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RECENT ADVANCES IN THE UNDERSTANDING AND MANAGEMENT OF ANCA-ASSOCIATED VASCULITIDES

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ABSTRACT

Background. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) constitute a group of systemic vasculitides, comprising granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). They primarily affect small vessels, resulting in a broad spectrum of clinical manifestations involving multiple organ systems, particularly those critical for sustaining vital functions. In recent years, substantial advances have been made in our understanding of these conditions.
Aim. The objective of this study was to collect, analyze and synthesize the most recent evidence regarding ANCA-associated vasculitides.
Material and methods. A comprehensive literature search of the PubMed database was conducted focusing on ANCA-associated vasculitides. The analysis encompassed the most recent and relevant case–control studies, observational studies, meta-analyses, as well as the latest recommendations of rheumatology societies concerning the etiopathogenesis, clinical presentation, diagnosis and management of AAV.
Results and conclusion. ANCA-associated vasculitides are defined by the presence of specific autoantibodies directed against neutrophil antigens: proteinase 3 (PR3-ANCA) and myeloperoxidase (MPO-ANCA). These autoantibodies activate neutrophils and the complement system, leading to vascular wall injury. The upper respiratory tract and kidneys are the most commonly affected sites. Current therapeutic strategies are based on glucocorticoids in combination with immunosuppressive agents, with an increasing role for biologics such as rituximab and mepolizumab, enabling reduction of glucocorticoid exposure. Advances in the understanding of disease pathogenesis have facilitated the development of novel agents, including avacopan. Ongoing research efforts are directed toward the identification of new diagnostic biomarkers and therapeutic targets, as well as improving long-term outcomes and minimizing organ damage.

KEYWORDS

ANCA-Associated Vasculitis, Rituximab, Pathophysiology, Prognosis, Treatment, Risk Factors, Classification Criteria

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Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) constitute a group of autoimmune disorders classified among the systemic vasculitides. According to the most widely applied classification of systemic vasculitides, established during the 2012 Chapel Hill Consensus Conference, these conditions are categorized based on the size of the vessels affected by the inflammatory process [1]. AAV encompass granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis), eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg–Strauss syndrome) and microscopic polyangiitis (MPA). They predominantly affect small-caliber vessels, including capillaries, arterioles, small arteries and venules, and are distinguished from other systemic vasculitides by the presence of ANCA in the serum. The principal antigens recognized by ANCA are myeloperoxidase (MPO) and proteinase 3 (PR3, also known as myeloblastin) [2].

Research Materials and Methods

The primary aim of this study was to present the current state of knowledge regarding ANCA-associated vasculitides, with particular emphasis on recent advances in pathogenesis and treatment. To this end, a comprehensive search of the PubMed database was conducted to identify recent publications related to AAV. The initial search yielded more than 100 scientific papers, which were subsequently screened for relevance to the study objectives. Eligible articles were subjected to detailed analysis, resulting in 63 publications forming the source base for this review. These comprised review articles, the most recent rheumatology society guidelines, and original research papers published between 2000 and 2025, including case-control, prospective and retrospective studies, as well as meta-analyses addressing the epidemiology, pathogenesis, clinical manifestations, diagnosis and treatment of ANCA-associated vasculitides.

Epidemiology and Risk Factors

The epidemiology of ANCA-associated vasculitides (AAV) remains challenging to define precisely. This is largely attributable to the rarity of these conditions in the general population and to diagnostic difficulties arising from variability in classification criteria and the presence of non-specific clinical manifestations that overlap with other diseases, often delaying diagnosis. Current epidemiological studies estimate the prevalence of AAV to range from 30 up to 218 cases per million population [3]. The annual incidence in Europe is estimated at approximately 10–20 cases per million [4, 5, 6], primarily for GPA and MPA, as EGPA is substantially rarer, with an incidence of only 1–4 cases per million annually. Over the past three decades, a marked increase in the incidence of AAV has been observed, most likely reflecting greater physician awareness, improved access to healthcare, refinement of diagnostic criteria and the widespread availability of serological assays for ANCA detection. The typical age of onset falls within the sixth and seventh decades of life, although in recent years a shift toward later onset, into the eighth decade, has been reported. Nonetheless, cases also occur in younger adults and in children. Most studies demonstrate a comparable frequency in men and women, with a slight male predominance [3, 7].

In recent years, considerable attention has been devoted to identifying potential genetic and environmental risk factors for AAV. Genome-wide association studies (GWAS) in European and North American populations have identified susceptibility haplotypes within the major histocompatibility complex (MHC) region: HLA-DP1 associated with GPA, HLA-DQ with MPA, and HLA-DRB4 with EGPA. Associations outside the MHC region have also been demonstrated, including variants in CTLA4, TLR9, SERPINA1, PTPN22 and FCGR2A [8].

Environmental factors have likewise been implicated. Several studies reported higher incidence of GPA and EGPA during autumn and winter, likely reflecting seasonal increases in infections that may act as immune triggers. Higher geographic latitude, associated with reduced ultraviolet exposure, has also been linked with increased risk. Patients with AAV were found to have significantly lower serum vitamin D levels compared with the general population, consistent with its role in immune regulation. Pathogenic microorganisms represent another important category of risk factors. Nasal dysbiosis has been associated with susceptibility to AAV, and chronic nasal carriage of Staphylococcus aureus has been linked to up to a sevenfold increased risk of GPA. The potential role of other pathogens, including Mycobacterium tuberculosis, Chlamydia, viruses and protozoa, remains less clear due to limited evidence. Additional risk factors described in the literature include exposure to silicone, environmental toxins (e.g., mercury, carbon monoxide), natural disasters and occupational exposure in agricultural settings and livestock handling. Interestingly, several studies have suggested a protective effect of trimethoprim–sulfamethoxazole therapy against the development of GPA [9].

Antineutrophil Cytoplasmic Antibodies (ANCA)

ANCA are divided into two major types based on the immunofluorescence staining patterns obtained by indirect immunofluorescence (IIF). Perinuclear ANCA (p-ANCA) produce a characteristic perinuclear staining pattern, with myeloperoxidase (MPO) as the principal target antigen. Cytoplasmic ANCA (c-ANCA), in contrast, yield a diffuse cytoplasmic staining pattern and are primarily directed against proteinase 3 (PR3). A second diagnostic method, enzyme-linked immunosorbent assay (ELISA), enables the identification of specific neutrophil antigens (MPO-ANCA and PR3-ANCA). Due to its superior sensitivity and specificity, ELISA is currently recommended as the first-line diagnostic test [10].

