituximab or cyclophosphamide, may be considered for induction of remission in GPA or MPA, as part of a strategy to substantially reduce exposure to GCs. Avacopan Vifor is also now part of the 2022 EULAR algorithm for the induction of remission in GPA and MPA (Figure 13).[5]

Figure 13. The 2022 EULAR algorithm for induction of remission in treatment of GPA and MPA includes Avacopan Vifor in combination with rituximab or cyclophosphamide[5]



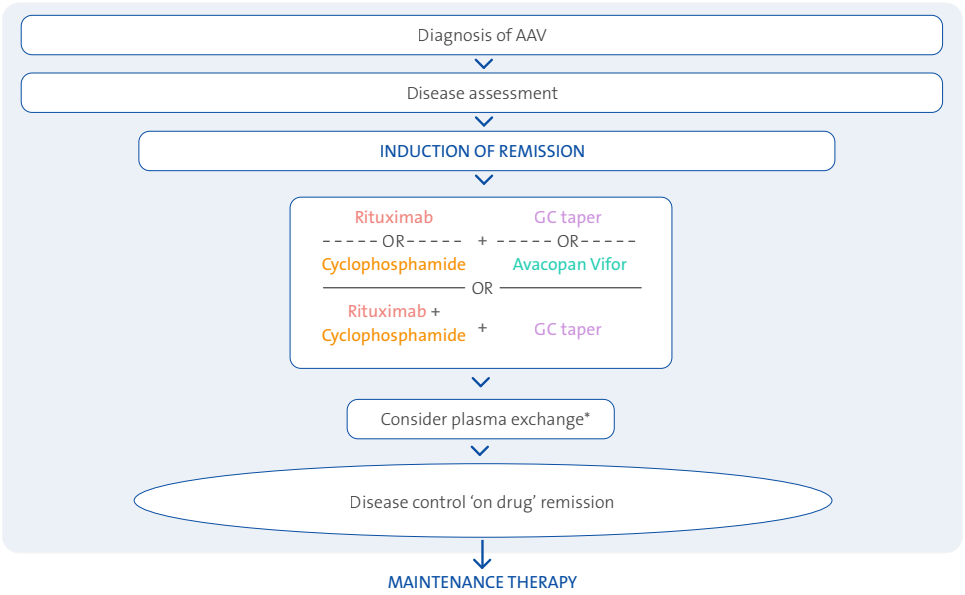


*In selected patients with serum creatinine >300 µmol/L due to active glomerulonephritis, plasma exchange may be considered taken into account individual risk for end-stage kidney disease and patient preferences[5]

†Not approved in the UK for the treatment of AAV (GPA/MPA).

Avacopan Vifor was also recognised by KDIGO in their 2024 clinical practice guidelines for the management of AAV, which acknowledged the ability of Avacopan Vifor in controlling disease and its potential to improve renal function, reduce GC exposure and improve patient quality of life. The guidelines state that Avacopan Vifor may be used as an alternative to GCs for the induction of remission in combination with rituximab or cyclophosphamide (Figure 14).[6]

Figure 14. Avacopan Vifor is part of the practical treatment algorithm for AAV with kidney involvement (practice point 9.3.1.1)[6]



*Practice Point 9.3.1.9: Consider plasma exchange for patients with serum creatinine >3.4 mg/dl (>300 µmol/l), patients requiring dialysis or with rapidly increasing serum creatinine, or patients with diffuse alveolar haemorrhage who have hypoxaemia.[6]

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Avacopan Vifor clinical trial programme

Avacopan Vifor clinical trial programme

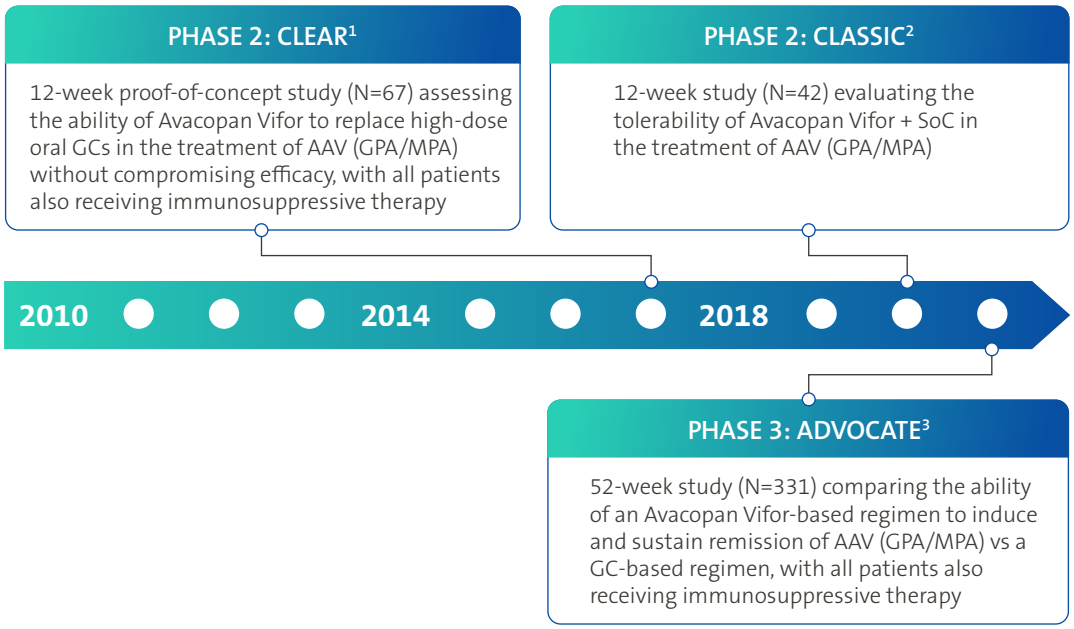
Key points

- The Avacopan Vifor clinical trial programme consisted of two phase 2 (CLEAR and CLASSIC) and one phase 3 (ADVOCATE) trials[1–3]
- CLEAR investigated whether Avacopan Vifor could replace high-dose oral GCs in the treatment of GPA and MPA without compromising efficacy, with all patients also receiving immunosuppressive therapy[1]
- CLASSIC evaluated the tolerability of Avacopan Vifor + SoC (oral GCs + immunosuppressive therapy) for the treatment of GPA and MPA[2]
- ADVOCATE compared the ability of Avacopan Vifor with that of tapered GCs to induce and sustain remission in GPA and MPA, with all patients also receiving immunosuppressive therapy[3]

Programme overview

The efficacy and tolerability of Avacopan Vifor were evaluated in a clinical trial programme that consisted of two phase 2 and one phase 3 studies (Figure 15).[1–3]

Figure 15. Clinical trial programme of Avacopan Vifor



Adapted from Jayne DRW et al. 2017,[1] Merkel PA et al. 2020[2] and Jayne DRW et al. 2021.[3]

Phase 2 clinical trials: CLEAR and CLASSIC

The objectives, designs, results and conclusions of the two phase 2 trials, CLEAR and CLASSIC, are summarised in tables 5 and 6.

