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EFFICACY AND SAFETY OF IMMUNOSUPPRESSIVE THERAPY IN ANCA-ASSOCIATED VASCULITIS. A NARRATIVE REVIEW

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Abstract:
Antineutrophil cytoplasmic antibody–associated vasculitis represents a group of severe systemic autoimmune diseases characterized by inflammation of small- and medium-sized blood vessels, often leading to life-threatening organ damage. Over recent decades, advances in immunosuppressive therapy have significantly improved patient survival and remission rates. However, long-term disease control remains limited by frequent relapses and treatment-related toxicity. This narrative review aims to evaluate the efficacy and safety of current immunosuppressive therapies used in the management of ANCA-associated vasculitis, with particular emphasis on emerging glucocorticoid-sparing strategies. Evidence from randomized controlled trials and observational studies demonstrates that conventional induction regimens combining high-dose glucocorticoids with cyclophosphamide or rituximab achieve high remission rates. Rituximab has emerged as an effective alternative to cyclophosphamide, showing comparable efficacy across different disease subtypes and patient populations. Despite these advances, infectious complications and cumulative glucocorticoid toxicity remain major challenges, contributing substantially to morbidity and mortality during both induction and maintenance therapy.
Recent data highlight the potential role of targeted therapies, particularly avacopan, a selective C5a receptor antagonist, in reducing glucocorticoid exposure while maintaining effective disease control. Avacopan-based regimens have been associated with improved safety profiles and enhanced health-related quality of life without an increased risk of serious infections. Overall, optimizing

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the balance between therapeutic efficacy and safety remains central to improving long-term outcomes in ANCA-associated vasculitis.

Keywords: ANCA-associated vasculitis; immunosuppressive therapy; rituximab; cyclophosphamide; avacopan; glucocorticoid-sparing therapy; safety.

Introduction

Anti-neutrophil cytoplasmic antibody–associated vasculitis constitutes a group of severe systemic autoimmune disorders characterized by inflammatory involvement of small and medium-sized blood vessels. The underlying pathological process is driven by immune-mediated injury to the vascular endothelium, resulting in progressive tissue damage and functional impairment of multiple organ systems. The disease spectrum encompasses granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis, which are unified by similar immunopathogenic mechanisms and overlapping clinical manifestations [8].

A defining feature of this group of disorders is the presence of circulating anti-neutrophil cytoplasmic antibodies, which interact with activated neutrophils and components of the complement system, thereby amplifying inflammatory cascades within the vascular wall. This immune activation contributes to necrotizing vasculitis and granulomatous inflammation, ultimately leading to organ-threatening complications [12]. Renal impairment, pulmonary hemorrhage, sinonasal involvement, peripheral neuropathy, and cutaneous lesions are among the most frequently observed clinical manifestations, underscoring the multisystemic nature of the disease and the necessity for timely diagnosis and intervention.

Therapeutic strategies for ANCA-associated vasculitis are traditionally divided into induction of remission and maintenance therapy. Induction regimens commonly rely on high-dose glucocorticoids in combination with potent immunosuppressive agents, such as cyclophosphamide or rituximab, aimed at rapid control of disease activity. Although these approaches have significantly improved survival rates and long-term outcomes, they remain associated with considerable treatment-related toxicity, including infectious complications, metabolic disturbances, and cardiovascular risks [1].

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Despite notable advances in immunosuppressive therapy and a marked improvement in patient prognosis over recent decades, relapse remains a major clinical challenge in the management of ANCA-associated vasculitis. Recurrent disease activity often necessitates repeated or prolonged immunosuppression, increasing the cumulative burden of adverse effects [13]. Consequently, optimizing therapeutic strategies to achieve sustained disease control while minimizing treatment-associated complications remains a critical objective in contemporary vasculitis research.