In granulomatosis with polyangiitis (GPA), the majority of patients (75–90%) are positive for PR3-ANCA (c-ANCA), while 5–20% present with MPO-ANCA (p-ANCA). Approximately 8.5% of patients, however, are ANCA-negative [11, 12]. Among patients with microscopic polyangiitis (MPA), 40–80% are MPO-ANCA positive, yet up to 24% remain ANCA-negative [11, 13]. In eosinophilic granulomatosis with polyangiitis (EGPA), ANCA are detected less frequently, with 30–40% of patients being MPO-ANCA positive. For this reason, ANCA play a limited role in the diagnosis of EGPA, while blood eosinophil count serves as a more reliable disease marker, as eosinophilia is observed in nearly all cases [14]. The substantial proportion of double-negative results for PR3- and MPO-ANCA poses a diagnostic challenge, driving the search for novel biomarkers of AAV. One such candidate is anti-pentraxin 3 (anti-PTX3) antibodies, which are detected at elevated levels in patients with vasculitides and other connective tissue autoimmune diseases. Their concentration correlates with AAV activity, and they are present in approximately 40% of AAV patients. Importantly, half of the patients with negative PR3- and MPO-ANCA results have detectable anti-PTX3 [15].

Pathogenesis

The pathogenesis of ANCA-associated vasculitides resembles that of other autoimmune disorders. In genetically predisposed individuals, exposure to environmental triggers leads to aberrant immune system activation. Central to this process are ANCAs directed against MPO and PR3, which drive neutrophil activation.

The precise mechanisms underlying the initiation of ANCA production remain incompletely elucidated, but dysregulated activation of B and T lymphocytes is thought to play a role [16]. Under physiological conditions, MPO and PR3 are stored in cytoplasmic granules of neutrophils. Upon exposure to certain stimuli - such as infections or drug reactions -neutrophils undergo a priming process, preparing them for rapid immune activation. During priming, these antigens translocate to the neutrophil cell surface, where they become accessible to ANCA binding. This triggers neutrophil activation, leading to the release of proinflammatory cytokines, reactive oxygen species, and lytic enzymes [16, 17]. Excessive neutrophil activation also promotes the formation of neutrophil extracellular traps (NETs). At high levels, NETs contribute directly to small-vessel injury. Moreover, NETs themselves can stimulate dendritic cells to induce ANCA production, thereby amplifying the inflammatory cascade and perpetuating the pathological cycle of autoimmunity. Ultimately, necrotic damage to the vascular wall compromises its barrier function, enabling immune cells to infiltrate surrounding tissues and extend inflammation to multiple organ systems [18].

Diagnosis and Clinical Presentation

The diagnosis of ANCA-associated vasculitides (AAV) is based on the integration of clinical manifestations with laboratory, imaging and histopathological findings. Due to the insidious onset and nonspecific nature of early symptoms, the interval between symptom onset and diagnosis is often prolonged, with a median of approximately six months [19]. Typical manifestations across different organ systems, stratified by AAV subtype, are summarized in Table 1.

Among laboratory investigations, detection of ANCA antibodies - preferably using ELISA - remains the most relevant diagnostic tool [20]. In cases of renal involvement, most commonly glomerulonephritis, urinalysis typically reveals features consistent with nephritic syndrome. In EGPA, peripheral blood eosinophilia is a characteristic finding. Imaging studies, including chest computed tomography (CT) and radiography, may reveal interstitial lung disease, diffuse infiltrates, cavitating nodules, pleural effusion, or alveolar hemorrhage. Paranasal sinus CT serves as the gold standard in the evaluation of chronic rhinosinusitis.

Less commonly employed modalities, such as 18F-fluorodeoxyglucose positron emission tomography (FDG-PET), can detect occult sites of disease activity, while pulmonary function tests may aid in disease assessment when conventional methods are inconclusive. Histopathological confirmation significantly enhances diagnostic certainty, although diagnostic yield depends on biopsy site. Skin biopsy has a diagnostic sensitivity of 70–90%, typically demonstrating necrotizing vasculitis of small vessels. In GPA and EGPA, granulomatous inflammation is often present, with EGPA additionally characterized by prominent eosinophilic infiltration. Percutaneous renal biopsy offers a diagnostic accuracy of 99%, usually revealing segmental, focal, necrotizing glomerulonephritis with crescent formation. In contrast, nasal mucosa biopsies have a low sensitivity of approximately 30%. Open lung biopsy provides a sensitivity of ~90%, but due to its invasiveness, it is reserved for selected cases; transbronchial biopsy, while less invasive, offers a sensitivity of only ~50% [19, 21].

Once histopathological evidence of small-vessel vasculitis is obtained, alternative causes must be excluded. Differential diagnosis includes other systemic vasculitides, such as polyarteritis nodosa, and anti–glomerular basement membrane (anti-GBM) disease. Granulomatous disorders, including tuberculosis and sarcoidosis, as well as head and neck malignancies, should also be considered. In suspected EGPA, conditions associated with hypereosinophilia must additionally be ruled out.

The final diagnosis should be established according to the 2022 ACR/EULAR classification criteria, which demonstrate high sensitivity and specificity: 92.5% and 93.8% for GPA, 90.8% and 94.2% for MPA, and 84.9% and 99.1% for EGPA, respectively [22].

Table 1. The most common clinical manifestations of AAV subtypes according to organ involvement.

Organ involvement	GPA	EGPA	MPA
Upper respiratory tract	Epistaxis, septal perforation, cartilage destruction, nasal mucosal ulceration, chronic sinusitis, hoarseness, subglottic stenosis, recurrent otitis media	Sinusitis, nasal polyps	Rare
Lower respiratory tract and lungs	Cough, dyspnea, hemoptysis, alveolar hemorrhage, pulmonary cavities, nodular changes, diffuse infiltrates with necrosis, bronchial inflammation	Asthma, pulmonary infiltrates, pulmonary nodules, alveolar hemorrhage, pleural effusion	Alveolar hemorrhage, dyspnea, hemoptysis
Kidneys	Necrotizing glomerulonephritis with crescents, hematuria, proteinuria, renal failure	Rapidly progressive glomerulonephritis	Rapidly progressive glomerulonephritis, hematuria, proteinuria
Nervous system	Mononeuritis multiplex, cranial nerve involvement, polyneuropathy	Mononeuritis multiplex, cranial nerve involvement, polyneuropathy, ischemic or hemorrhagic stroke	Mononeuritis multiplex, polyneuropathy
Cardiovascular system	Myocarditis, pericarditis, arrhythmias (SVT, AF, AFl)	Endocarditis, myocarditis, pericarditis, arrhythmias, cardiomyopathy	Arrhythmias
Skin	Palpable purpura, ulcerative nodules, granulomatous lesions, subcutaneous nodules, erythema	Palpable purpura, subcutaneous nodules, Churg–Strauss sign, Raynaud's phenomenon, urticaria	Palpable purpura
Gastrointestinal tract	Abdominal pain, bloody diarrhea, gastric and intestinal ulcerations, often asymptomatic	Abdominal pain, diarrhea, gastrointestinal bleeding, intestinal ischemia	Abdominal pain, gastrointestinal bleeding
Eye involvement	Inflammation of all ocular structures, orbital pseudotumor, superior orbital fissure syndrome, orbital apex syndrome	Inflammation of all ocular structures	Rare