Table 5. Overview of CLEAR[1]

DESIGN		12-week, randomised, placebo-controlled, three-arm, phase 2, proof-of-concept trial
OBJECTIVE		To determine whether Avacopan Vifor could replace high-dose oral GCs in the treatment of GPA and MPA without compromising efficacy
POPULATION		Adults (N=67) with newly diagnosed or relapsing GPA or MPA
INTERVENTIONS		• Treatment arm 1 (n=22): Avacopan Vifor (30 mg orally, twice daily) + reduced-dose prednisone (20 mg daily) • Treatment arm 2 (n=22): Avacopan Vifor (30 mg orally, twice daily) without prednisone • Control arm (n=23): placebo + prednisone starting at 60 mg daily All patients received cyclophosphamide followed by azathioprine or rituximab
PRIMARY ENDPOINT		Proportion of patients achieving clinical response at Week 12, defined as ≥50% reduction of BVAS from baseline, with no worsening in any body system
RESULTS	**PRIMARY ENDPOINT (EFFICACY)**	Clinical response at Week 12 was achieved in: • 19/22 (86.4%) patients in the Avacopan Vifor + reduced-dose prednisone arm (difference from control: 16.4%; p=0.002 for non-inferiority) • 17/21 (81.0%) patients in the Avacopan Vifor without prednisone arm (difference from control: 11.0%; p=0.01 for non-inferiority) • 14/20 (70.0%) patients in the placebo + prednisone arm
	TOLERABILITY	AEs of any kind occurred in: • 19/22 (86%) patients in the Avacopan Vifor + reduced-dose prednisone arm • 21/22 (96%) patients in the Avacopan Vifor without prednisone arm • 21/23 (91%) patients in the placebo + prednisone arm
CONCLUSION		Avacopan Vifor is effective at replacing high-dose oral GCs in the treatment of adults with newly diagnosed/relapsing GPA or MPA

Table 6. Overview of CLASSIC[2]

DESIGN		12-week, randomised, placebo-controlled, three-arm, phase 2 trial
OBJECTIVE		To evaluate the tolerability of Avacopan Vifor + SoC (oral GCs + cyclophosphamide or rituximab) for the treatment of GPA and MPA
POPULATION		Adults (N=42) with newly diagnosed or relapsing GPA or MPA
INTERVENTIONS		• Treatment arm 1 (n=13): Avacopan Vifor (10 mg orally, twice daily**) + SoC • Treatment arm 2 (n=16): Avacopan Vifor (30 mg orally, twice daily) + SoC • Control arm (n=13): placebo + SoC
ENDPOINTS	**PRIMARY**	Incidence of AEs
	MAIN EFFICACY	Proportion of patients achieving clinical response at Day 85, defined as ≥50% reduction of BVAS from baseline, with no worsening in any body system
RESULTS*	**PRIMARY ENDPOINT (TOLERABILITY)**	AEs of any kind occurred in: • 11/13 (85%) patients in the Avacopan Vifor 10 mg + SoC arm • 15/16 (94%) patients in the Avacopan Vifor 30 mg + SoC arm • 13/13 (100%) patients in the placebo + SoC arm
	MAIN EFFICACY ENDPOINT	Clinical response at Day 85 was achieved in: • 11/12 (92%) patients in the Avacopan Vifor 10 mg + SoC arm • 12/15 (80%) patients in the Avacopan Vifor 30 mg + SoC arm • 11/13 (85%) patients in the placebo + SoC arm
CONCLUSIONS		Avacopan Vifor + SoC is well tolerated in the treatment of adults with newly diagnosed/relapsing GPA or MPA, and the higher (30 mg) dose appeared to improve time to remission

*Because CLASSIC was primarily a safety study, efficacy results are descriptive, and neither safety nor efficacy outcomes were powered statistically.[2]

**Licensed dosing of Avacopan is 30mg BD

Phase 3 clinical trial: ADVOCATE

The study design of the phase 3 clinical trial, ADVOCATE, is provided in Table 7 and Figure 16. Baseline patient characteristics are presented in Table 8. The results and conclusions of the trial are presented in detail in the following efficacy (page 36) and tolerability (page 43) sections.

Table 7. The objectives, design and endpoints of ADVOCATE

DESIGN[3]	52-week, randomised, double-dummy, controlled, phase 3 trial
OBJECTIVE[3]	To compare the ability of Avacopan Vifor with that of tapered GCs to induce and sustain remission in GPA and MPA patients, with both arms also receiving immunosuppressive therapy
POPULATION[3]	Patients (N=331) with newly diagnosed or relapsing GPA or MPA
INCLUSION CRITERIA[4]	• Age ≥12 years* • Newly diagnosed/relapsing GPA or MPA according to Chapel Hill Consensus Conference definitions • Indicated for treatment with rituximab or cyclophosphamide • PR3- or MPO-positivity • eGFR of ≥15 mL/min/1.73 m^2 • At least one major or three non-major BVAS items, or at least two renal BVAS items of haematuria and proteinuria
EXCLUSION CRITERIA[4]	• Alveolar haemorrhage requiring invasive pulmonary ventilation anticipated to last beyond screening • Any other multisystem autoimmune disease • Coagulopathy or bleeding disorder • Dialysis or plasma exchange within 12 weeks prior to screening • Kidney transplant • Any of the following treatments prior to screening: – Cyclophosphamide within 12 weeks – Rituximab within 12 months (or 6 months with B cell reconstitution, CD19 count >0.01 x 10^9/L) – Cumulative dose of IV GCs >3 g within 4 weeks – Oral GCs of >10 mg per day prednisone (or equivalent) for >6 weeks continuously
INTERVENTIONS[3]	• Treatment arm (n=166): Avacopan Vifor + placebo oral GCs • Control arm (n=164): oral GCs + placebo Avacopan Vifor All patients also received either rituximab or cyclophosphamide, with the latter being followed by azathioprine

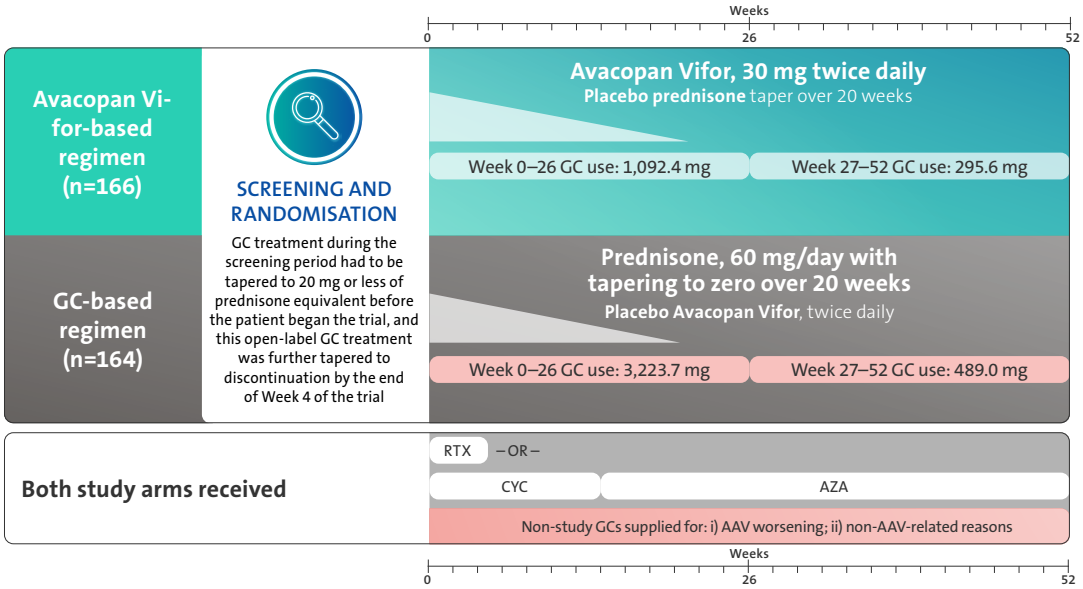
CO-PRIMARY ENDPOINTS[3]	• Proportion of patients achieving remission at Week 26, defined as a BVAS of 0 and no use of GCs in the previous 4 weeks • Proportion of patients achieving sustained remission, defined as remission at weeks 26 and 52 and no use of GCs in the previous 4 weeks Both endpoints were tested for non-inferiority and superiority
SECONDARY ENDPOINTS[3†]	• Change in GC-induced toxicity as measured by change from baseline over the first 26 weeks in the GTI • Early remission, defined as BVAS 0 at Week 4 • Change from baseline over 52 weeks in health-related QoL as measured by the domains and component scores of the SF-36v2 and EQ-5D-5L visual analogue scale (VAS) and index • Proportion of patients and time to experiencing a relapse‡ • In patients with renal disease at baseline (based on the BVAS renal component), the percent change in eGFR from baseline over 52 weeks • In patients with renal disease at baseline (based on the BVAS renal component), the percent change in UACR from baseline over 52 weeks • In patients with renal disease at baseline (based on the BVAS renal component), the percent change in urinary MCP-1:creatinine ratio from baseline over 52 weeks • Change in the VDI from baseline over 52 weeks

*The mean age of patients in ADVOCATE was 61.2 and 60.5 years for the Avacopan Vifor and GC arms, respectively.[3] For additional details, visit clinicaltrials.gov (study code: NCT02994927).

