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Review

The Expanding Role of JAK Inhibitors in Vasculitis: From Large-Vessel Disease to Emerging Evidence in Monogenic Syndromes

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Abstract: Janus kinase (JAK) inhibitors have emerged as a potential therapeutic class across immune-mediated diseases, prompting interest in their application to vasculitis. Although data remain limited, early evidence suggests that JAK inhibition may offer clinical benefit in selected settings, including large-vessel vasculitis and Behçet's disease and monogenic vasculopathies such as adenosine deaminase 2 deficiency (DADA2) and VEXAS syndrome, where treatment options are often restricted and disease control is challenging. In these conditions, modulation of intracellular signaling pathways may translate into improvements across systemic, cutaneous, and hematologic domains. Overall, while JAK inhibitors represent a promising and biologically plausible therapeutic avenue for difficult-to-treat vasculitic conditions, current evidence is derived almost entirely from retrospective studies and case series. Ongoing and future investigations are needed to define efficacy and optimal treatment strategies.

Keywords: janus kinase inhibitors; vasculitis; large-vessel vasculitis; Behçet's disease; DADA2; VEXAS syndrome; autoimmunity

1. Introduction

Vasculitides comprise a heterogeneous group of systemic inflammatory disorders characterized by immune-mediated injury of blood vessel walls of varying caliber, leading to ischemia, tissue damage and organ dysfunction [1]. Despite differences in clinical expression across large-, medium-, and small-vessel diseases, many forms of vasculitis share convergent immunopathologic pathways driven by dysregulated cytokine signaling. Increasing evidence places the JAK–STAT axis at the crossroads of vascular inflammation, particularly in large-vessel vasculitis (LVV), giant cell arteritis (GCA), Takayasu arteritis (TAK) and Behçet's disease (BD) [2].

In LVV, vascular lesions are characterized by granulomatous inflammation sustained by dendritic cells, macrophages, and highly activated Th1 and Th17 cells, whose functions depend on STAT1/2/4 and STAT3 signaling pathways, respectively. These effector populations depend heavily on JAK-STAT–mediated cytokine circuits, including IFN-γ, IL-6, IL-12, IL-23, and IL-17 [3–6]. These cytokines drive not only immune activation but also the vascular remodeling that ultimately leads to luminal compromise [7–9]. Transcriptomic studies confirm marked activation of these pathways in arteritic lesions, accompanied by increased production of IFN-γ, IL-17, and IL-21 [10,11]. In parallel, in BD, innate immune activation is more prominent, with increased STAT3 phosphorylation in monocytes and T cells contributing to neutrophil hyperreactivity and endothelial dysfunction [12,13].

The Janus kinase (JAK)–signal transducer and activator of transcription (STAT) pathway represents a central intracellular signaling hub for more than 50 cytokines and growth factors [14]. Upon ligand binding, paired JAKs (JAK1, JAK2, JAK3, TYK2) phosphorylate STAT proteins, which translocate to the nucleus and drive transcription of inflammatory, angiogenic, and tissue-remodeling genes [15]. Aberrant activation of this pathway

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has been documented in arterial lesions of GCA and TAK [16,17] and in circulating immune cells of BD[12], providing a biologically coherent rationale for the use of pharmacologic JAK inhibition.

JAK inhibitors (JAKi), including agents with preferential selectivity for JAK1 (upadacitinib, filgotinib), JAK1/2 (baricitinib, ruxolitinib), JAK1/3 (tofacitinib), or TYK2 [18], have been approved for the treatment of several immune-mediated diseases. Their capacity to simultaneously modulate multiple inflammatory cytokines distinguishes them from single-target biologics.

Over the past decade, the therapeutic use of JAK inhibitors has expanded considerably across immune-mediated rheumatic diseases. Beyond inflammatory arthritis, growing evidence supports their efficacy in several connective tissue diseases, where they have shown promising effects on disease activity and glucocorticoid sparing [19–24]. These clinical observations, together with increasing knowledge of the role of the JAK–STAT pathway in immune regulation, have provided a strong biological rationale for investigating JAK inhibition in vasculitis.

By blocking multiple upstream cytokine networks, JAKi offer the possibility of simultaneously targeting different immune pathways, attenuating Th1/Th17-driven pathology in large-vessel vasculitis while dampening innate effector responses in BD (Figure 1).