Treatment of ANCA-Associated Vasculitides

In 2022, the European Alliance of Associations for Rheumatology (EULAR) published an update of the 2016 recommendations on the management of ANCA-associated vasculitides (AAV) [23]. One of the principal changes was the introduction of separate recommendations for EGPA. For GPA and MPA, a shared therapeutic algorithm remained. In addition, the Kidney Disease: Improving Global Outcomes (KDIGO) initiative released updated guidelines in 2024 [24].

Granulomatosis with Polyangiitis and Microscopic Polyangiitis

The standard approach to remission induction in newly diagnosed GPA and MPA, as well as in relapsing disease, depends on the presence of life- or organ-threatening manifestations. These include glomerulonephritis, alveolar hemorrhage, orbital involvement, meningeal or central nervous system disease, mononeuritis multiplex and cardiac or mesenteric vasculitis [23].

In such cases, induction therapy consists of high-dose oral glucocorticoids (initially 50–75 mg/kg body weight of prednisone equivalent per day, tapered to 5 mg/day over 4–5 months), combined with either cyclophosphamide (15 mg/kg body weight, maximum 1200 mg/day, administered intravenously; the first three infusions every two weeks, followed by every three weeks) or rituximab, a monoclonal anti-CD20 antibody (375 mg/m² body surface area weekly for four infusions). In relapsing disease, rituximab is the preferred agent [25]. Comparative studies demonstrated superior remission rates with rituximab at 6 and 12 months among

relapsing patients, while efficacy was similar between rituximab and cyclophosphamide in newly diagnosed cases [26, 27]. Cyclophosphamide carries significant risks with long-term use, including premature ovarian failure, infertility in men [28, 29] and an increased risk of malignancies such as bladder carcinoma and myelodysplastic syndromes [30, 31]. For this reason, rituximab is a safer option in relapsing disease [32]. Combination therapy with rituximab and low-dose cyclophosphamide has been shown to provide comparable efficacy to full-dose cyclophosphamide, with retrospective data suggesting its potential utility in glucocorticoid-sparing strategies [33, 34]. The conventional rituximab dosing regimen (375 mg/m² weekly × 4) demonstrates comparable efficacy to the alternative two-dose regimen (1 g intravenously on days 1 and 15), as confirmed by recent meta-analyses [35]. A novel therapeutic agent, avacopan - a C5a receptor antagonist and cytochrome P450 3A3 inhibitor - may be considered in combination with rituximab or cyclophosphamide as part of a glucocorticoid-sparing induction regimen. In the Avacopan for the Treatment of ANCA-associated Vasculitis (ADVOCATE) trial, avacopan-based therapy achieved higher remission rates at week 26 (72.3% vs. 70.1% with standard glucocorticoid regimen), superior renal outcomes in patients with active glomerulonephritis, and fewer glucocorticoid-related adverse events. After one year, cumulative glucocorticoid exposure was reduced by approximately 2300 mg in the avacopan group compared with standard therapy. Currently, no data are available on treatment beyond one year. The proposed dosing regimen is 30 mg orally twice daily for 6–12 months [36]. In patients with active glomerulonephritis and serum creatinine >300 μmol/L, plasma exchange may be considered as an adjunct to pharmacological induction therapy [37].

In patients with GPA or MPA presenting without life- or organ-threatening manifestations, induction therapy is based on oral glucocorticoids combined with rituximab (administered in the same dosing regimens as outlined above). Alternatively, methotrexate or mycophenolate mofetil may be considered [23]. However, methotrexate was associated with lower remission rates, more frequent relapses at one year, shorter time to relapse and a higher probability of subsequent relapses after treatment discontinuation compared with cyclophosphamide [38]. Similarly, mycophenolate mofetil achieved lower remission rates and higher relapse rates than cyclophosphamide [39], although comparable efficacy was observed in selected patients with MPA [40]. Taken together, rituximab should be regarded as the first-line option in this setting.

When standard remission induction regimens fail, the disease is classified as refractory. In such cases, other potential causes of the patient's symptoms should be reassessed, comorbidities reviewed and treatment strategies reconsidered. Options include increasing glucocorticoid doses or combining cyclophosphamide with rituximab. In patients with persistent disease activity, particularly those at risk of infection, intravenous immunoglobulins may be beneficial. Importantly, patients with refractory disease should be referred to, or managed in close collaboration with, specialized centers [23, 41].

Rituximab is the preferred agent for maintenance therapy, with azathioprine or methotrexate serving as alternatives [23]. Large randomized controlled trials have demonstrated lower relapse rates and improved survival in patients treated with rituximab compared with azathioprine, with follow-up extending beyond 60 months [42, 43]. Nevertheless, prolonged rituximab use carries risks such as hypogammaglobulinemia [44] and impaired vaccine responses [45]. In patients at risk of these complications or with prior allergic reactions to rituximab, classical immunosuppressive agents remain valid options. Obinutuzumab, another anti-CD20 monoclonal antibody, has been reported as an effective alternative for induction and maintenance in patients who experienced rituximab-induced anaphylaxis [46]. Leflunomide may be considered in GPA patients with contraindications to rituximab, azathioprine, or methotrexate [47]. Maintenance therapy is most often combined with low-dose glucocorticoids, although the dosing should be individualized. Complete discontinuation of glucocorticoids may be associated with an increased risk of relapse [48]. Maintenance treatment should be continued for 24–48 months after remission is achieved, with extension considered in patients with relapsing disease, increased relapse risk, or based on patient preferences and the risks of chronic immunosuppression [41].