†This study was not powered to detect differences in the secondary/exploratory endpoints.[3] There was no prespecified plan for adjustment of confidence intervals for multiplicity of the secondary endpoints, and no definite conclusions can be drawn from these data.[3]

‡Relapse was defined as worsening of disease after previous achievement of a BVAS of 0.[3] Worsening was defined as recording at least one major BVAS item, three or more minor BVAS items, or one or two minor BVAS items at two consecutive trial visits.[3]

Figure 16. Study design of ADVOCATE[3,4]



Patients were randomised in a 1:1 ratio to receive either the Avacopan Vifor- or GC-based regimen. The patients in the Avacopan Vifor arm received 30 mg of Avacopan Vifor twice daily for 52 weeks + placebo prednisone tapered over 20 weeks. The patients in the GC arm received placebo Avacopan Vifor twice daily for 52 weeks + prednisone tapered from 60 mg/day to zero over 20 weeks. All patients also received one of three regimens: intravenous rituximab (RTX) at a dose of 375 mg per square metre of body-surface area per week for 4 weeks; intravenous cyclophosphamide (CYC) at a dose of 15 mg per kg of body weight up to 1.2 g on day 1 and at weeks 2, 4, 7, 10 and 13; or oral cyclophosphamide at a dose of 2 mg per kg of body weight up to 200 mg per day for 14 weeks. No rituximab was given beyond the first 4 weeks. From week 15 onwards, cyclophosphamide was followed by oral azathioprine (AZA) at a dose of 2 mg per kg per day. Investigators were instructed that the use of additional GCs, not supplied as trial medication, was to be avoided as much as possible. Adapted from Jayne DRW et al. 2021[3] and Jayne DRW et al. 2021 Suppl.[4]

Table 8. Baseline characteristics of patients in ADVOCATE[3]

AGE, mean ± SD	61.2 ± 14.6	60.5 ± 14.5
MALE, number (%)	98 (59.0)	88 (53.7)
GRANULOMATOSIS WITH POLYANGIITIS, number (%)	91 (54.8)	90 (54.9)
MICROSCOPIC POLYANGIITIS, number (%)	75 (45.2)	74 (45.1)
RELAPSED PATIENTS, number (%)	51 (30.7)	50 (30.5)
NEWLY DIAGNOSED PATIENTS, number (%)	115 (69.3)	114 (69.5)
BVAS SCORE, mean ± SD	16.3 ± 5.9	16.2 ± 5.7
GC USE DURING SCREENING PERIOD, number (%)	125 (75.3)	135 (82.3)

References

1. Jayne DRW, et al. *J Am Soc Nephrol* 2017;28(9):2756–67. **2.** Merkel PA, et al. *ACR Open Rheumatol* 2020;2(11):662–7. **3.** Jayne DRW, et al. *N Engl J Med* 2021;384(7):599–609. **4.** Jayne DRW, et al. *N Engl J Med* 2021;384(7):599–609. [Suppl Appendix]

Avacopan Vifor efficacy profile

Avacopan Vifor efficacy profile

Key points

In the phase 3 trial, ADVOCATE, the Avacopan Vifor-based regimen:[1]

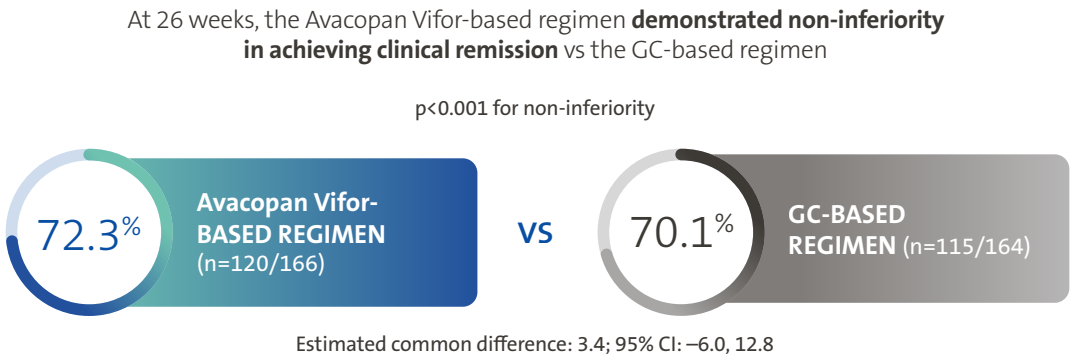
- Demonstrated a non-inferior remission rate at Week 26 and a statistically superior sustained remission rate at Week 52 versus the GC-based regimen
- Was associated with reduced use of GCs and a larger reduction in GC toxicity compared with the GC-based regimen
- Was associated with fewer potentially GC-related AEs in all AE categories than was the GC-based regimen
- Produced a larger numerical increase in eGFR at weeks 26 and 52 versus the GC-based regimen in patients with renal disease at baseline
- Led to greater numerical improvements in physical domains of HRQoL than did the GC-based regimen

Co-primary endpoints

Remission at 26 weeks

The Avacopan Vifor-based regimen was non-inferior to the GC-based regimen with regards to achieving remission at 26 weeks, with clinical remission being observed in 120/166 (72.3%) patients in the Avacopan Vifor group and 115/164 (70.1%) patients in the GC group (p<0.001 for non-inferiority; p=0.24 for superiority; Figure 17).[1]

Figure 17. Proportion (%) of patients achieving remission at 26 weeks[1]

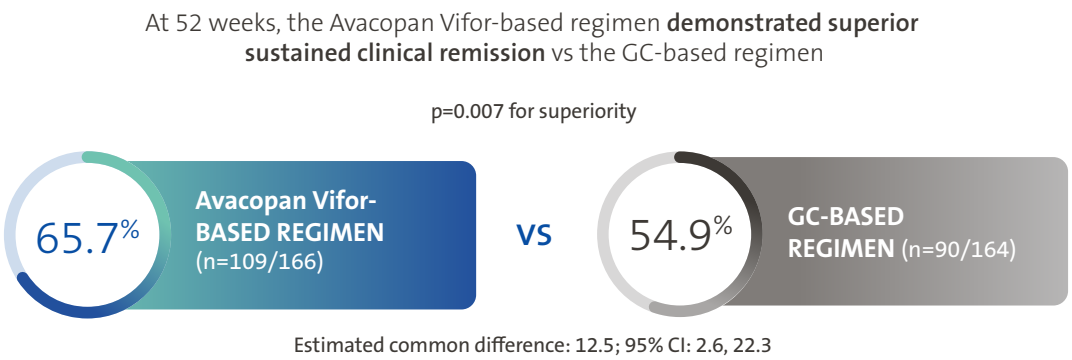


Adapted from Jayne DRW et al. 2021.[1]

Sustained remission at 52 weeks

Compared with the GC-based regimen, the Avacopan Vifor-based regimen demonstrated superior sustained remission at 52 weeks, with sustained clinical remission being observed in 109/166 (65.7%) patients in the Avacopan Vifor group and in 90/164 (54.9%) patients in the GC group (p<0.001 for non-inferiority; p=0.007 for superiority; Figure 18).[1]

Figure 18. Proportion (%) of patients achieving sustained clinical remission at 52 weeks[1]



Adapted from Jayne DRW et al. 2021.[1]

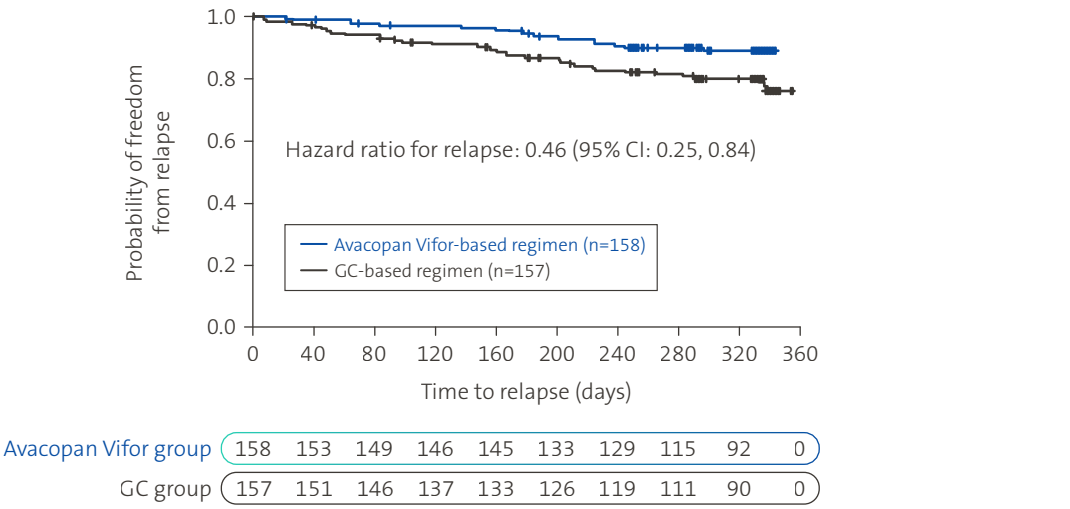
Secondary endpoints

This study was not powered to detect differences in the secondary/exploratory endpoints.[1] There was no prespecified plan for adjustment of confidence intervals for multiplicity of the secondary endpoints, so no definite conclusions can be drawn from these data.[1]