Efficacy of immunosuppressive therapy in ANCA-associated vasculitis

Immunosuppressive therapy remains the cornerstone of treatment for antineutrophil cytoplasmic antibody associated vasculitis and aims to achieve rapid disease control, prevent irreversible organ damage, and maintain long term remission. Standard management strategies are divided into an induction phase lasting three to six months followed by a prolonged maintenance phase. Despite advances in therapy, disease relapse continues to represent a major clinical challenge [14].

Randomized and non-randomized clinical studies consistently demonstrate high remission rates with current induction regimens. Conventional therapy based on high dose glucocorticoids combined with cyclophosphamide has historically achieved remission in approximately seventy to ninety percent of patients [6]. However, cumulative toxicity and relapse risk have prompted the development of alternative immunosuppressive strategies.

Table 1. PICO framework used to define study eligibility criteria

Element	Description
Population	Adult patients diagnosed with ANCA-associated vasculitis, including granulomatosis with polyangiitis and microscopic polyangiitis
Intervention	Treatment regimens containing avacopan administered alone or in combination with rituximab or cyclophosphamide
Comparison	Conventional immunosuppressive strategies based on glucocorticoids combined with rituximab or cyclophosphamide
Outcomes	Rates of remission at predefined time points, sustained remission, frequency of disease relapse, renal function outcomes, health-related quality of life measures, and incidence of adverse events

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Rituximab has emerged as a highly effective induction agent and has been extensively evaluated in comparison with cyclophosphamide. Large randomized trials have demonstrated that rituximab is not inferior to cyclophosphamide in inducing remission, including in patients with severe disease manifestations and renal involvement. Importantly, comparable remission rates have been observed across different age groups and disease subtypes, supporting the broad applicability of rituximab-based regimens [4].

Beyond induction therapy, maintenance immunosuppression plays a critical role in sustaining remission and reducing relapse rates. Evidence from long term follow up studies indicates that rituximab-based maintenance strategies are effective in prolonging remission and delaying disease recurrence when compared with conventional agents such as azathioprine [17]. Although complete prevention of relapse is not achievable, maintenance therapy significantly improves disease control over time.

Safety and adverse effects of immunosuppressive therapy in ANCA-associated vasculitis

Immunosuppressive therapy plays a central role in the management of ANCA-associated vasculitis; however, its use is frequently limited by treatment-related adverse events. Among these, infectious complications represent one of the most significant safety concerns and contribute substantially to morbidity and mortality [2]. The risk of adverse outcomes reflects a complex interaction between disease-related immune dysfunction and the immunosuppressive effects of therapeutic regimens.

Patients with ANCA-associated vasculitis are inherently susceptible to infections due to disease involvement of the upper and lower respiratory tract, as well as renal impairment. This vulnerability is further amplified by intensive immunosuppressive treatment, particularly during the induction phase, which commonly includes high-dose glucocorticoids in combination with cytotoxic or biologic agents [15]. Despite the implementation of preventive strategies such as vaccination, antimicrobial prophylaxis, and dose reduction of glucocorticoids, infectious complications remain a persistent clinical challenge.

Evidence from systematic reviews and meta-analyses indicates that serious infections occur across all commonly used immunosuppressive regimens,

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including rituximab, cyclophosphamide, and azathioprine. The incidence of severe infections is highest during the induction period but continues to be observed during maintenance therapy. Although fatal infections are relatively uncommon, they constitute a major cause of treatment-related mortality and warrant careful risk assessment and monitoring [8].

Table 2. Distribution of serious infection categories during maintenance immunosuppressive therapy

Infection category	Relative frequency among reported cases
Respiratory infections	Most frequently reported
Gastrointestinal infections	Moderately reported
Genitourinary infections	Less frequently reported
Sepsis	Clinically significant but less common
Other or unspecified infections	Reported in a minority of cases

Rituximab-based regimens have demonstrated an acceptable safety profile when compared with conventional cyclophosphamide-based therapy. While rituximab does not appear to increase the overall risk of severe infections beyond expected levels, specific adverse events such as hypogammaglobulinemia, cytopenia, and delayed immune reconstitution have been reported, particularly with repeated or prolonged exposure [5]. These findings highlight the importance of individualized treatment strategies and long-term surveillance.