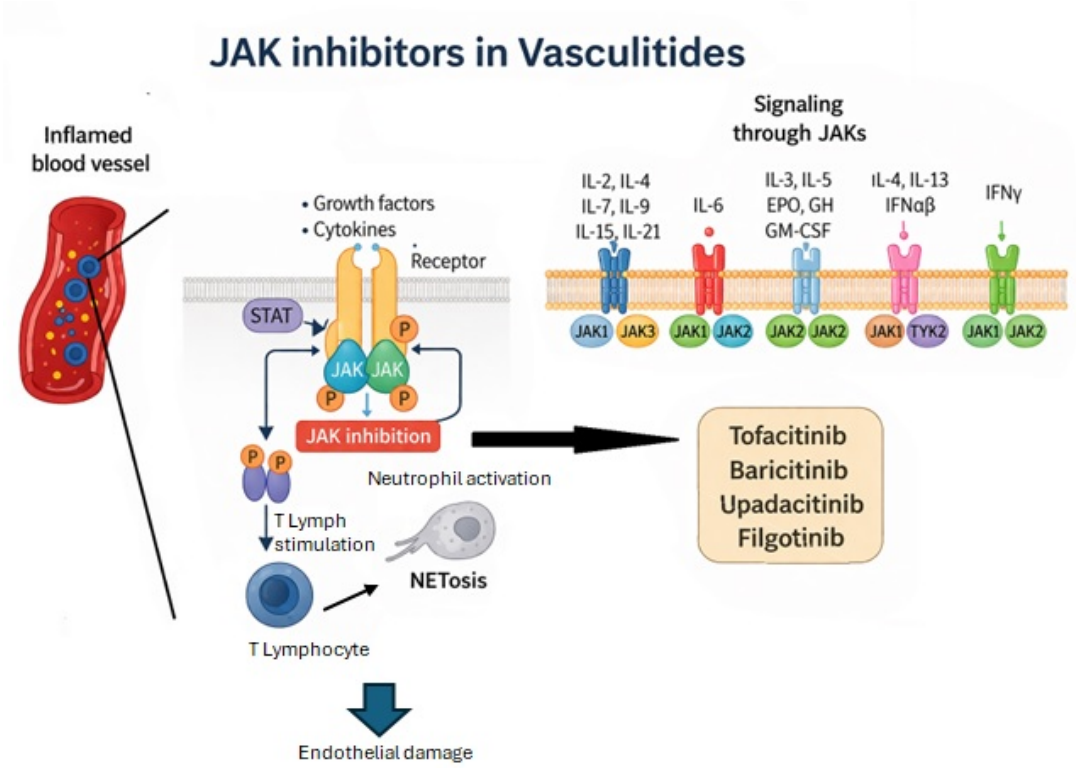


Figure 1. Pro-inflammatory cytokines relevant to vascular inflammation activate JAK–STAT pathways downstream of their receptors, promoting transcriptional programs that sustain Th1/Th17 responses, innate immune activation, and vascular remodeling. JAKi target this intracellular signaling hub, enabling simultaneous modulation of multiple cytokine networks involved in vasculitic disease.

Early translational and clinical data across GCA, TAK, and BD suggest meaningful steroid-sparing effects, prevention of relapse, and improvement in vascular inflammation, highlighting JAK inhibition as one of the most promising emerging approaches for refractory or relapsing vasculitis.

Emerging observations from rare conditions affecting vessels, such as DADA2 and VEXAS syndrome, highlight the potential involvement of JAK-related mechanisms. While clinical experience with JAK inhibitors is increasing in VEXAS syndrome, evidence in DADA2 remains largely limited to mechanistic studies supporting activation of the IFN-JAK-STAT pathway.

Data on other forms of vasculitis are limited. Preliminary signals suggest a broader role of JAK/STAT dysregulation. In polyarteritis nodosa, increased STAT3 activation has been reported in circulating T cells [25], while in Kawasaki disease elevated CXCL10, a STAT-induced chemokine, has been detected during active phases [26,27].

2. Large-Vessel Vasculitis

Large-vessel vasculitis refers to inflammatory disorders that primarily involve large-caliber vessels, leading to vascular wall damage, stenosis, and ischemic complications [28]. Preclinical studies have begun to delineate how suppression of JAK-STAT pathway alters the course of vascular inflammation. *In vitro* exposure of T cells from patients with TAK to ruxolitinib or tofacitinib suppressed Th1 and Th17 polarization, promoted regulatory T-cell differentiation, and reduced CD25 expression [29]. In a GCA mouse model, tofacitinib disrupted the survival of tissue-resident memory T cells, downregulated key transcriptional programs, and reduced the production of IFN-γ, IL-17, and IL-21, directly linking JAK/STAT blockade to attenuation of vascular inflammation [30]. These mechanisms extend beyond immune modulation: JAK inhibition also attenuates vascular remodeling by reducing endothelial expression of growth factors, such as platelet-derived growth factor (PDGF), fibroblast growth factor 2 (FGF2), vascular endothelial growth factor (VEGF), thereby suppressing angiogenesis and intimal hyperplasia [30–33]. In experimental aortitis, JAK blockade restored physiological STAT3 phosphorylation and suppressed endothelial IL-17A expression, collectively dampening vascular injury [34].

Clinical experience, though still evolving, increasingly supports these biological predictions. In GCA, retrospective studies [35,36] reported clinically meaningful improvement, substantial glucocorticoid-sparing effects, and an acceptable safety profile in patients with relapsing or refractory disease treated with tofacitinib, baricitinib, or upadacitinib. Treatment with JAKi has been associated not only with clinical improvement but also with measurable reductions in vascular inflammation, as demonstrated by decreased ^18F-FDG uptake on PET/CT [37,38].

These signals were corroborated by a prospective open-label pilot trial, in which baricitinib 4 mg/day achieved sustained disease control and allowed steroid discontinuation in the majority of relapsing patients, with only a single relapse over 52 weeks [39].