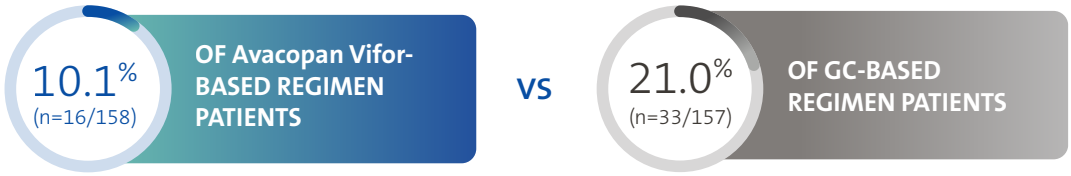
Time to relapse, and proportion of patients who experienced relapse

A total of 16 of 158 patients (10.1%) in the Avacopan Vifor group and 33 of 157 patients (21.0%) in the GC group experienced relapses.[1] The patients taking the Avacopan Vifor-based regimen had a 54% relative reduced risk of relapse over 52 weeks compared with the patients taking the GC-based regimen (Figure 19).[1]

Figure 19. Kaplan–Meier plot of time to relapse and proportion (%) of patients who experienced a relapse in each group[1]



Proportions of **patients who had a relapse** over 52 weeks of treatment



Adapted from Jayne DRW et al. 2021.[1]

Reduced glucocorticoid use

An Avacopan Vifor-based regimen allowed physicians to reduce GC use (Figure 20).[2] Between Weeks 27–52, 73% of patients on the Avacopan Vifor-based regimen (n=121/166) were GC free vs 61% on a GC-based regimen (n=100/164), with a lower cumulative dose of GCs.[3]

Figure 20. Reduction of the use of GCs by the Avacopan Vifor-based regimen[2]

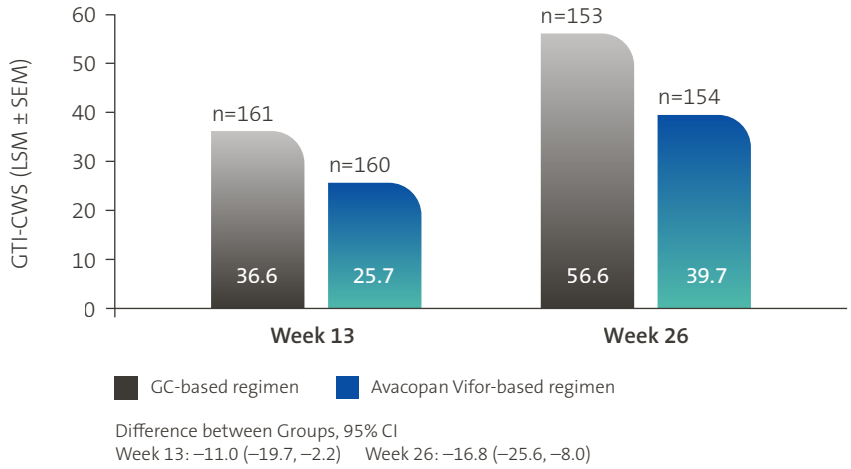
lower total GC dose on an Avacopan Vifor-based regimen[2]

Mean total GC dose: 1,676 mg vs 3,847 mg

Reduction of GC toxicity

Patients on the Avacopan Vifor-based regimen manifested a numerically larger reduction in the measures of GC toxicity at weeks 13 and 26 compared with the patients on the GC-based regimen.[1] This was indicated by reductions in both Glucocorticoid Toxicity Index (GTI) Cumulative Worsening Score (CWS; Figure 21) and GTI Aggregate Improvement Score (AIS; Figure 22).[1]

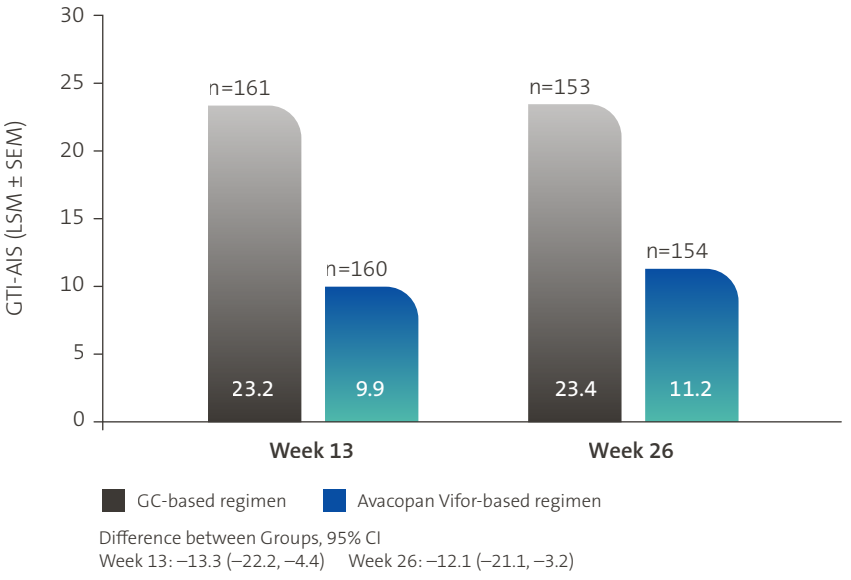
Figure 21. GTI-CWS at weeks 13 and 26[1,3]



Difference between Groups, 95% CI
Week 13: –11.0 (–19.7, –2.2) Week 26: –16.8 (–25.6, –8.0)

The GTI-CWS ranges from 0 to 410, with higher scores indicating greater severity of toxic effects.[1] When calculating GTI-CWS, new toxicities that occur are added, but transient toxicities that resolve on follow-up are not removed.[4] Adapted from Jayne DRW et al. 2021[1] and Jayne DRW et al. 2021 Suppl.[3]

Figure 22. GTI-AIS at weeks 13 and 26[1,3]



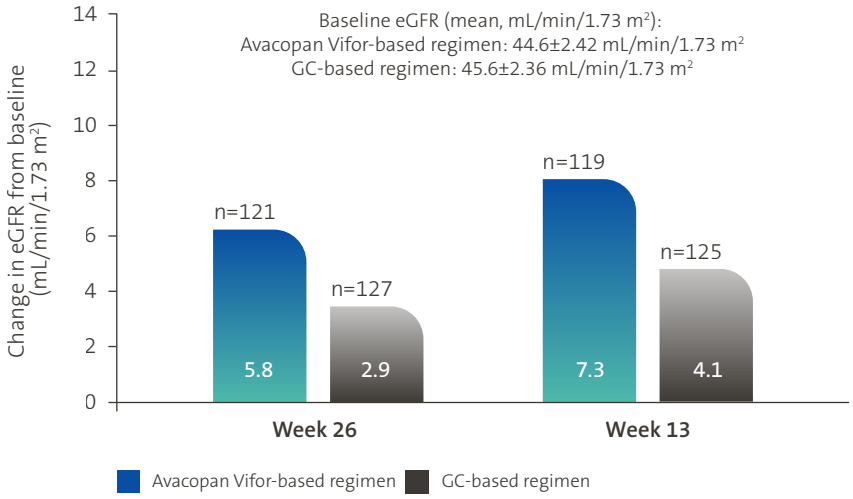
Difference between Groups, 95% CI
Week 13: –13.3 (–22.2, –4.4) Week 26: –12.1 (–21.1, –3.2)