Eosinophilic Granulomatosis with Polyangitis (EGPA)

Similar to microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA), the treatment of EGPA depends on the presence of life-threatening manifestations or risk of organ damage. Prognosis is assessed using the Five Factor Score (FFS), which includes renal dysfunction, proteinuria, cardiomyopathy, gastrointestinal involvement and central nervous system involvement. An FFS ≥1 indicates poor prognosis. In such cases, the recommended therapy consists of high-dose glucocorticoids in combination with cyclophosphamide (15 mg/kg, maximum 1200 mg). Rituximab may be considered as an alternative to cyclophosphamide [23]. In a recent study of EGPA patients with cardiac involvement treated with high-dose

glucocorticoids and cyclophosphamide, no deaths related to cardiac disease were reported during a 10-year follow-up [49]. Another study demonstrated that among patients with poor prognosis, an intensified regimen of cyclophosphamide consisting of 12 cycles, compared with 6, reduced the incidence of minor relapses but did not improve overall remission rates or reduce the frequency of major relapses [50]. In the prospective REOVAS trial, the efficacy of rituximab was compared with cyclophosphamide, both administered alongside high-dose glucocorticoids in patients with FFS ≥1. Rituximab, administered as two infusions (1 g on days 1 and 15), demonstrated comparable efficacy to cyclophosphamide (nine infusions over 13 weeks) at both 6 and 12 months after initiation of treatment [51]. Unlike in GPA and MPA, however, the impact of ANCA status on the effectiveness of rituximab in EGPA remains less conclusive [52].

For non–life- or organ-threatening disease, glucocorticoid monotherapy remains the standard of care. This approach achieves remission rates exceeding 90%. Nonetheless, tapering glucocorticoids is frequently associated with relapses [53], whereas long-term exposure to high doses increases the risk of adverse effects. This often prompts the addition of another immunosuppressive agent to enable glucocorticoid sparing, though the evidence supporting such combinations is limited [54]. In contrast to GPA and MPA, combining azathioprine with glucocorticoids in patients with FFS = 0 did not improve remission rates, glucocorticoid dose reduction, adverse event profile, or relapse frequency compared with glucocorticoids plus placebo [55]. Similarly, in the REOVAS trial, rituximab combined with glucocorticoids did not achieve superior efficacy compared with glucocorticoids plus placebo in this patient group [51].

In refractory or relapsing disease, mepolizumab is recommended. This humanized monoclonal antibody inhibits interleukin-5 (IL-5). Its efficacy was demonstrated in the randomized, double-blind, placebo-controlled MIRRA trial including 136 patients with refractory or relapsing non–life-threatening, non–organ-threatening EGPA of at least 6 months' duration. Subcutaneous mepolizumab at a dose of 300 mg every 4 weeks resulted in longer remission duration with reduced prednisone dose (4 mg), higher remission rates at weeks 36 and 48, lower relapse rates and reduced cumulative glucocorticoid exposure compared with placebo [56, 57]. In patients with contraindications to mepolizumab, individualized use of azathioprine, methotrexate, mycophenolate mofetil, or rituximab should be considered [23]. Other IL-5–targeting agents, such as reslizumab and benralizumab, have also shown favorable outcomes in EGPA, though confirmatory data remain limited [58, 59]. In contrast, omalizumab (a humanized anti-IgE antibody) has proven less effective than mepolizumab [55].

For maintenance therapy in relapsing, non–life-threatening, non–organ-threatening EGPA, mepolizumab is the treatment of choice. This recommendation is supported by MIRRA trial results, which showed prolonged remission and fewer relapses with mepolizumab, with an adverse event profile similar to that of glucocorticoids plus placebo [56, 57]. In cases of life- or organ-threatening disease, methotrexate, azathioprine, mepolizumab, or rituximab may be considered [23]. However, only one prospective study has specifically addressed this issue [60], and therefore treatment decisions should be individualized.

Monitoring Disease Course and Management of Complications

Effective management of chronic autoimmune diseases, including ANCA-associated vasculitides, requires regular follow-up assessments aimed at the early detection of relapse, drug-related adverse effects, and comorbidities. Physical examination remains of critical importance, particularly in an era of wide access to extensive laboratory and imaging tests. In addition, patients should be adequately educated about their disease and potential complications. The choice of ancillary investigations depends on the organs involved; however, they should routinely include assessment of renal function (urinalysis for proteinuria and hematuria, serum creatinine) and imaging of the heart and respiratory system [61].

Long-term rituximab therapy may lead to hypogammaglobulinemia; therefore, serum immunoglobulin levels should be measured before each infusion to exclude secondary immunodeficiency. Routine monitoring of CD19+ cell counts (B lymphocytes) and ANCA titers should not be considered the primary approach to evaluating treatment response or relapse, but rather as complementary to the aforementioned basic assessments [62]. In patients treated with cyclophosphamide, the increased risk of malignancy must be taken into account [31]. Nasal carriage of pathogens may also warrant evaluation, as infections represent the most significant early complication of treatment and constitute the leading cause of death during the first year of therapy. Consequently, patients receiving rituximab, cyclophosphamide, or high-dose glucocorticoids should receive trimethoprim–sulfamethoxazole prophylaxis to prevent Pneumocystis jirovecii pneumonia and other infections [63]. Immunization against influenza and pneumococcus is also recommended. Management of organ-related complications - including nasal cartilage destruction, airway stenosis, end-stage renal disease and heart failure - should be undertaken in specialized centers with expertise in treating such manifestations.

Conclusions

ANCA-associated vasculitides (AAV) represent a heterogeneous group of diseases with a broad spectrum of clinical manifestations. Early recognition is essential to reduce the risk of irreversible damage to vital organs; therefore, it is crucial that clinicians possess fundamental knowledge of these disorders and their presenting features to facilitate timely and accurate diagnosis.

In recent years, there has been a substantial expansion of knowledge regarding AAV, encompassing risk factors (including genetic predisposition), disease pathogenesis, advances in diagnostic modalities, and the development of novel biologic therapies. A deeper understanding of disease mechanisms and their impact on the immune system has enabled the design of targeted therapies directed at specific steps of the inflammatory cascade. Examples include the demonstrated efficacy of rituximab in GPA and MPA, as well as mepolizumab in EGPA. Furthermore, these advances have led to the introduction of new therapeutic agents, such as avacopan (a C5a receptor inhibitor), for GPA and MPA. Nonetheless, the long-term need for immunosuppressive therapies, particularly glucocorticoids, remains a significant challenge.

Ongoing research is also focused on the identification of novel diagnostic markers to improve disease classification and prognostication, which is of particular importance in EGPA, given its frequent ANCA-negative presentation. The future of AAV research will therefore center on the development of innovative therapeutic strategies and diagnostic biomarkers, as well as on approaches to managing organ-specific complications and reducing their incidence.