Most importantly, the phase 3 SELECT-GCA trial [40] has now provided the first high-quality randomized evidence for JAK inhibition in vasculitis. In 209 patients with new-onset or relapsing GCA, upadacitinib 15 mg once daily combined with a 26-week glucocorticoid taper achieved significantly higher rates of sustained remission at 52 weeks compared with placebo plus a 52-week taper. Benefits extended to key secondary endpoints, including sustained complete remission, time to flare, cumulative steroid exposure, and patient-reported outcomes. The safety profile was encouraging, with no major cardiovascular events and an overall tolerability comparable to that observed in other immune-mediated diseases. Notably, the 7.5 mg dose did not demonstrate superiority over placebo, underscoring the importance of achieving sufficient JAK1 inhibition.

In TAK, evidence is more fragmented but increasingly compelling. Kong et al. [41] reported that tofacitinib was superior to methotrexate in controlling disease activity and preventing relapses in a prospective cohort. Complementing this, several small case series and reports have documented responses to tofacitinib in patients with highly refractory TAK, often after failure of multiple biologics [42–47]. Notably, a recent multicentre international retrospective study further supported these findings, showing a complete response in 50% of patients at 6 months, together with significant reductions in disease activity, C-reactive protein levels and glucocorticoid requirements [48].

Imaging and biomarker studies provide additional mechanistic support, demonstrating reductions in arterial inflammation and normalization of cytokine profiles in parallel with clinical improvement after tofacitinib therapy [49].

A prospective cohort from a tertiary referral centre [50] showed that baricitinib may also induce remission in refractory TAK, further reinforcing the therapeutic relevance of JAK inhibition in this setting. Additional data regarding the efficacy of tofacitinib in TAK are anticipated from an ongoing clinical trial (NCT04299971) [51]. Concurrently, the JAK1-selective inhibitor upadacitinib is being examined in a phase-3, multicenter, placebo-controlled study (SELECT-Takayasu; NCT04161898) [52].

3. Behçet's Disease

Behçet's disease is a multisystem inflammatory disorder characterized by recurrent mucocutaneous lesions, ocular involvement, vascular inflammation, and, in some patients, neurologic or gastrointestinal disease [53]. Early clinical experience with JAKi in BD is encouraging but heterogeneous. Tofacitinib has shown potential efficacy in intestinal disease and in vascular and systemic features [54–56]. Baricitinib has demonstrated broader benefit, achieving mucosal healing in intestinal Behçet's [57] and improving vascular manifestations [58]. More recently, upadacitinib induced rapid remission in anti-TNF–refractory uveitis with macular edema [59], raising the possibility that selective JAK1 inhibition may be especially effective in ocular inflammation, a domain traditionally difficult to manage and associated with considerable morbidity. The prominence of STAT3 signaling in BD provides a plausible mechanistic foundation for these clinical results.

4. Adenosine Deaminase 2 Deficiency

Adenosine deaminase 2 deficiency (DADA2) is a rare monogenic vasculopathy resulting from biallelic loss-of-function mutations in ADA2 (formerly CECR1). Its clinical expression is remarkably heterogeneous, including mucocutaneous ulcers, intestinal involvement, livedo racemosa, and thrombotic complications [60]. Because of its rarity, therapeutic evidence derives almost entirely from case series, and no controlled clinical trials have yet been conducted. Anti-TNF agents remain the cornerstone of therapy, reflecting the central role of TNF-driven macrophage activation in the disease; however, even these agents fail to adequately control all disease manifestations. Responses to IL-1 blockade have generally been incomplete, and the role of B-cell depletion with rituximab remains uncertain because of limited follow-up and variable outcomes reported across isolated cases [61].

The pathogenesis of DADA2 is defined by a complex interplay between innate and adaptive immune cells, initiated by the insufficient or absent enzymatic activity of ADA2. Loss of ADA2 function impairs the conversion of adenosine to inosine, leading to extracellular adenosine accumulation. This metabolic disturbance promotes chronic activation of innate immune cells, with increased NETosis and a shift of macrophages toward an M1 inflammatory phenotype with increased TNF-α production while endothelial and myeloid cells sustain inflammation through NF-κB and interferon pathways. Recent evidence indicates that the IFN–JAK–STAT1 axis is prominently activated in DADA2, with the strongest signatures observed in monocytes and T cells. Persistent STAT1 signaling amplifies pro-inflammatory macrophage responses, disturbs T-cell homeostasis, and impairs B-cell maturation, suggesting that immune dysregulation in DADA2 extends beyond the TNF- and NF-κB–dependent mechanisms traditionally described in the disease. These findings provide a biological rationale for considering JAK inhibition as a potential therapeutic strategy.

By modulating a key intracellular pathway through which interferons drive disease activity, JAK inhibitors could theoretically target components of immune dysregulation that persist despite TNF blockade, expanding the therapeutic options for this complex vasculopathy [62–64]. However, it is important to emphasize that no clinical studies or systematic evaluations of JAKi in DADA2 are currently available, and this therapeutic rationale remains entirely speculative. Rigorous preclinical work and dedicated clinical trials will be required to determine whether JAK inhibition can meaningfully modulate disease activity in this setting.