GTI-AIS ranges from –317 to 410, with higher scores indicating greater severity of toxic effects.[1] In contrast to GTI-CWS, GTI-AIS increases when toxicities are reported and decreases when improvement occurs.[4] Adapted from Jayne DRW et al. 2021[1] and Jayne DRW et al. 2021 Suppl.[3]

Numerical improvements of eGFR in patients with chronic kidney disease (CKD) at baseline

At weeks 26 and 52, numerical increases in eGFR were seen in both the Avacopan Vifor and GC groups, with greater improvements in the former (Figure 23).[1] The mean changes in eGFR from baseline at Week 52 were 7.3 and 4.1 mL/min/1.73 m^2 in the Avacopan Vifor and GC groups, respectively (difference: 3.2 mL/min/1.73 m^2).[1]

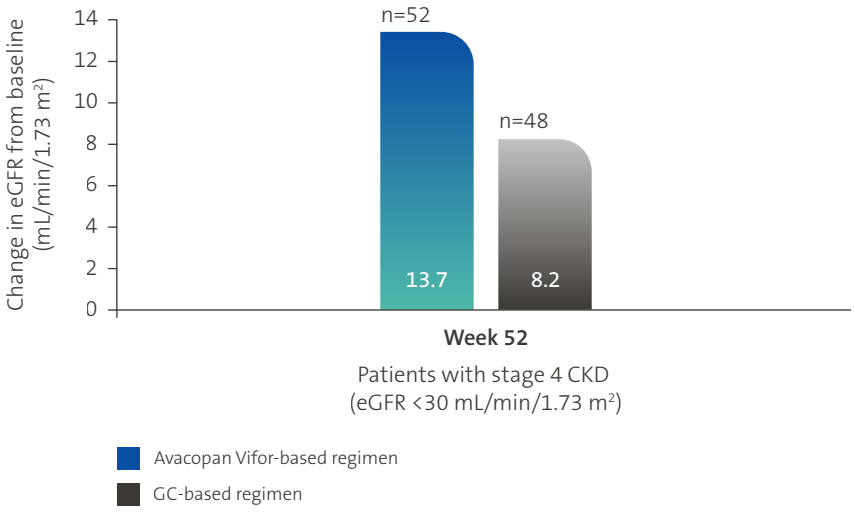
Figure 23. Mean changes in eGFR at weeks 26 and 52 in patients with CKD[1,3]



Adapted from Jayne DRW et al. 2021[1] and Jayne DRW et al. 2021 Suppl.[3]

Furthermore, based on a post-hoc analysis, the numerical increase in eGFR in patients with stage 4 CKD was 13.7 and 8.2 mL/min/1.73 m^2 in the Avacopan Vifor and GC arms, respectively (Figure 24).[1]

Figure 24. Mean changes in eGFR at Week 52 in patients with stage 4 CKD[1,3]



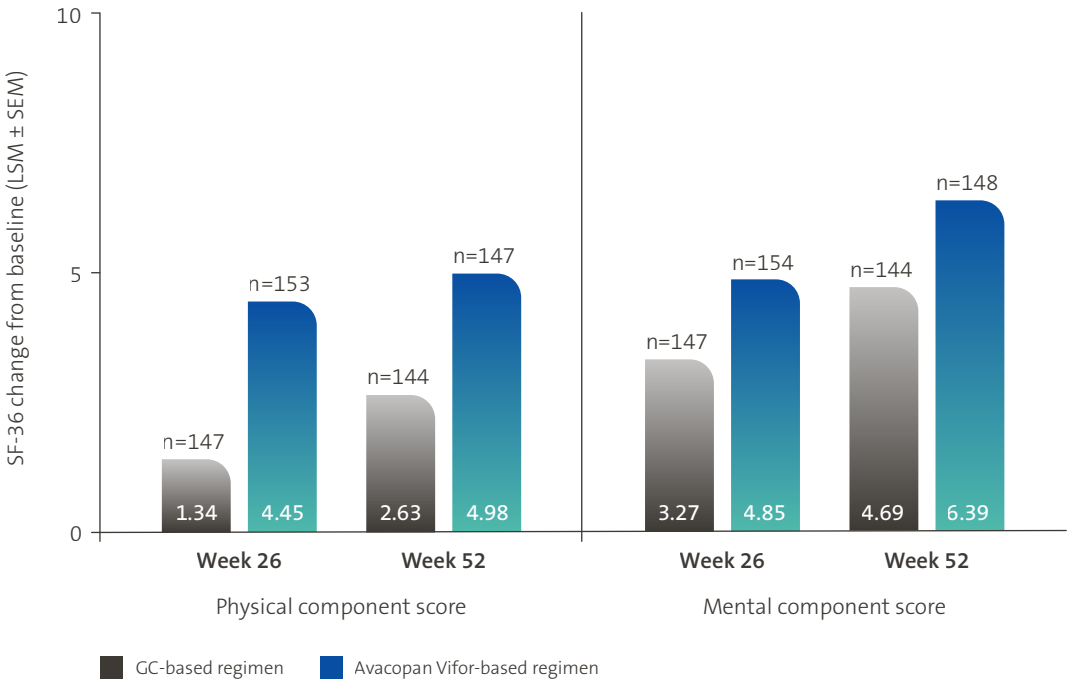
Adapted from Jayne DRW et al. 2021[1] and Jayne DRW et al. 2021 Suppl.[3]

Numerical improvement of physical and mental HRQoL

HRQoL was measured using version 2 of the 36-Item Short Form Health Survey (SF-36).[1]

Compared with the GC-based regimen, at weeks 26 and 52, greater numerical improvements were seen in the Avacopan Vifor-based regimen in both SF-36 physical component score and SF-36 mental component score (Figure 25).[1,3]

Figure 25. Impact of the two treatment arms on physical and mental health based on SF-36[1,3]



The SF-36 score ranges from 0 to 100, with a higher score indicating a better QoL.[1] The SF-36 physical component score domains measured were physical functioning, 'role physical' (limitations due to physical functioning), bodily pain and general health perception.[3] The mental component score domains measured were mental health, 'role emotional' (limitations due to emotional functioning), social functioning and vitality.[3] Adapted from Jayne DRW et al. 2021[1] and Jayne DRW et al. 2021 Suppl.[3]

The greater numerical improvement in SF-36 scores in the Avacopan Vifor-based regimen is consistent with results from the phase 2 CLEAR and CLASSIC trials, which assessed HRQoL as a secondary endpoint.[5,6] The Avacopan Vifor-based regimens in these two trials were associated with greater numerical increases in HRQoL than were prednisone + immunosuppressive therapy (CLEAR)[6] and SoC (CLASSIC).[5]

References

1. Jayne DRW, et al. *N Engl J Med* 2021;384(7):599–609. **2.** Avacopan Vifor UK SmPC. **3.** Jayne DRW, et al. *N Engl J Med* 2021;384(7):599–609. [Suppl. Appendix]. **4.** Jayne DRW, et al. *Kidney Int Rep* 2021;6(4):S162–S163. Abstract only. **5.** Merkel PA, et al. *ACR Open Rheumatol* 2020;2(11):662–7. **6.** Jayne DRW, et al. *J Am Soc Nephrol* 2017;28(9):2756–67.