Disclosure

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REFERENCES

1. Jennette, J. C., Falk, R. J., Bacon, P. A., Basu, N., Cid, M. C., Ferrario, F., Flores-Suarez, L. F., Gross, W. L., Guillevin, L., Hagen, E. C., Hoffman, G. S., Jayne, D. R., Kallenberg, C. G., Lamprecht, P., Langford, C. A., Luqmani, R. A., Mahr, A. D., Matteson, E. L., Merkel, P. A., Ozen, S., … Watts, R. A. (2013). 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis and rheumatism*, *65*(1), 1–11. https://doi.org/10.1002/art.37715
2. Geetha, D., & Jefferson, J. A. (2020). ANCA-Associated Vasculitis: Core Curriculum 2020. *American journal of kidney diseases : the official journal of the National Kidney Foundation*, *75*(1), 124–137. https://doi.org/10.1053/j.ajkd.2019.04.031
3. Mohammad A. J. (2020). An update on the epidemiology of ANCA-associated vasculitis. *Rheumatology (Oxford, England)*, *59*(Suppl 3), iii42–iii50. https://doi.org/10.1093/rheumatology/keaa089
4. Gonzalez-Gay, M. A., Garcia-Porrua, C., Guerrero, J., Rodriguez-Ledo, P., & Llorca, J. (2003). The epidemiology of the primary systemic vasculitides in northwest Spain: implications of the Chapel Hill Consensus Conference definitions. *Arthritis and rheumatism*, *49*(3), 388–393. https://doi.org/10.1002/art.11115
5. Watts, R. A., Lane, S. E., Bentham, G., & Scott, D. G. (2000). Epidemiology of systemic vasculitis: a ten-year study in the United Kingdom. *Arthritis and rheumatism*, *43*(2), 414–419. https://doi.org/10.1002/1529-0131(200002)43:2%3C414::aid-anr23%3E3.0.co;2-0
6. Mohammad, A. J., Jacobsson, L. T., Westman, K. W., Sturfelt, G., & Segelmark, M. (2009). Incidence and survival rates in Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome and polyarteritis nodosa. Rheumatology (Oxford, England), 48(12), 1560–1565. https://doi.org/10.1093/rheumatology/kep304
7. Hellmich, B., Lamprecht, P., Spearpoint, P., Götte, D., Deichmann, A., Buchholz, I., Schönermark, M. P., & Rutherford, P. (2021). New insights into the epidemiology of ANCA-associated vasculitides in Germany: results from a claims data study. Rheumatology (Oxford, England), 60(10), 4868–4873. https://doi.org/10.1093/rheumatology/keaa924
8. Zhao, W. M., Wang, Z. J., Shi, R., Zhu, Y. Y., Zhang, S., Wang, R. F., & Wang, D. G. (2022). Environmental factors influencing the risk of ANCA-associated vasculitis. Frontiers in immunology, 13, 991256. https://doi.org/10.3389/fimmu.2022.991256
9. Scott, J., Hartnett, J., Mockler, D., & Little, M. A. (2020). Environmental risk factors associated with ANCA associated vasculitis: A systematic mapping review. Autoimmunity reviews, 19(11), 102660. https://doi.org/10.1016/j.autrev.2020.102660
10. Walker, B. S., Peterson, L. K., Koening, C., White, S. K., Schmidt, R. L., & Tebo, A. E. (2022). Performance of MPO-ANCA and PR3-ANCA immunoassays for the stratification of specific ANCA-associated vasculitis: A systematic review and meta-analysis. Autoimmunity reviews, 21(6), 103100. https://doi.org/10.1016/j.autrev.2022.103100
11. Yaseen, K., & Mandell, B. F. (2023). ANCA associated vasculitis (AAV): a review for internists. Postgraduate medicine, 135(sup1), 3–13. https://doi.org/10.1080/00325481.2022.2102368
12. Puéchal, X., Iudici, M., Perrodeau, E., Bonnotte, B., Lifermann, F., Le Gallou, T., Karras, A., Blanchard-Delaunay, C., Quéméneur, T., Aouba, A., Aumaître, O., Cottin, V., Hamidou, M., Ruivard, M., Cohen, P., Mouthon, L., Guillevin, L., Ravaud, P., Porcher, R., Terrier, B., … French Vasculitis Study Group (2022). Rituximab vs Cyclophosphamide Induction Therapy for Patients With Granulomatosis With Polyangiitis. *JAMA network open*, *5*(11), e2243799. https://doi.org/10.1001/jamanetworkopen.2022.43799
13. Damoiseaux, J., Csernok, E., Rasmussen, N., Moosig, F., van Paassen, P., Baslund, B., Vermeersch, P., Blockmans, D., Cohen Tervaert, J. W., & Bossuyt, X. (2017). Detection of antineutrophil cytoplasmic antibodies (ANCAs): a multicentre European Vasculitis Study Group (EUVAS) evaluation of the value of indirect immunofluorescence (IIF) versus antigen-specific immunoassays. Annals of the rheumatic diseases, 76(4), 647–653. https://doi.org/10.1136/annrheumdis-2016-209507
14. Matucci, A., Vivarelli, E., Perlato, M., Mecheri, V., Accinno, M., Cosmi, L., Parronchi, P., Rossi, O., & Vultaggio, A. (2023). EGPA Phenotyping: Not Only ANCA, but Also Eosinophils. Biomedicines, 11(3), 776. https://doi.org/10.3390/biomedicines11030776
15. Potentas-Policewicz, M., & Fijolek, J. (2024). Granulomatosis with polyangiitis: clinical characteristics and updates in diagnosis. Frontiers in medicine, 11, 1369233. https://doi.org/10.3389/fmed.2024.1369233
16. Kronbichler, A., Lee, K. H., Denicolò, S., Choi, D., Lee, H., Ahn, D., Kim, K. H., Lee, J. H., Kim, H., Hwang, M., Jung, S. W., Lee, C., Lee, H., Sung, H., Lee, D., Hwang, J., Kim, S., Hwang, I., Kim, D. Y., Kim, H. J., … Shin, J. I. (2020). Immunopathogenesis of ANCA-Associated Vasculitis. International journal of molecular sciences, 21(19), 7319. https://doi.org/10.3390/ijms21197319
17. Leacy, E., Brady, G., & Little, M. A. (2020). Pathogenesis of ANCA-associated vasculitis: an emerging role for immunometabolism. Rheumatology (Oxford, England), 59(Suppl 3), iii33–iii41. https://doi.org/10.1093/rheumatology/keaa023