5. VEXAS Syndrome

VEXAS syndrome is an adult-onset autoinflammatory disorder caused by somatic UBA1 mutations in hematopoietic progenitors, leading to defective ubiquitination in myeloid precursors and a systemic inflammatory phenotype characterized by cytopenia, chondritis, vasculitic features and recurrent fever [65]. The inflammatory signature is broad, with activation of type I and type II interferon pathways, upregulation of NF-κB–related signals and production of proinflammatory cytokines by dysregulated myeloid cells [66,67]. The marked interferon activation in VEXAS provides a biological rationale for considering JAK inhibition, given the central role of the JAK–STAT signaling in interferon-dependent immune activation.

Clinical evidence for JAKi in VEXAS, although still limited, is growing. The most informative data derive from a multicenter retrospective cohort of 30 patients [68] in which ruxolitinib, tofacitinib, baricitinib and upadacitinib were administered after extensive treatment failure; approximately half achieved clinical improvement within one month. Ruxolitinib showed the most consistent effects, particularly on hematologic abnormalities, with particularly consistent improvement in hemoglobin levels. This may reflect its JAK1/2 inhibition profile and additional activity on TYK2, a kinase broadly expressed in hematopoietic cells and implicated in type I interferon signaling. Improvement in inflammatory manifestations has also been reported, including resolution of cutaneous vasculitis with ruxolitinib and disease remission with upadacitinib in patients with underlying myelodysplastic features. However, these findings are currently supported only by small retrospective series and individual case reports. The successful use of filgotinib has also been described after two months of therapy [69,70].

Despite these encouraging findings, available evidence remains limited by heterogeneous endpoints, variable dosing strategies, frequent concomitant therapies, and the absence of prospective or controlled studies. Consequently, it remains unclear how durable these responses are or which VEXAS phenotypes might derive the greatest benefit from JAK inhibition. While the interferon-driven biology of the disease provides a compelling rationale for further investigation, current use of JAK inhibitors in VEXAS should still be regarded as experimental.

6. Conclusions

Although evidence is still evolving, JAK inhibition has emerged as a promising therapeutic strategy for several forms of vasculitis. The strongest clinical evidence is currently available for GCA, while encouraging

results have also been reported in TAK, BD and other forms of vasculitis. However, the available data are still insufficient to define how JAK inhibitors should be used in clinical practice, and whether these agents can be used earlier in the disease course rather than being reserved for refractory disease remains to be established. Several important questions still remain, including the optimal dosing strategies and the selection of appropriate candidates are not yet fully defined. The lack of efficacy observed with the 7.5-mg dose underscores a fundamental question about the minimal pharmacologic threshold required to suppress vascular inflammation. Future studies integrating pharmacokinetic and pharmacodynamic data may help answer this question by correlating systemic drug exposure with p-STAT suppression within vascular lesions. They may also clarify whether selective JAK1 inhibition offers advantages over broader JAK inhibition in large-vessel vasculitis as well as provide information on the optimal duration of treatment and the risk of relapse after treatment discontinuation.

Safety also remains an important consideration: boxed warnings for this drug class include major adverse cardiovascular events, venous thromboembolism, malignancy and serious infections, including herpes zoster [71,72]. Although the available studies in vasculitis have not identified new disease-specific safety signals, these data are still limited by small sample size and relatively short follow-up [35,36,39–41,50]. Because patients with vasculitis often have an increased baseline risk of cardiovascular and thrombotic events related to chronic inflammation and vascular damage [28], careful assessment of individual risk factors remains essential when considering JAK inhibitor therapy.

Another important consideration is that the JAK–STAT pathway is only one component of the complex inflammatory network involved in vasculitis. The persistence of inflammation driven by alternative pathways, such as NF-κB, may explain the variable response observed across different vasculitic phenotypes, particularly in those that are less dependent on Th1/Th17 cytokine circuits. A better understanding of these mechanisms may support the development of more personalized therapeutic strategies and, where appropriate, combination approaches.

Overall, further prospective controlled studies are needed to better define the efficacy, safety and optimal use of JAK inhibitors across the different forms of vasculitis. If future studies confirm the available evidence, JAK inhibitors may become an important therapeutic option, particularly for GCA, TAK and BD where the strongest evidence is currently available. However, more evidence will be needed before they can be widely adopted in clinical practice.

Author Contributions

L.B.: investigation, literature review, writing—original draft preparation; G.C.: investigation, literature review, writing—review and editing; R.d.P.: investigation, visualization, writing—review and editing; E.B.: supervision, validation, writing—review and editing; C.P.: conceptualization, methodology, supervision, validation, writing—original draft preparation, writing—review and editing. All authors have read and agreed to the published version of the manuscript and agree to be accountable for their respective contributions and for ensuring that questions concerning the accuracy or integrity of the work are appropriately investigated and resolved.

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Conflicts of Interest

The authors declare no conflicts of interest.

Use of AI and AI-Assisted Technologies

During the preparation of this work, the authors used ChatGPT (OpenAI) to assist with language editing, grammatical corrections, improving the clarity and readability of the manuscript, and graphical refinement and amendment of the figure. After using this tool, the authors carefully reviewed and edited the text and figure as needed, verified their scientific accuracy, and take full responsibility for the content of the published article.