Avacopan Vifor tolerability profile

Avacopan Vifor tolerability profile

Key points

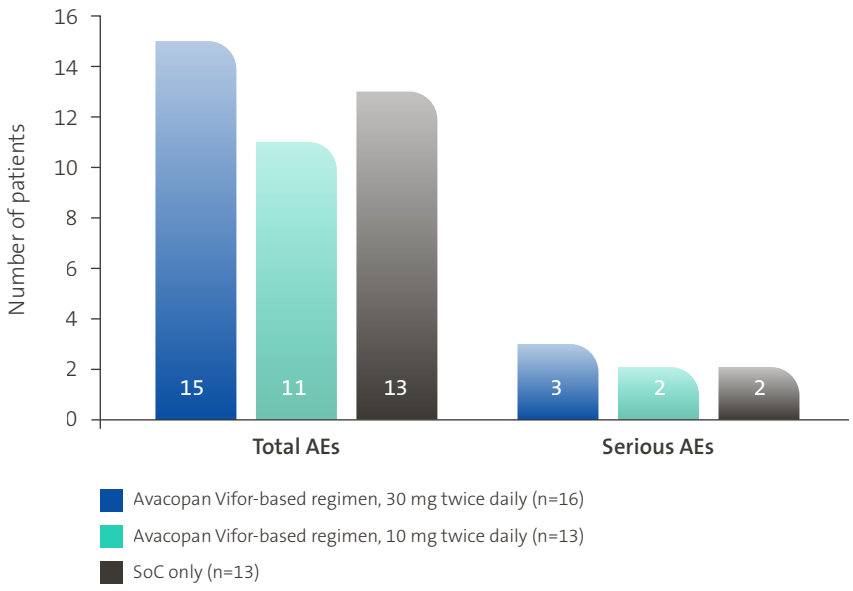
- Preliminary data from a small sample in the phase 2 trial, CLASSIC, indicated that Avacopan Vifor is generally well tolerated[1]
- The favourable tolerability profile of Avacopan Vifor was echoed in the phase 3 trial, ADVOCATE[2]
- In ADVOCATE, the Avacopan Vifor-based regimen was associated with fewer AEs of any kind, serious AEs, deaths, infections and potentially GC-related AEs versus the GC-based regimen[2]
- In the post-marketing setting, drug-induced liver injury and vanishing bile duct syndrome (VBDS), including cases with fatal outcome, have been reported[3]

Phase 2 trial tolerability profile

The phase 2 trial CLASSIC was specifically designed to evaluate the tolerability of Avacopan Vifor + SoC (oral GCs + cyclophosphamide or rituximab) in the treatment of GPA and MPA.[1]

In CLASSIC, the rate of AEs was comparable between the Avacopan Vifor and placebo arms of the trial.[1] Over the 12-week treatment period, a similar number of total and serious AEs was seen across all treatment groups (Figure 25).[1] The overall conclusion of CLASSIC was that Avacopan Vifor is well tolerated.[1]

Figure 25. Total and serious AEs over 12 weeks in the phase 2 trial, CLASSIC[1]



Adapted from Merkel PA et al. 2020.[1]

Avacopan Vifor tolerability profile

As per the Avacopan Vifor SmPC the most common AEs were nausea (23.5%), headache (20.5%), a decrease in white blood cell (WBC) count (18.7%), upper respiratory tract infection (14.5%), diarrhoea (15.1%), vomiting (15.1%) and nasopharyngitis (15.1%) (Table 10).[3] The most common serious AEs were liver function abnormalities (5.4%) and pneumonia (4.8%).[3]

In the post-marketing setting, drug-induced liver injury and VBDS, including cases with fatal outcome, have been reported (frequency unknown).[3]

Table 10. AEs observed in the phase 3 trial, ADVOCATE, and the post marketing setting, with the AEs in each cell being presented in the order of decreasing seriousness[3]

SYSTEM ORGAN CLASS	VERY COMMON (≥1/10)	COMMON (≥1/100 TO <1/10)	UNCOMMON (≥1/1,000 TO <1/100)	NOT KNOWN
Infections and infestations	Upper respiratory tract infection, Nasopharyngitis	Pneumonia, Rhinitis, Urinary tract infection, Sinusitis, Bronchitis, Gastroenteritis, Lower respiratory tract infection, Cellulitis, Herpes zoster, Influenza, Oral candidiasis, Oral herpes, Otitis media		
Blood and lymphatic system disorders		Neutropenia		
Nervous system disorders	Headache			
Gastrointestinal disorders	Nausea, Diarrhoea, Vomiting	Upper abdominal pain		
Hepatobiliary disorders	Increased liver function test*			Drug induced liver injury, Vanishing bile duct syndrome
Skin and subcutaneous tissue disorders			Angioedema	
Investigations	Decreased WBC count†	Increased blood creatine phosphokinase		

*Increased alanine aminotransferase, increased total blood bilirubin, abnormal hepatic function, increased gamma-glutamyl transferase, increased hepatic enzyme and increased transaminases.[3]

† Includes leukopenia.[3]

Serious AEs were experienced by 42.2% of patients taking the Avacopan Vifor-based regimen and 45.1% of patients taking the GC-based regimen.[2] A numerically higher number of AEs, deaths and infections was observed in the GC group (Table 11).[2]

Table 11. Comparison of AEs at 52 weeks in the phase 3 trial, ADVOCATE[2]

	Avacopan Vifor BASED REGIMEN (n=166)	GC-BASED REGIMEN (n=164)
AEs		
Patients with any AEs, n (%)	164 (98.8)	161 (98.2)
Number of events	1,779	2,139
SERIOUS AEs		
Patients with serious AEs, n (%)	70 (42.2)	74 (45.1)
Number of events	116	166
Patients with any life-threatening AEs, n (%)	8 (4.8)	14 (8.5)
Number of events	8	22
Patients with serious AEs related to vasculitis worsening	17 (10.2)	23 (14.0)
Number of events	18	36
Patients with serious AEs not related to vasculitis worsening	62 (37.3)	64 (39.0)
Number of events	98	130
DEATHS		
Total number of deaths, n (%)	2 (1.2)	4 (2.4)
INFECTIONS		
Number of serious infection events	25	31
PATIENTS WITH ANY POTENTIALLY GC-RELATED AEs		
Investigator-blinded assessment, n (%)	110 (66.3)	132 (80.5)

References

1. Merkel PA, et al. *ACR Open Rheumatol* 2020;2(11):662–7. **2.** Jayne DRW, et al. *N Engl J Med* 2021;384(7):599–609. **3.** Avacopan Vifor UK SmPC.

Avacopan Vifor dosage, administration and management

Avacopan Vifor dosage, administration and management

Key points[1]

Avacopan Vifor is contraindicated in patients with a hypersensitivity to the active substance, avacopan, or to any of the excipients

- Avacopan Vifor is taken as a fixed oral dose, with required monitoring
- The recommended dose is 30 mg taken orally twice daily, in the morning and evening, with food. Avacopan Vifor should be swallowed whole with water, and must not be crushed, chewed or opened
- Avacopan Vifor should be administered in combination with either rituximab or cyclophosphamide, with the latter being followed by either oral azathioprine or mycophenolate mofetil. GCs may also be used as clinically indicated
- Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and other parameters must be monitored, and treatment with Avacopan Vifor should be either temporarily or permanently stopped if certain criteria are met

Dosage

Treatment with Avacopan Vifor should be initiated and monitored by healthcare professionals who are experienced in the diagnosis and treatment of GPA or MPA.[1]

Avacopan Vifor is taken as a fixed oral dose.[1] The recommended dose is 30 mg (3 hard capsules of 10 mg each) taken orally, twice daily, morning and evening, with food.[1]

Avacopan Vifor should be administered in combination with either a rituximab or cyclophosphamide regimen as follows:[1]

Rituximab for 4 weekly intravenous doses

or

intravenous or oral cyclophosphamide for 13 or 14 weeks, followed by oral azathioprine or mycophenolate mofetil

GCs may also be used as clinically indicated.[1]

The twice-daily oral dose of Avacopan Vifor provides 24-hour C5aR1 coverage.[2]

Method of administration[1]

Avacopan Vifor is for oral use. The hard capsules should be taken with food and swallowed whole with water. They must not be crushed, chewed or opened.

Missed doses[1]

If a patient misses a dose, the missed dose should be taken as soon as possible unless within three hours of the next scheduled dose. If within three hours, the missed dose should be skipped.

Monitoring and dose management[1]

Monitoring[1]

Patients must be monitored for:

- Hepatic transaminases and total bilirubin at least least every 4 weeks after the start of therapy for the first 6 months of treatment, and as clinically indicated thereafter
- WBC count as clinically indicated and as part of the routine follow-up of the patient's underlying condition

Dose suspensions[1]

Treatment with Avacopan Vifor must be reassessed clinically and temporarily stopped if either ALT or AST is more than 3 times the upper limit of normal (ULN).