18. Nakazawa, D., Masuda, S., Tomaru, U., & Ishizu, A. (2019). Pathogenesis and therapeutic interventions for ANCA-associated vasculitis. Nature reviews. Rheumatology, 15(2), 91–101. https://doi.org/10.1038/s41584-018-0145-y
19. Kronbichler, A., Bajema, I. M., Bruchfeld, A., Mastroianni Kirsztajn, G., & Stone, J. H. (2024). Diagnosis and management of ANCA-associated vasculitis. Lancet (London, England), 403(10427), 683–698. https://doi.org/10.1016/S0140-6736(23)01736-1
20. Guchelaar, N. A. D., Waling, M. M., Adhin, A. A., van Daele, P. L. A., Schreurs, M. W. J., & Rombach, S. M. (2021). The value of anti-neutrophil cytoplasmic antibodies (ANCA) testing for the diagnosis of ANCA-associated vasculitis, a systematic review and meta-analysis. Autoimmunity reviews, 20(1), 102716. https://doi.org/10.1016/j.autrev.2020.102716
21. Ross, C., Makhzoum, J. P., & Pagnoux, C. (2022). Updates in ANCA-associated vasculitis. European journal of rheumatology, 9(3), 153–166. https://doi.org/10.5152/eujrheum.2022.20248
22. Rathmann, J., & Mohammad, A. J. (2024). Classification Criteria for ANCA Associated Vasculitis - Ready for Prime Time?. Current rheumatology reports, 26(9), 332–342. https://doi.org/10.1007/s11926-024-01154-9
23. Hellmich, B., Sanchez-Alamo, B., Schirmer, J. H., Berti, A., Blockmans, D., Cid, M. C., Holle, J. U., Hollinger, N., Karadag, O., Kronbichler, A., Little, M. A., Luqmani, R. A., Mahr, A., Merkel, P. A., Mohammad, A. J., Monti, S., Mukhtyar, C. B., Musial, J., Price-Kuehne, F., Segelmark, M., … Jayne, D. (2024). EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. Annals of the rheumatic diseases, 83(1), 30–47. https://doi.org/10.1136/ard-2022-223764
24. Kidney Disease: Improving Global Outcomes (KDIGO) ANCA Vasculitis Work Group (2024). KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis. Kidney international, 105(3S), S71–S116. https://doi.org/10.1016/j.kint.2023.10.008
25. Yazici Y. (2024). Current treatment approach to ANCA-associated vasculitis. Current opinion in rheumatology, 36(1), 35–39. https://doi.org/10.1097/BOR.0000000000000982
26. Stone, J. H., Merkel, P. A., Spiera, R., Seo, P., Langford, C. A., Hoffman, G. S., Kallenberg, C. G., St Clair, E. W., Turkiewicz, A., Tchao, N. K., Webber, L., Ding, L., Sejismundo, L. P., Mieras, K., Weitzenkamp, D., Ikle, D., Seyfert-Margolis, V., Mueller, M., Brunetta, P., Allen, N. B., … RAVE-ITN Research Group (2010). Rituximab versus cyclophosphamide for ANCA-associated vasculitis. The New England journal of medicine, 363(3), 221–232. https://doi.org/10.1056/NEJMoa0909905
27. Specks, U., Merkel, P. A., Seo, P., Spiera, R., Langford, C. A., Hoffman, G. S., Kallenberg, C. G., St Clair, E. W., Fessler, B. J., Ding, L., Viviano, L., Tchao, N. K., Phippard, D. J., Asare, A. L., Lim, N., Ikle, D., Jepson, B., Brunetta, P., Allen, N. B., Fervenza, F. C., … RAVE-ITN Research Group (2013). Efficacy of remission-induction regimens for ANCA-associated vasculitis. The New England journal of medicine, 369(5), 417–427. https://doi.org/10.1056/NEJMoa1213277
28. Clowse, M. E., Copland, S. C., Hsieh, T. C., Chow, S. C., Hoffman, G. S., Merkel, P. A., Spiera, R. F., Davis, J. C., Jr, McCune, W. J., Ytterberg, S. R., St Clair, E. W., Allen, N. B., Specks, U., Stone, J. H., & WGET Research Group (2011). Ovarian reserve diminished by oral cyclophosphamide therapy for granulomatosis with polyangiitis (Wegener's). Arthritis care & research, 63(12), 1777–1781. https://doi.org/10.1002/acr.20605
29. Soares, P. M., Borba, E. F., Bonfa, E., Hallak, J., Corrêa, A. L., & Silva, C. A. (2007). Gonad evaluation in male systemic lupus erythematosus. Arthritis and rheumatism, 56(7), 2352–2361. https://doi.org/10.1002/art.22660
30. Knight, A., Hjorton, K., Sundström, C., Höglund, M., Backlin, C., Smedby, K. E., Askling, J., & Baecklund, E. (2015). Leukemia and myelodysplastic syndrome in granulomatosis with polyangiitis: subtypes, clinical characteristics, and outcome. The Journal of rheumatology, 42(4), 690–694. https://doi.org/10.3899/jrheum.141104
31. Faurschou, M., Mellemkjaer, L., Voss, A., Keller, K. K., Hansen, I. T., & Baslund, B. (2015). Prolonged risk of specific malignancies following cyclophosphamide therapy among patients with granulomatosis with polyangiitis. Rheumatology (Oxford, England), 54(8), 1345–1350. https://doi.org/10.1093/rheumatology/keu372
32. van Daalen, E. E., Rizzo, R., Kronbichler, A., Wolterbeek, R., Bruijn, J. A., Jayne, D. R., Bajema, I. M., & Rahmattulla, C. (2017). Effect of rituximab on malignancy risk in patients with ANCA-associated vasculitis. Annals of the rheumatic diseases, 76(6), 1064–1069. https://doi.org/10.1136/annrheumdis-2016-209925
33. Pepper, R. J., McAdoo, S. P., Moran, S. M., Kelly, D., Scott, J., Hamour, S., Burns, A., Griffith, M., Galliford, J., Levy, J. B., Cairns, T. D., Gopaluni, S., Jones, R. B., Jayne, D., Little, M. A., Pusey, C. D., & Salama, A. D. (2019). A novel glucocorticoid-free maintenance regimen for anti-neutrophil cytoplasm antibody-associated vasculitis. Rheumatology (Oxford, England), 58(2), 260–268. https://doi.org/10.1093/rheumatology/key288
34. Cortazar, F. B., Muhsin, S. A., Pendergraft, W. F., 3rd, Wallace, Z. S., Dunbar, C., Laliberte, K., & Niles, J. L. (2017). Combination Therapy With Rituximab and Cyclophosphamide for Remission Induction in ANCA Vasculitis. Kidney international reports, 3(2), 394–402. https://doi.org/10.1016/j.ekir.2017.11.004
35. Bénard, V., Farhat, C., Zarandi-Nowroozi, M., Durand, M., Charles, P., Puéchal, X., Guillevin, L., Pagnoux, C., & Makhzoum, J. P. (2021). Comparison of Two Rituximab Induction Regimens for Antineutrophil Cytoplasm Antibody-Associated Vasculitis: Systematic Review and Meta-Analysis. ACR open rheumatology, 3(7), 484–494. https://doi.org/10.1002/acr2.11274