References

1. Watts, R.A.; Robson, J. Introduction, epidemiology and classification of vasculitis. *Best. Pract. Res. Clin. Rheumatol.* **2018**, *32*, 3–20. https://doi.org/10.1016/j.berh.2018.10.003.
2. Bursi, R.; Cafaro, G.; Perricone, C.; et al. Contribution of Janus-Kinase/Signal Transduction Activator of Transcription Pathway in the Pathogenesis of Vasculitis: A Possible Treatment Target in the Upcoming Future. *Front. Pharmacol.* **2021**, *12*, 635663. https://doi.org/10.3389/fphar.2021.635663.
3. Deng, J.; Younge, B.; Olshen, R.; et al. Th17 and Th1 T-cell responses in giant cell arteritis. *Circulation* **2010**, *121*, 906–915. https://doi.org/10.1161/circulationaha.109.872903.
4. Watanabe, R.; Hashimoto, M. Vasculitogenic T Cells in Large Vessel Vasculitis. *Front. Immunol.* **2022**, *13*, 923582. https://doi.org/10.3389/fimmu.2022.923582.
5. Qin, Z.; Wang, R.; Hou, P.; et al. TCR signaling induces STAT3 phosphorylation to promote TH17 cell differentiation. *J. Exp. Med.* **2024**, *221*, e20230683. https://doi.org/10.1084/jem.20230683.
6. Kaplan, M.H.; Grusby, M.J. Regulation of T helper cell differentiation by STAT molecules. *J. Leukoc. Biol.* **1998**, *64*, 2–5. https://doi.org/10.1002/jlb.64.1.2.
7. Weyand, C.; Younge, B.; Goronzy, J. IFN-γ and IL-17: The two faces of T-cell pathology in giant cell arteritis. *Curr. Opin. Rheumatol.* **2011**, *23*, 43–49. https://doi.org/10.1097/bor.0b013e32833ee946.
8. Weyand, C.M.; Goronzy, J.J. Immune mechanisms in medium and large-vessel vasculitis. *Nat. Rev. Rheumatol.* **2013**, *9*, 731–740. https://doi.org/10.1038/nrrheum.2013.161.
9. Koster, M.J.; Warrington, K.J. Giant cell arteritis: Pathogenic mechanisms and new potential therapeutic targets. *BMC Rheumatol.* **2017**, *1*, 2. https://doi.org/10.1186/s41927-017-0004-5.
10. Watanabe, R.; Berry, G.J.; Liang, D.H.; et al. Cellular Signaling Pathways in Medium and Large Vessel Vasculitis. *Front. Immunol.* **2020**, *11*, 587089. https://doi.org/10.3389/fimmu.2020.587089.
11. Greigert, H.; Genet, C.; Ramon, A.; et al. New Insights into the Pathogenesis of Giant Cell Arteritis: Mechanisms Involved in Maintaining Vascular Inflammation. *J. Clin. Med.* **2022**, *11*, 2905. https://doi.org/10.3390/jcm11102905.
12. Tulunay, A.; Dozmorov, M.; Ture-Ozdemir, F.; et al. Activation of the JAK/STAT pathway in Behcet's disease. *Genes Immun.* **2015**, *16*, 170–175. https://doi.org/10.1038/gene.2014.64.
13. van der Houwen, T.B.; van Hagen, P.M.; van Laar, J.A.M. Immunopathogenesis of Behçet's disease and treatment modalities. *Semin. Arthritis Rheum.* **2022**, *52*, 151956. https://doi.org/10.1016/j.semarthrit.2022.151956.