Treatment must be temporarily stopped in the event of any of the following:

- ALT or AST >5 × ULN
- A patient develops leukopenia (WBCs $<2 \times 10^9$/L) or neutropenia (neutrophils $<1 \times 10^9$/L) or lymphopenia (lymphocytes $<0.2 \times 10^9$/L)
- A patient has an active, serious infection (that is, requires hospitalisation or prolonged hospitalisation)

Treatment may be resumed after normalisation of values and based on an individual benefit–risk assessment. If treatment is resumed, hepatic transaminases and total bilirubin should be monitored closely.

Dose discontinuations[1]

Permanent discontinuation of treatment with Avacopan Vifor must be considered in the event of any of the following:

- ALT or AST >8 × ULN
- ALT or AST >5 × ULN for more than 2 weeks
- ALT or AST >3 × ULN and total bilirubin >2 × ULN or >1.5 x international normalised ratio
- 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 Vifor and hepatic dysfunction has been established

Special populations[1]

Dose-adjustment recommendations for Avacopan Vifor in special populations are presented in Table 12.

Table 12. Dose-adjustment recommendations as per special populations[1]

POPULATION	DOSE ADJUSTMENT
Elderly	No dose adjustment is required
Hepatic impairment	No dose adjustment is required in patients with mild/moderate hepatic impairment. Avacopan Vifor has not been studied in patients with severe hepatic impairment (Child-Pugh Class C); therefore, it is not recommended for use in this population
Renal impairment	No dose adjustment is needed based on renal function. Avacopan Vifor has not been studied in patients with an eGFR <15 mL/min/1.73 m^2 who are on dialysis, or patients who are in need of dialysis or plasma exchange
Severe disease manifested as alveolar haemorrhage	Avacopan Vifor has not been studied in these patients
Paediatric population	The safety and efficacy of Avacopan Vifor has not been studied in adolescents (12–17 years of age) or children (<12 years of age); therefore, it is not recommended for use in these populations

Overdose[1]

Avacopan Vifor was studied in healthy subjects at a maximum total daily dose of 200 mg (given as 100 mg twice daily) for 7 days without evidence of dose-limiting toxicities. In the event of an overdose, it is recommended that the patient be monitored for any signs or symptoms of AEs and given appropriate symptomatic treatment and supportive care.

Reference

1. Avacopan Vifor UK SmPC. **2.** Bekker P, et al. *PLoS One* 2016;11(10):e0164646.

Avacopan Vifor special warnings and precautions for use

Avacopan Vifor special warnings and precautions for use

Key points[1]

- Avacopan Vifor must be avoided in patients with signs of liver disease
- Hepatic transaminases, total bilirubin and WBC count must be obtained prior to initiation of Avacopan Vifor, and these parameters must be monitored as clinically indicated and as part of the routine follow-up of the patient's underlying condition
- Patients taking Avacopan Vifor must be assessed for serious infections
- *Pneumocystis jirovecii* pneumonia prophylaxis is recommended during Avacopan Vifor treatment
- Avacopan Vifor must be withheld in patients who develop angioedema while taking Avacopan Vifor
- Avacopan Vifor contains macrogolglycerol hydroxystearate, which may cause stomach upset and diarrhoea
- Avacopan Vifor is not recommended during pregnancy or in women of childbearing potential not using contraception
- Immunomodulatory medicinal products may increase the risk of malignancies
- Cardiac risk: A treatment regimen based on the combination with cyclophosphamide followed by azathioprine may carry an increased risk of cardiac disorders as compared with a regimen based on the combination with rituximab

Contraindications[1]

Avacopan Vifor is contraindicated in patients with a hypersensitivity to the active substance, avacopan, or to any of the excipients.

Hepatoxicity[1]

Avacopan Vifor must be avoided in patients with signs of liver disease, such as:

- Elevated AST, ALT or alkaline phosphatase (ALP)
- Total bilirubin >3 x ULN

Hepatic transaminases and total bilirubin must be obtained prior to initiation of therapy. Patients must be monitored for hepatic transaminases and total bilirubin as clinically indicated and as part of the routine follow-up of the patient's underlying condition.

Blood and immune system[1]

WBC count must be obtained prior to initiation of therapy. Patients must be monitored for WBC count as clinically indicated and as part of the routine follow-up of the patient's underlying condition.

Treatment with Avacopan Vifor must not be initiated if either one of the following are observed:

- WBC count <3.5 x 10^9 /L
- Neutrophil count <1.5 x 10^9 /L
- Lymphocyte count <0.5 x 10^9 /L

Serious infections[1]

Patients must be assessed for any serious infections. Avacopan Vifor has not been studied in patients with hepatitis B, hepatitis C or HIV infections; therefore, caution should be exercised when treating patients with a history of these infections, as well as tuberculosis.

Patients should also be monitored for clinical signs and symptoms of *Neisseria* infections according to standard practice.

Pneumocystis jirovecii pneumonia prophylaxis[1]

Pneumocystis jirovecii pneumonia prophylaxis is recommended for adult GPA/MPA patients during Avacopan Vifor treatment according to local clinical practice guidelines.

Immunisation[1]

The safety of immunisation with live vaccines following Avacopan Vifor therapy has not been studied. Administer vaccinations preferably prior to initiation of treatment with Avacopan Vifor or during a quiescent phase of the disease.

Angioedema[1]

Angioedema has been reported in patients receiving Avacopan Vifor, and Avacopan Vifor must be withheld in cases of angioedema.

Cardiac disorders[1]

Patients with GPA or MPA are at risk of cardiac disorders such as myocardial infarction, cardiac failure and cardiac vasculitis. A treatment regimen based on the combination with cyclophosphamide followed by azathioprine may carry an increased risk of cardiac disorders as compared with a regimen based on the combination with rituximab.

Malignancy[1]

Immunomodulatory medicinal products may increase the risk of malignancies. The clinical data are currently limited.

Macrogolglycerol hydroxystearate content[1]

Avacopan Vifor contains macrogolglycerol hydroxystearate, which may cause stomach upset and diarrhoea.

Pregnancy and breastfeeding[1]

Avacopan Vifor is not recommended for use during pregnancy or in women of childbearing potential who are not using contraception.

A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from using Avacopan Vifor, taking into account the benefit of breastfeeding for the child and the benefit of an Avacopan Vifor-based regimen for the woman.

Fertility[1]

There are no data on the effects of Avacopan Vifor on human fertility. Animal data did not indicate any impairment of male or female fertility.

Please see the link to the full UK Avacopan Vifor summary of product characteristics at the front of this document for full details on the special warnings and precautions

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Reference

1. Avacopan Vifor UK SmPC.

Avacopan Vifor pharmacokinetic profile

Avacopan Vifor pharmacokinetic profile

Key points[1]

- The maximum plasma concentration (C_{max}) of Avacopan Vifor occurs at a median time to maximum plasma concentration (T_{max}) of approximately 2 hours if administered without food
- When Avacopan Vifor is stopped after steady state has been reached, the residual plasma concentration is projected to decrease to approximately <5% of the steady state C_{max} after approximately 10 weeks
- The main route of clearance is metabolism, followed by biliary excretion of the metabolites into faeces

Absorption[1]

Avacopan Vifor has shown an approximate dose-proportional increase in systemic exposure in the dose range of 10 to 30 mg.

When administered without food, the C_{max} of Avacopan Vifor occurs at a median T_{max} of approximately 2 hours. When 30 mg of Avacopan Vifor is administered in capsule formulation with a high-fat, high-calorie meal, plasma exposure increases by approximately 72% and T_{max} is delayed by approximately 3 hours; however, C_{max} is not affected.

Elimination[1]

Based on a population pharmacokinetic analysis:

- The total apparent body clearance (CL/F) of Avacopan Vifor is 16.3 L/h
- The median terminal elimination half-life of Avacopan Vifor is 510 hours (21 days)

When Avacopan Vifor is stopped after steady state has been reached, the residual plasma concentration is projected to decrease to approximately 20%, <10% and <5% of the steady state C_{max} after approximately 4 weeks, 7 weeks and 10 weeks, respectively.

The main route of clearance of Avacopan Vifor is metabolism, followed by biliary excretion of the metabolites into faeces. Direct excretion of Avacopan Vifor into urine or faeces via bile is negligible.