Emerging therapeutic strategies and future directions in ANCA-associated vasculitis

The safety of immunosuppressive therapy represents a major concern in the management of ANCA-associated vasculitis, particularly in the context of prolonged glucocorticoid exposure. Although glucocorticoids remain a central component of remission induction, their long-term use is associated with substantial toxicity, including metabolic disturbances, neuropsychiatric complications, osteoporosis, cardiovascular events, and increased susceptibility to infection [9]. These limitations have driven the development of glucocorticoid-sparing strategies aimed at maintaining disease control while reducing treatment-related harm.

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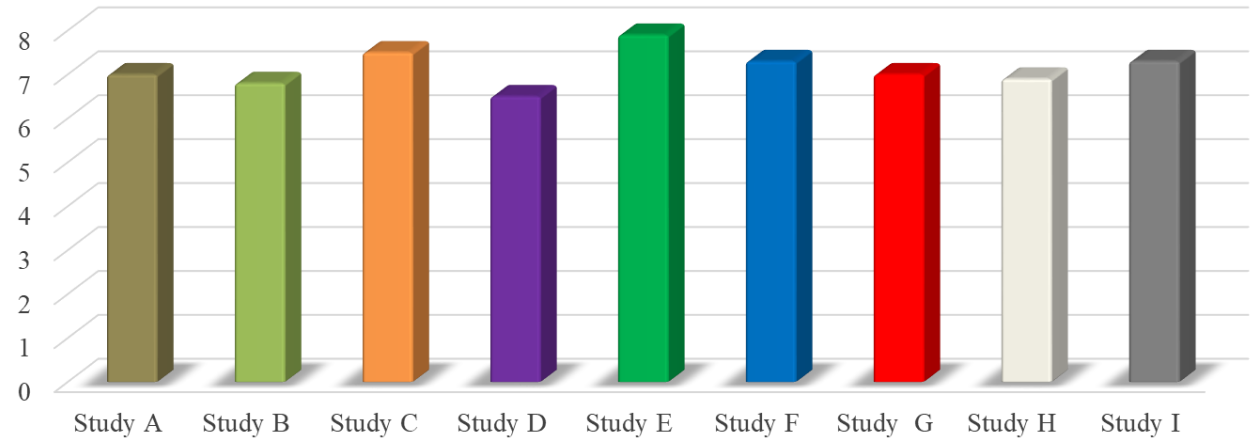

Fig. 3. Health-related quality of life outcomes reported across studies evaluating avacopan-based therapy in ANCA-associated vasculitis.

**a) Geetha et al. b) Harigai & Takada c) Jayne et al. d) Jayne et al. e) Jayne et al. f) Jayne et al. g) Krohklär et al. h) Merkel et al. i) Zonozi et al.*

Recent evidence indicates that avacopan, a selective C5a receptor antagonist, offers a favorable safety profile when used as part of induction and maintenance regimens for ANCA-associated vasculitis. By inhibiting C5a-mediated neutrophil activation without suppressing the entire complement cascade, avacopan provides targeted immunomodulation while preserving host defense mechanisms [3]. This mechanism distinguishes avacopan from conventional immunosuppressive agents and may account for its improved tolerability.

Across randomized controlled trials and post hoc analyses, avacopan-based regimens have been associated with a reduced burden of glucocorticoid-related adverse events. Patients receiving avacopan experienced lower rates of metabolic complications, including weight gain and hyperglycemia, as well as fewer neuropsychiatric side effects such as mood disturbances and sleep disorders [16]. Importantly, avacopan therapy was also linked to improved health-related quality of life measures, reflecting both reduced toxicity and better functional outcomes.

Infectious complications remain a critical safety endpoint in patients with ANCA-associated vasculitis. Available data suggest that avacopan does not increase the incidence of serious infections compared with standard glucocorticoid-containing regimens. Most reported adverse events in avacopan-treated patients were mild to moderate in severity, with a lower frequency of treatment discontinuation due

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to toxicity [11]. These findings support the notion that selective complement inhibition may mitigate inflammation without substantially compromising immune competence.