14. Lv, Y.; Mi, P.; Babon, J.J.; et al. Small molecule drug discovery targeting the JAK-STAT pathway. *Pharmacol. Res.* **2024**, *204*, 107217. https://doi.org/10.1016/j.phrs.2024.107217.
15. Hu, X.; Li, J.; Fu, M.; et al. The JAK/STAT signaling pathway: From bench to clinic. *Signal Transduct. Target. Ther.* **2021**, *6*, 402. https://doi.org/10.1038/s41392-021-00791-1.
16. Bonacini, M.; Rossi, A.; Ferrigno, I.; et al. The importance of defining which Janus kinases are activated in giant cell arteritis. *Clin. Exp. Rheumatol.* **2023**, *41*, 784–786. https://doi.org/10.55563/clinexprheumatol/u7elc2.
17. Watanabe, R.; Hashimoto, M. Perspectives of JAK Inhibitors for Large Vessel Vasculitis. *Front. Immunol.* **2022**, *13*, 881705. https://doi.org/10.3389/fimmu.2022.881705.
18. Virtanen, A.; Palmroth, M.; Liukkonen, S.; et al. Differences in JAK Isoform Selectivity Among Different Types of JAK Inhibitors Evaluated for Rheumatic Diseases Through *In Vitro* Profiling. *Arthritis Rheumatol.* **2023**, *75*, 2054–2061. https://doi.org/10.1002/art.42547.
19. Bruno, L.; Cafaro, G.; Dal Pozzolo, R.; et al. JAK inhibitors in areas outside of inflammatory arthritis: Focus on connective tissue diseases. *Rheumatology* **2026**, *65*, keag317. https://doi.org/10.1093/rheumatology/keag317.
20. Ma, C.; Liu, M.; Cheng, Y.; et al. Therapeutic efficacy and safety of JAK inhibitors in treating polymyositis/dermatomyositis: A single-arm systemic meta-analysis. *Front. Immunol.* **2024**, *15*, 1382728. https://doi.org/10.3389/fimmu.2024.1382728.
21. Fazeli, P.; Bahramian, S.; Farahmand, K.; et al. JAK Inhibitors for Treatment of SAPHO Syndrome: A Systematic Review of 72 Cases. *ACR Open Rheumatol.* **2025**, *7*, e70101. https://doi.org/10.1002/acr2.70101.
22. Ma, L.; Peng, L.; Zhao, J.; et al. Efficacy and safety of Janus kinase inhibitors in systemic and cutaneous lupus erythematosus: A systematic review and meta-analysis. *Autoimmun. Rev.* **2023**, *22*, 103440. https://doi.org/10.1016/j.autrev.2023.103440.
23. Ansari, M.S.; Vahabi, S.M.; Memari, H.; et al. Use of the oral Janus kinase inhibitor tofacitinib in the treatment of morphea: A retrospective study. *J. Am. Acad. Dermatol.* **2025**, *93*, 769–771. https://doi.org/10.1016/j.jaad.2025.05.1377.
24. Crisler, W.J.; Rowley, R.; Oke, O.; et al. Eosinophilic Fasciitis and Morphea Share Gene Signatures of Inflammatory Cell Death, Self-DNA Recognition, and Enhanced Jak/Signal Transducer and Activator of Transcription Signaling. *J. Investig. Dermatol.* **2026**, *146*, 64–77.e1. https://doi.org/10.1016/j.jid.2025.05.023.
25. Rimar, D.; Alpert, A.; Starosvetsky, E.; et al. Tofacitinib for polyarteritis nodosa: A tailored therapy. *Ann. Rheum. Dis.* **2016**, *75*, 2214–2216. https://doi.org/10.1136/annrheumdis-2016-209330.