Reference

1. Avacopan Vifor UK SmPC.

Avacopan Vifor drug–drug interactions

Avacopan Vifor drug–drug interactions

Key points[1]

- Inducers of CYP3A4 may reduce the exposure of Avacopan Vifor, impacting its efficacy
- The use of strong CYP3A4 enzyme inducers (e.g. rifampicin, carbamazepine, enzalutamide, mitotane, phenobarbital, phenytoin and St. John's Wort) with Avacopan Vifor is to be avoided
- Inhibitors of CYP3A4, including grapefruit and grapefruit juice, may increase the exposure of Avacopan Vifor, raising the risk of side effects
- Avacopan Vifor may enhance exposure to CYP3A4 substrates that have a narrow therapeutic index
- Avacopan Vifor is a moderate inhibitor of CYP3A4 *in vivo*. In a clinical study, co-administration of Avacopan Vifor and simvastatin, a sensitive CYP3A4 substrate, increased the total systemic exposure of simvastatin
- An excipient of Avacopan Vifor, macrogolglycerol hydroxystearate, may have a clinically relevant impact on P-glycoprotein (P-gp) substrates that have a relatively low bioavailability

Effect of CYP3A4 inducers and inhibitors on Avacopan Vifor[1]

Avacopan, the active ingredient in Avacopan Vifor, is a substrate of cytochrome P450 family 3 subfamily A member 4 (CYP3A4). Therefore, co-administration of inducers or inhibitors of CYP3A4 may affect the pharmacokinetics of Avacopan Vifor (Table 13).

Table 13. Effect of strong and moderate CYP3A4 inducers and inhibitors on Avacopan Vifor[1]

DRUG	EFFECT ON AVACOPAN VIFOR	CLINICAL CONSIDERATIONS WITH AVACOPAN VIFOR
Strong CYP3A4 inducers (e.g. rifampicin, carbamazepine, enzalutamide, mitotane, phenobarbital, phenytoin, St. John's Wort)	May reduce the efficacy of Avacopan Vifor by decreasing its area under the plasma concentration time curve (AUC) and C_{max}	Patients who require long-term administration of strong CYP3A4 enzyme inducers should not be treated with Avacopan Vifor. If short-term co-administration is unavoidable, the patient must be closely monitored for reoccurrence of disease activity
Moderate CYP3A4 inducers (e.g. bosentan, efavirenz, etravirine, modafinil)	May reduce the efficacy of Avacopan Vifor by decreasing its AUC and C_{max}	Caution should be exercised when co-administering moderate CYP3A4 inducers, and the benefit–risk ratio of Avacopan Vifor should be carefully evaluated
Strong CYP3A4 inhibitors (e.g. itraconazole, boceprevir, clarithromycin, conivaptan, indinavir, ketoconazole, lopinavir/ritonavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole)	May increase the exposure of Avacopan Vifor by increasing its AUC and C_{max}	Caution should be exercised when co-administering strong CYP3A4 inhibitors, and patients must be monitored for a potential increase in side effects of Avacopan Vifor

Since grapefruit and grapefruit juice are inhibitors of CYP3A4, they, too, should be avoided in patients taking Avacopan Vifor.[1]

Effect of Avacopan Vifor and its excipient on other medicinal products[1]

Avacopan is a moderate inhibitor of CYP3A4 *in vivo*, and one of the excipients of Avacopan Vifor may interact with sensitive P-gp substrates. As such, the pharmacokinetics of certain CYP3A4 and P-gp substrates may be affected by Avacopan Vifor (Table 14).

Table 14. Effect of Avacopan Vifor/its excipient on CYP3A4 and P-gp substrates[1]

EFFECT OF Avacopan Vifor/ITS EXCIPIENT	CLINICAL CONSIDERATIONS
Avacopan Vifor may increase the exposure of CYP3A4 substrates that have a narrow therapeutic index (e.g. alfentanil, ciclosporin, dihydroergotamine, ergotamine, fentanyl, sirolimus, tacrolimus)	Caution should be exercised when co-administering CYP3A4 substrates that have a narrow therapeutic index, and patients must be managed according to the respective summary of product characteristics of each CYP3A4 substrate. Dose reductions or monitoring of AEs may be necessary
In a clinical study, the co-administration of Avacopan Vifor with simvastatin, a sensitive CYP3A4 substrate, increased the total systemic exposure (AUC) of simvastatin by 3.5-fold and C_{max} by 3.2-fold	Please consult simvastatin's summary of product characteristics for appropriate dose adjustments
An excipient of Avacopan Vifor, macrogolglycerol hydroxystearate, may have a clinically relevant impact on sensitive P-gp substrates that have a relatively low bioavailability (e.g. dabigatran etexilate)	Caution should be exercised when co-administering P-gp substrates that have a relatively low bioavailability

Reference

1. Avacopan Vifor UK SmPC.

Avacopan Vifor UK pricing and purchasing

Avacopan Vifor UK pricing and purchasing

Key points

- The list price of Avacopan Vifor is £5,547.95 per pack of 180 x 10 mg capsules[1]
- A discount is available for NHS organisations[1]
- Orders can be made through Alloga UK via email (allogauk.orders@alloga.co.uk) or telephone (+44 [0] 01773 441702)
- There are two ordering codes: one for Great Britain (USP7515) and another for Northern Ireland (USP7818)

Avacopan Vifor UK pricing

The list price of Avacopan Vifor is £5,547.95 per pack of 180 x 10 mg capsules.[1]

Discount for NHS organisations

CSL Vifor has a commercial arrangement with the NHS (simple discount patient access scheme).[1] This makes Avacopan Vifor available to the NHS at a discount.[1] To learn about the discount, please contact Alloga UK, the wholesaler of Avacopan Vifor in the UK, using the contact details below.

Contact and purchasing information

Avacopan Vifor is available to order through Alloga UK. Orders can be made via email or telephone using the appropriate ordering code, with one being available for Great Britain and another for Northern Ireland.

ADDRESS	Alloga UK, Amber Park 1, Berristow Lane, South Normanton, Derbyshire DE55 2FH
TELEPHONE	+44 (0) 01773 441702
EMAIL	allogauk.orders@alloga.co.uk
ORDERING CODE FOR GREAT BRITAIN	USP7515
ORDERING CODE FOR NORTHERN IRELAND	USP7818

Reference

1. National Institute for Health and Care Excellence, 2022. Avacopan for treating severe active granulomatosis with polyangiitis or microscopic polyangiitis. Technology appraisal guidance [TA825]. Available at: https://www.nice.org.uk/guidance/TA825. Date Accessed: July 2025.

Avacopan Vifor summary

Avacopan Vifor summary

Unmet needs in the treatment of AAV (GPA/MPA)

- AAV (GPA/MPA) is a rare condition that can cause irreversible organ damage and lead to a high mortality risk[1–8]
- GPA/MPA may have a substantial impact on QoL[9–11]
- SoC therapies for AAV can lead to a high cumulative burden for patients[12–18]
- The current SoC does not target a key mechanism of disease in GPA/MPA[1,17,18]
- Many patients do not achieve or sustain remission, and risk of relapse persists[12–14]

Avacopan Vifor-based regimen

- Selectively targets C5aR1 to achieve and sustain remission at 52 weeks[19–21]
- Non-inferior to the GC-based regimen at achieving disease remission at 26 weeks and superior at sustaining remission at 52 weeks[20]
- Lower absolute risk of relapse vs the GC-based regimen[20]
- Larger reduction in GC toxicity vs the GC-based regimen[20]
- Greater numerical increase in eGFR vs the GC-based regimen at weeks 26 and 52[20,22]
- Larger numerical increase in physical domains of HRQoL vs the GC-based reigmen[20]
- Fewer AEs of any kind vs the GC-based regimen, including potentially GC-related AEs, serious AEs, deaths and infections[20]
- Taken as a fixed oral dose, with required monitoring[21]

Ordering Avacopan Vifor

- The list price of Avacopan Vifor is £5,547.95 per pack of 180 x 10 mg capsules[23]
- A discount is available for NHS organisations[23]
- Orders can be made through Alloga UK via email (allogauk.orders@alloga.co.uk) or telephone (+44 [0] 01773 441702)
- There are two ordering codes: one for Great Britain (USP7515) and another for Northern Ireland (USP7818)

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