36. Jayne, D. R. W., Merkel, P. A., Schall, T. J., Bekker, P., & ADVOCATE Study Group (2021). Avacopan for the Treatment of ANCA-Associated Vasculitis. The New England journal of medicine, 384(7), 599–609. https://doi.org/10.1056/NEJMoa2023386
37. Jayne, D. R., Gaskin, G., Rasmussen, N., Abramowicz, D., Ferrario, F., Guillevin, L., Mirapeix, E., Savage, C. O., Sinico, R. A., Stegeman, C. A., Westman, K. W., van der Woude, F. J., de Lind van Wijngaarden, R. A., Pusey, C. D., & European Vasculitis Study Group (2007). Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. Journal of the American Society of Nephrology : JASN, 18(7), 2180–2188. https://doi.org/10.1681/ASN.2007010090
38. Faurschou, M., Westman, K., Rasmussen, N., de Groot, K., Flossmann, O., Höglund, P., Jayne, D. R., & European Vasculitis Study Group (2012). Brief Report: long-term outcome of a randomized clinical trial comparing methotrexate to cyclophosphamide for remission induction in early systemic antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis and rheumatism, 64(10), 3472–3477. https://doi.org/10.1002/art.34547
39. Tuin, J., Stassen, P. M., Bogdan, D. I., Broekroelofs, J., van Paassen, P., Cohen Tervaert, J. W., Sanders, J. S., & Stegeman, C. A. (2019). Mycophenolate Mofetil Versus Cyclophosphamide for the Induction of Remission in Nonlife-Threatening Relapses of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: Randomized, Controlled Trial. Clinical journal of the American Society of Nephrology : CJASN, 14(7), 1021–1028. https://doi.org/10.2215/CJN.11801018
40. Han, F., Liu, G., Zhang, X., Li, X., He, Q., He, X., Li, Q., Wang, S., Wang, H., & Chen, J. (2011). Effects of mycophenolate mofetil combined with corticosteroids for induction therapy of microscopic polyangiitis. American journal of nephrology, 33(2), 185–192. https://doi.org/10.1159/000324364
41. Chalkia, A., & Jayne, D. (2024). ANCA-associated vasculitis-treatment standard. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 39(6), 944–955. https://doi.org/10.1093/ndt/gfad237
42. Guillevin, L., Pagnoux, C., Karras, A., Khouatra, C., Aumaître, O., Cohen, P., Maurier, F., Decaux, O., Ninet, J., Gobert, P., Quémeneur, T., Blanchard-Delaunay, C., Godmer, P., Puéchal, X., Carron, P. L., Hatron, P. Y., Limal, N., Hamidou, M., Ducret, M., Daugas, E., … French Vasculitis Study Group (2014). Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. The New England journal of medicine, 371(19), 1771–1780. https://doi.org/10.1056/NEJMoa1404231
43. Terrier, B., Pagnoux, C., Perrodeau, É., Karras, A., Khouatra, C., Aumaître, O., Cohen, P., Decaux, O., Desmurs-Clavel, H., Maurier, F., Gobert, P., Quémeneur, T., Blanchard-Delaunay, C., Bonnotte, B., Carron, P. L., Daugas, E., Ducret, M., Godmer, P., Hamidou, M., Lidove, O., … French Vasculitis Study Group (2018). Long-term efficacy of remission-maintenance regimens for ANCA-associated vasculitides. Annals of the rheumatic diseases, 77(8), 1150–1156. https://doi.org/10.1136/annrheumdis-2017-212768
44. Wijetilleka, S., Mukhtyar, C., Jayne, D., Ala, A., Bright, P., Chinoy, H., Harper, L., Kazmi, M., Kiani-Alikhan, S., Li, C., Misbah, S., Oni, L., Price-Kuehne, F., Salama, A., Workman, S., Wrench, D., & Karim, M. Y. (2019). Immunoglobulin replacement for secondary immunodeficiency after B-cell targeted therapies in autoimmune rheumatic disease: Systematic literature review. Autoimmunity reviews, 18(5), 535–541. https://doi.org/10.1016/j.autrev.2019.03.010
45. Spiera, R., Jinich, S., & Jannat-Khah, D. (2021). Rituximab, but not other antirheumatic therapies, is associated with impaired serological response to SARS- CoV-2 vaccination in patients with rheumatic diseases. Annals of the rheumatic diseases, 80(10), 1357–1359. https://doi.org/10.1136/annrheumdis-2021-220604
46. Amudala, N. A., Boukhlal, S., Sheridan, B., Langford, C. A., Geara, A., Merkel, P. A., & Cornec, D. (2022). Obinutuzumab as treatment for ANCA-associated vasculitis. Rheumatology (Oxford, England), 61(9), 3814–3817. https://doi.org/10.1093/rheumatology/keab916
47. Metzler, C., Fink, C., Lamprecht, P., Gross, W. L., & Reinhold-Keller, E. (2004). Maintenance of remission with leflunomide in Wegener's granulomatosis. Rheumatology (Oxford, England), 43(3), 315–320. https://doi.org/10.1093/rheumatology/keh009
48. Emejuaiwe N. (2019). Treatment Strategies in ANCA-Associated Vasculitis. Current rheumatology reports, 21(7), 33. https://doi.org/10.1007/s11926-019-0835-8
49. Sartorelli, S., Chassagnon, G., Cohen, P., Dunogué, B., Puéchal, X., Régent, A., Mouthon, L., Guillevin, L., Terrier, B., & French Vasculitis Study Group (FVSG) (2022). Revisiting characteristics, treatment and outcome of cardiomyopathy in eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss). Rheumatology (Oxford, England), 61(3), 1175–1184. https://doi.org/10.1093/rheumatology/keab514
50. Cohen, P., Pagnoux, C., Mahr, A., Arène, J. P., Mouthon, L., Le Guern, V., André, M. H., Gayraud, M., Jayne, D., Blöckmans, D., Cordier, J. F., Guillevin, L., & French Vasculitis Study Group (2007). Churg-Strauss syndrome with poor-prognosis factors: A prospective multicenter trial comparing glucocorticoids and six or twelve cyclophosphamide pulses in forty-eight patients. Arthritis and rheumatism, 57(4), 686–693. https://doi.org/10.1002/art.22679