26. Shikishima, Y.; Saeki, T.; Matsuura, N. Chemokines in Kawasaki disease: Measurement of CCL2, CCL22 and CXCL10. *Asian Pac. J. Allergy Immunol.* **2003**, *21*, 139–143.
27. Hosaka, S.; Imagawa, K.; Yano, Y.; et al. The CXCL10-CXCR3 axis plays an important role in Kawasaki disease. *Clin. Exp. Immunol.* **2024**, *216*, 104–111. https://doi.org/10.1093/cei/uxad125.
28. Pugh, D.; Karabayas, M.; Basu, N.; et al. Large-vessel vasculitis. *Nat. Rev. Dis. Prim.* **2022**, *7*, 93. https://doi.org/10.1038/s41572-021-00327-5.
29. Régnier, P.; Le Joncour, A.; Maciejewski-Duval, A.; et al. Targeting JAK/STAT pathway in Takayasu's arteritis. *Ann. Rheum. Dis.* **2020**, *79*, 951–959. https://doi.org/10.1136/annrheumdis-2019-216900.
30. Zhang, H.; Watanabe, R.; Berry, G.J.; et al. Inhibition of JAK-STAT Signaling Suppresses Pathogenic Immune Responses in Medium and Large Vessel Vasculitis. *Circulation* **2018**, *137*, 1934–1948. https://doi.org/10.1161/circulationaha.117.030423.
31. Maleszewski, J.J.; Younge, B.R.; Fritzlen, J.T.; et al. Clinical and pathological evolution of giant cell arteritis: A prospective study of follow-up temporal artery biopsies in 40 treated patients. *Mod. Pathol.* **2017**, *30*, 788–796. https://doi.org/10.1038/modpathol.2017.10.
32. Samson, M.; Corbera-Bellalta, M.; Audia, S.; et al. Recent advances in our understanding of giant cell arteritis pathogenesis. *Autoimmun. Rev.* **2017**, *16*, 833–844. https://doi.org/10.1016/j.autrev.2017.05.014.
33. Cid, M.C.; Ríos-Garcés, R.; Terrades-García, N.; et al. Treatment of giant-cell arteritis: From broad spectrum immunosuppressive agents to targeted therapies. *Rheumatology* **2020**, *59*, iii17–iii27. https://doi.org/10.1093/rheumatology/kez645.
34. Cai, X.Y.; Ge, J.R.; Xu, L.; et al. Paeoniflorin 6′-o-benzene sulfonate (CP-25) improves vasculitis through inhibiting IL 17A/JAK/STAT3 signaling pathway in endothelial cells of HFD CIA rats. *Phytother Res.* **2021**, *35*, 1033-1047. https://doi.org/10.1002/ptr.6870.
35. Eriksson, P.; Skoglund, O.; Hemgren, C.; et al. Clinical experience and safety of Janus kinase inhibitors in giant cell arteritis: A retrospective case series from Sweden. *Front. Immunol.* **2023**, *14*, 1187584. https://doi.org/10.3389/fimmu.2023.1187584.
36. Loricera, J.; Tofade, T.; Prieto-Peña, D.; et al. Effectiveness of janus kinase inhibitors in relapsing giant cell arteritis in real-world clinical practice and review of the literature. *Arthritis Res. Ther.* **2024**, *26*, 116. https://doi.org/10.1186/s13075-024-03314-9.
37. Prigent, K.; Aouba, A.; Aide, N.; et al. JAK inhibitor effectiveness in giant-cell arteritis with large-vessel involvement assessed by 18F-FDG PET-CT. *Clin. Nucl. Med.* **2022**, *47*, 234–235. https://doi.org/10.1097/rlu.0000000000003913.
38. Régent, A.; Terrier, B.; Legendre, P.; et al. Efficacy of baricitinib for refractory large-vessel vasculitis. *Rheumatology* **2021**, *60*, e389–e391. https://doi.org/10.1093/rheumatology/keab541.
39. Koster, M.J.; Crowson, C.S.; Giblon, R.E.; et al. Baricitinib for relapsing giant cell arteritis: A prospective open-label 52-week pilot study. *Ann. Rheum. Dis.* **2022**, *81*, 861–867. https://doi.org/10.1136/annrheumdis-2021-221961.
40. Blockmans, D.; Penn, S.K.; Setty, A.R.; et al. A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis. *N. Engl. J. Med.* **2025**, *392*, 2013–2024. https://doi.org/10.1056/nejmoa2413449.
41. Kong, X.; Sun, Y.; Dai, X.; et al. Treatment efficacy and safety of tofacitinib versus methotrexate in Takayasu arteritis: A prospective observational study. *Ann. Rheum. Dis.* **2022**, *81*, 117–123. https://doi.org/10.1136/annrheumdis-2021-220832.
42. Palermo, A.; Marvisi, C.; Casali, M.; et al. Tofacitinib for the treatment of refractory Takayasu's arteritis: Description of 2 cases. *Clin. Exp. Rheumatol.* **2020**, *38*, 234–235.
43. Li, J.; Li, M.; Tian, X.; et al. Tofacitinib in patients with refractory Takayasu's arteritis. *Rheumatology* **2020**, *59*, e95–e98. https://doi.org/10.1093/rheumatology/keaa281.
44. Yamamura, Y.; Matsumoto, Y.; Asano, Y.; et al. Refractory Takayasu arteritis responding to the oral Janus kinase inhibitor, tofacitinib. *Rheumatol. Adv. Pract.* **2020**, *4*, rkz050. https://doi.org/10.1093/rap/rkz050.
45. Sato, S.; Matsumoto, H.; Temmoku, J.; et al. A case of Takayasu arteritis complicated by refractory ulcerative colitis successfully treated with tofacitinib. *Rheumatology* **2020**, *59*, 1773–1775. https://doi.org/10.1093/rheumatology/kez580.
46. Kuwabara, S.; Tanimura, S.; Matsumoto, S.; et al. Successful remission with tofacitinib in a patient with refractory Takayasu arteritis complicated by ulcerative colitis. *Ann. Rheum. Dis.* **2020**, *79*, 1125–1126. https://doi.org/10.1136/annrheumdis-2019-216606.
47. Wang, C.; Tsai, Y.; Liu, Y.; et al. Extended-release tofacitinib improves refractory Takayasu's arteritis. *Scand. J. Rheumatol.* **2022**, *51*, 72–75. https://doi.org/10.1080/03009742.2021.1911054.
48. Mekinian, A.; Meneses, S.; Biard, L.; et al. Salvage therapy with JAK inhibitors in refractory Takayasu arteritis: A multicentre experience. *RMD Open* **2026**, *12*, e006501. https://doi.org/10.1136/rmdopen-2025-006501.
49. Ino, K.; Kinoshita, N.; Arinuma, Y.; et al. Improvements in PET/CT results and serum cytokine profile of HLA-B52-positive patients with Takayasu's arteritis and ulcerative colitis post-tofacitinib. *Clin. Exp. Rheumatol.* **2022**, *40*, 849–850. https://doi.org/10.55563/clinexprheumatol/i9chku.