Discussion

The management of ANCA-associated vasculitis has evolved substantially over recent decades, leading to significant improvements in patient survival and disease control. Current immunosuppressive strategies are highly effective in inducing remission; however, long-term outcomes remain limited by frequent relapses and treatment-related toxicity. The present analysis highlights the ongoing challenge of balancing therapeutic efficacy with safety and tolerability in this complex multisystem disease.

Evidence from randomized and observational studies confirms that conventional immunosuppressive regimens, including cyclophosphamide- and rituximab-based therapies, achieve high remission rates during the induction phase. Rituximab, in particular, has emerged as a reliable alternative to cyclophosphamide, demonstrating comparable efficacy across different disease severities and patient subgroups [6]. Nevertheless, sustained remission remains difficult to achieve, and a substantial proportion of patients experience disease relapse despite maintenance therapy.

Safety considerations represent a major determinant of long-term treatment success. Infectious complications are among the most clinically relevant adverse events associated with immunosuppressive therapy and contribute significantly to morbidity and mortality. Available data indicate that serious infections occur across all commonly used maintenance regimens, with no striking differences between rituximab- and azathioprine-based approaches [7]. These findings underscore the importance of careful patient selection, vigilant monitoring, and the implementation of preventive strategies to mitigate infection risk.

The emergence of glucocorticoid-sparing therapies represents a critical advance in addressing treatment-related toxicity. Avacopan, through selective inhibition of the C5a receptor, offers a targeted mechanism that reduces reliance on high-dose glucocorticoids while maintaining effective disease control. Clinical trials and pooled analyses suggest that avacopan-based regimens are associated with reduced glucocorticoid-related adverse effects and improved patient-reported

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quality of life, without a concomitant increase in serious infections [2]. These outcomes highlight the potential of complement-targeted therapy to improve both clinical and patient-centered endpoints.

Despite these encouraging findings, several limitations warrant consideration. Heterogeneity in study design, patient populations, and outcome definitions complicates direct comparisons across trials. Additionally, long-term real-world data on the safety and durability of newer therapeutic approaches remain limited. Future research should focus on identifying biomarkers for treatment response, optimizing individualized maintenance strategies, and evaluating long-term outcomes in diverse patient populations [11].

In conclusion, while current immunosuppressive therapies remain effective for the management of ANCA-associated vasculitis, treatment-related toxicity continues to pose significant challenges. Glucocorticoid-sparing strategies such as avacopan represent a promising step toward more personalized and tolerable treatment paradigms. Continued refinement of therapeutic approaches is essential to improve long-term disease control while minimizing adverse effects.

Conclusion

Immunosuppressive therapy has fundamentally transformed the prognosis of ANCA-associated vasculitis, enabling effective remission induction and improved survival across diverse patient populations. Both cyclophosphamide- and rituximab-based regimens demonstrate high efficacy during the induction phase, while maintenance strategies contribute to prolonged disease control. Nevertheless, sustained remission remains challenging, and disease relapse continues to affect a substantial proportion of patients, highlighting the inherent limitations of current therapeutic approaches despite their proven effectiveness.

Treatment-related toxicity, particularly infectious complications and glucocorticoid-associated adverse effects, represents a major barrier to long-term treatment success. Serious infections occur across all commonly used immunosuppressive regimens and remain a leading cause of morbidity and mortality, underscoring the need for careful risk stratification, vigilant monitoring, and preventive measures. The cumulative burden of glucocorticoid toxicity further emphasizes the importance of minimizing prolonged exposure while maintaining adequate disease suppression.