51. Terrier, B., Pugnet, G., de Moreuil, C., Bonnotte, B., Benhamou, Y., Chauveau, D., Besse, M. C., Duffau, P., Limal, N., Néel, A., Urbanski, G., Jourde-Chiche, N., Martin-Silva, N., Campagne, J., Mekinian, A., Schleinitz, N., Ackermann, F., Fauchais, A. L., Froissart, A., Le Gallou, T., … French Vasculitis Study Group (2025). Rituximab Versus Conventional Therapy for Remission Induction in Eosinophilic Granulomatosis With Polyangiitis : A Randomized Controlled Trial. Annals of internal medicine, 10.7326/ANNALS-24-03947. Advance online publication. https://doi.org/10.7326/ANNALS-24-03947
52. Moiseev, S., Bossuyt, X., Arimura, Y., Blockmans, D., Csernok, E., Damoiseaux, J., Emmi, G., Flores-Suárez, L. F., Hellmich, B., Jayne, D., Jennette, J. C., Little, M. A., Mohammad, A. J., Moosig, F., Novikov, P., Pagnoux, C., Radice, A., Sada, K. E., Segelmark, M., Shoenfeld, Y., … European EGPA Study Group (2020). International Consensus on ANCA Testing in Eosinophilic Granulomatosis with Polyangiitis. American journal of respiratory and critical care medicine, 10.1164/rccm.202005-1628SO. Advance online publication. https://doi.org/10.1164/rccm.202005-1628SO
53. Samson, M., Puéchal, X., Devilliers, H., Ribi, C., Cohen, P., Stern, M., Pagnoux, C., Mouthon, L., Guillevin, L., & French Vasculitis Study Group (2013). Long-term outcomes of 118 patients with eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) enrolled in two prospective trials. Journal of autoimmunity, 43, 60–69. https://doi.org/10.1016/j.jaut.2013.03.003
54. White, J., & Dubey, S. (2023). Eosinophilic granulomatosis with polyangiitis: A review. Autoimmunity reviews, 22(1), 103219. https://doi.org/10.1016/j.autrev.2022.103219
55. Puéchal, X., Pagnoux, C., Baron, G., Quémeneur, T., Néel, A., Agard, C., Lifermann, F., Liozon, E., Ruivard, M., Godmer, P., Limal, N., Mékinian, A., Papo, T., Ruppert, A. M., Bourgarit, A., Bienvenu, B., Geffray, L., Saraux, J. L., Diot, E., Crestani, B., … French Vasculitis Study Group (2017). Adding Azathioprine to Remission-Induction Glucocorticoids for Eosinophilic Granulomatosis With Polyangiitis (Churg-Strauss), Microscopic Polyangiitis, or Polyarteritis Nodosa Without Poor Prognosis Factors: A Randomized, Controlled Trial. Arthritis & rheumatology (Hoboken, N.J.), 69(11), 2175–2186. https://doi.org/10.1002/art.40205
56. Wechsler, M. E., Akuthota, P., Jayne, D., Khoury, P., Klion, A., Langford, C. A., Merkel, P. A., Moosig, F., Specks, U., Cid, M. C., Luqmani, R., Brown, J., Mallett, S., Philipson, R., Yancey, S. W., Steinfeld, J., Weller, P. F., Gleich, G. J., & EGPA Mepolizumab Study Team (2017). Mepolizumab or Placebo for Eosinophilic Granulomatosis with Polyangiitis. The New England journal of medicine, 376(20), 1921–1932. https://doi.org/10.1056/NEJMoa1702079
57. Steinfeld, J., Bradford, E. S., Brown, J., Mallett, S., Yancey, S. W., Akuthota, P., Cid, M. C., Gleich, G. J., Jayne, D., Khoury, P., Langford, C. A., Merkel, P. A., Moosig, F., Specks, U., Weller, P. F., & Wechsler, M. E. (2019). Evaluation of clinical benefit from treatment with mepolizumab for patients with eosinophilic granulomatosis with polyangiitis. The Journal of allergy and clinical immunology, 143(6), 2170–2177. https://doi.org/10.1016/j.jaci.2018.11.041
58. Shiomi, M., Watanabe, R., Ishihara, R., Tanaka, S., Nakazawa, T., & Hashimoto, M. (2025). Comparative Insights on IL-5 Targeting with Mepolizumab and Benralizumab: Enhancing EGPA Treatment Strategies. Biomolecules, 15(4), 544. https://doi.org/10.3390/biom15040544
59. Manka, L. A., Guntur, V. P., Denson, J. L., Dunn, R. M., Dollin, Y. T., Strand, M. J., & Wechsler, M. E. (2021). Efficacy and safety of reslizumab in the treatment of eosinophilic granulomatosis with polyangiitis. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology, 126(6), 696–701.e1. https://doi.org/10.1016/j.anai.2021.01.035
60. Maritati, F., Alberici, F., Oliva, E., Urban, M. L., Palmisano, A., Santarsia, F., Andrulli, S., Pavone, L., Pesci, A., Grasselli, C., Santi, R., Tumiati, B., Manenti, L., Buzio, C., & Vaglio, A. (2017). Methotrexate versus cyclophosphamide for remission maintenance in ANCA-associated vasculitis: A randomised trial. PloS one, 12(10), e0185880. https://doi.org/10.1371/journal.pone.0185880
61. Kitching, A. R., Anders, H. J., Basu, N., Brouwer, E., Gordon, J., Jayne, D. R., Kullman, J., Lyons, P. A., Merkel, P. A., Savage, C. O. S., Specks, U., & Kain, R. (2020). ANCA-associated vasculitis. Nature reviews. Disease primers, 6(1), 71. https://doi.org/10.1038/s41572-020-0204-y
62. Raffray, L., & Guillevin, L. (2020). Rituximab treatment of ANCA-associated vasculitis. Expert opinion on biological therapy, 20(8), 899–910. https://doi.org/10.1080/14712598.2020.1748597
63. Kronbichler, A., Jayne, D. R., & Mayer, G. (2015). Frequency, risk factors and prophylaxis of infection in ANCA-associated vasculitis. European journal of clinical investigation, 45(3), 346–368. https://doi.org/10.1111/eci.12410