50. Zhou, Z.; Fang, C.; Wang, L.; et al. Baricitinib for refractory Takayasu arteritis: A prospective cohort study in a tertiary referral centre. *RMD Open* **2024**, *10*, e003985. https://doi.org/10.1136/rmdopen-2023-003985.
51. ClinicalTrials.gov. Efficiency of Methotrexate and Tofacitinib in Mild and Moderate Patients with Takayasu Arteritis. Available online: https://clinicaltrials.gov/study/NCT04299971 (accessed on 19 October 2026).
52. ClinicalTrials.gov. A Study to Evaluate the Efficacy and Safety of Upadacitinib in Participants with Takayasu Arteritis (TAK). Available online: https://clinicaltrials.gov/study/NCT04161898 (accessed on 19 October 2026).
53. Pak, D.; Park, H.J. Behcet disease: An undifferentiating and complex vasculitis. *Postgrad. Med.* **2023**, *135*, 33–43. https://doi.org/10.1080/00325481.2022.2159205.
54. Liu, J.; Hou, Y.; Sun, L.; et al. A pilot study of tofacitinib for refractory Behçet's syndrome. *Ann. Rheum. Dis.* **2020**, *79*, 1517–1520. https://doi.org/10.1136/annrheumdis-2020-217307.
55. Zhao, N.; Tang, Y.; Wang, S.; et al. Case report: Refractory intestinal Behçet's syndrome successfully treated with tofacitinib: A report of four cases. *Front. Immunol.* **2022**, *13*, 981502. https://doi.org/10.3389/fimmu.2022.981502.
56. Zou, J.; Cai, J.F.; Ye, J.F.; et al. Tofacitinib as an alternative therapy for refractory intestinal Behçet's syndrome. *Ther. Adv. Musculoskelet. Dis.* **2022**, *14*, 1759720X221124014. https://doi.org/10.1177/1759720x221124014.
57. Liu, J.; Yu, X.; Wang, Z.; et al. Baricitinib for the treatment of intestinal Behçet's disease: A pilot study. *Clin. Immunol.* **2023**, *247*, 109241. https://doi.org/10.1016/j.clim.2023.109241.
58. Wang, Z.; Wang, X.; Liu, W.; et al. Baricitinib for the treatment of refractory vascular Behçet's disease. *Clin. Immunol.* **2023**, *250*, 109298. https://doi.org/10.1016/j.clim.2023.109298.
59. Tao, T.; He, D.; Peng, X.; et al. Successful Remission with Upadacitinib in Two Patients with Anti-TNF-Refractory Macular Edema Associated with Behçet's Uveitis. *Ocul. Immunol. Inflamm.* **2024**, *32*, 1897–1900. https://doi.org/10.1080/09273948.2023.2263557.
60. Colangelo, A.; Tromby, F.; Cafaro, G.; et al. Vasculitis associated with adenosine deaminase 2 deficiency: At the crossroads between Behçet's disease and autoinflammation. A viewpoint. *Reumatismo* **2023**, *18*, 75. https://doi.org/10.4081/reumatismo.2023.1578.
61. Sharma, V.; Deo, P.; Sharma, A. Deficiency of adenosine deaminase 2 (DADA2): Review. *Best. Pract. Res. Clin. Rheumatol.* **2023**, *37*, 101844. https://doi.org/10.1016/j.berh.2023.101844.
62. Signa, S.; Bertoni, A.; Penco, F.; et al. Adenosine deaminase 2 deficiency (DADA2): A crosstalk between innate and adaptive immunity. *Front. Immunol.* **2022**, *13*, 935957. https://doi.org/10.3389/fimmu.2022.935957.
63. Nihira, H.; Izawa, K.; Ito, M.; et al. Detailed Analysis of Japanese Patients with Adenosine Deaminase 2 Deficiency Reveals Characteristic Elevation of Type II Interferon Signature and STAT1 Hyperactivation. *J. Allergy Clin. Immunol.* **2021**, *148*, 550–562. https://doi.org/10.1016/j.jaci.2021.01.018.
64. Wu, Z.; Gao, S.; Watanabe, N.; et al. Single-Cell Profiling of T Lymphocytes in Deficiency of Adenosine Deaminase 2. *J. Leukoc. Biol.* **2022**, *111*, 301–312. https://doi.org/10.1002/jlb.5a0621-314r.
65. Nakajima, H.; Kunimoto, H. VEXAS syndrome. *Int. J. Hematol.* **2025**, *122*, 341–350. https://doi.org/10.1007/s12185-024-03799-9.
66. Holden, R.; Jeelall, Y.; McLean-Tooke, A.; et al. VEXAS: A review of current understandings and emerging treatment strategies. *Front. Immunol.* **2025**, *16*, 1644404. https://doi.org/10.3389/fimmu.2025.1644404.
67. Kosmider, O.; Possémé, C.; Templé, M.; et al. VEXAS syndrome is characterized by inflammasome activation and monocyte dysregulation. *Nat. Commun.* **2024**, *15*, 910. https://doi.org/10.1038/s41467-024-44811-4.
68. Heiblig, M.; Ferrada, M.; Koster, M.; et al. Ruxolitinib is more effective than other JAK inhibitors to treat VEXAS syndrome: A retrospective multicenter study. *Blood* **2022**, *140*, 927–931. https://doi.org/10.1182/blood.2022016642.
69. Bahramian, S.; Fazeli, P.; Rafati, A.; et al. JAK Inhibitors for Treatment of VEXAS Syndrome: A Systematic Review of 186 Cases. *Dermatol. Res. Pract.* **2025**, *2025*, 9127126. https://doi.org/10.1155/drp/9127126.
70. Bindoli, S.; Baggio, C.; Doria, A.; et al. JAK inhibitors for the treatment of VEXAS syndrome. *Exp. Biol. Med. Maywood* **2023**, *248*, 394–398. https://doi.org/10.1177/15353702231165030.
71. Ytterberg, S.R.; Bhatt, D.L.; Mikuls, T.R.; et al. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. *N. Engl. J. Med.* **2022**, *386*, 316–326. https://doi.org/10.1056/nejmoa2109927.
72. Szekanecz, Z.; Buch, M.H.; Charles-Schoeman, C.; et al. Efficacy and safety of JAK inhibitors in rheumatoid arthritis: Update for the practising clinician. *Nat. Rev. Rheumatol.* **2024**, *20*, 101–115. https://doi.org/10.1038/s41584-023-01062-9.