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The emergence of glucocorticoid-sparing strategies marks an important step toward optimizing the balance between efficacy and safety in ANCA-associated vasculitis. Avacopan, through selective inhibition of the C5a receptor, offers a targeted therapeutic approach that reduces glucocorticoid-related toxicity without compromising disease control. Evidence demonstrating improved health-related quality of life and a favorable safety profile supports its potential role in more personalized and patient-centered treatment paradigms. Future research should focus on long-term real-world outcomes, biomarker-guided therapy selection, and the integration of novel agents to further refine management strategies and improve both clinical and patient-reported outcomes.

References

1. Jayne DRW, Merkel PA, Schall TJ, Bekker P. **Avacopan for the Treatment of ANCA-Associated Vasculitis.** *N Engl J Med.* 2021.
2. Hellmich B, Sanchez-Alamo B, Schirmer JH, et al. **EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update.** *Ann Rheum Dis.* 2024;83:30–45.
3. Floege J, et al. **KDIGO 2024 Clinical Practice Guideline for the Management of ANCA–Associated Vasculitis.** *Kidney International.* 2024.
4. Biddle K, et al. **The 2025 British Society for Rheumatology management guideline for ANCA-associated vasculitis.** *Rheumatology (Oxford).* 2025.
5. Chalkia A, Karras A. **ANCA-associated vasculitis—treatment standard.** *[Review]* 2023.
6. Schirmer JH, et al. **Systematic literature review informing the 2022 update of the EULAR recommendations for the management of AAV: part 1 (treatment of GPA/MPA).** *RMD Open.* 2023;9:e003082/e003083.
7. Sanchez-Alamo B, Schirmer JH, Hellmich B, et al. **Systematic literature review informing the 2022 update of the EULAR recommendations: part 2.** *RMD Open.* 2023.
8. Habibi MA, et al. **The Efficacy and Safety of Rituximab in ANCA-Associated Vasculitis: a Systematic Review.** *Biology (Basel).* 2022;11(12):1767.

Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 04, April, 2026
Website: https://researchiapress.com

9. Geetha D, et al. **Efficacy and safety of avacopan in patients with AAV receiving background induction therapy with rituximab.** *Ann Rheum Dis.* 2024;83(2):223–231.
10. Berke I, et al. **Systematic Review of Efficacy and Safety of Avacopan in ANCA-Associated Vasculitis (clinical trials + real-world).** *Kidney Int Rep.* 2025.
11. Berdieva D. U., Nurmukhamedova N. S., Azimova S. B. Difficulties in diagnosing the human immunodeficiency virus (hiv) occurring under the guise of systemic lupus erythematosus //World Bulletin of Public Health. – 2022. – T. 13. – C. 188-191.
12. Dilfuza Berdiyeva. Assessment of clinical and diagnostic indicators of Grunulematosis with Polyangiitis// British Medical Journal Volume-1, No 2 - 2021. P 238-249
13. Бердиева Д.У. Гранулематоз полиангиитнинг этиопатогенетик ривожланиш механизмларига замонавий қарашлар// JOURNALOFIQRO–ЖУРНАЛИҚРО–IQROJURNALI– volume17,issue02,2025 P 84-89
14. BerdiyevaD.U.,OrolovB.N. Respirator va buyrak tizimlariga tahdid: poliangitli granulematozni tashxislash va davolash// journalofiqro– volume17,issue02,2025 P 542-548
15. Berdieva D. U. Evaluating the effectiveness of targeted therapy in the treatment of patients with granulomatosis with polyangiitis // Modern American Journal of Medical and Health Sciences. - 2025. - Volume 01. - P 9-24
16. Berdieva D.U. (2025). Evaluation of the efficiency of methods of diagnostics of various variants of granulomatosis with polyangiitis. International Journal of Medical Sciences And Clinical Research, 5(03), 40–45. https://doi.org/10.37547/ijmscr/Volume05Issue03-08
17. Rizamuxamedova M.Z., Berdieva D.U., Nurmuxamedova N.S., Orolov B.N. Poliangiitli granulematozning faolligi va zararlanish ko‘rsatkichlarini baholash // Toshkent tibbiyot akademiyasi axborotnomasi2025 yil mart P 148-152.