VEXAS Syndrome: Expert Consensus on Multidisciplinary Care at EULAR 2026

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VEXAS syndrome, a recently identified adult-onset inflammatory disease, presents a diagnostic and therapeutic challenge due to its varied clinical manifestations and often severe, refractory course. Expert discussions at EULAR 2026 underscored the critical need for a coordinated, multidisciplinary strategy to improve patient outcomes, emphasizing early recognition and tailored management.1

KEY TAKEAWAYS

- The Pivot: VEXAS syndrome requires a unified, multidisciplinary approach for diagnosis and management, moving beyond siloed specialty care.
- The Data: Early genetic testing for UBA1 mutations is crucial for definitive diagnosis, particularly in patients with unexplained systemic inflammation and cytopenias.
- The Action: Clinicians should consider VEXAS in older male patients presenting with refractory inflammatory conditions, myelodysplastic features, and dermatological or pulmonary involvement, facilitating prompt referral to specialized centers.

VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome is a severe, adult-onset inflammatory disorder caused by somatic mutations in the UBA1 gene, primarily affecting males.1 The clinical presentation is heterogeneous, often including refractory fevers, dermatological manifestations such as neutrophilic dermatosis or vasculitis, pulmonary infiltrates, chondritis, and myelodysplastic features.2 Hematological abnormalities, including macrocytic anemia, thrombocytopenia, and leukopenia, are common.3 The disease carries a high mortality rate, reported to be approximately 40% within five years of diagnosis.4 Given its rarity and diverse symptomatology, VEXAS syndrome often leads to diagnostic delays, with patients frequently undergoing extensive investigations across multiple specialties before a definitive diagnosis is established.5

The underlying pathophysiology of VEXAS syndrome involves impaired ubiquitylation due to mutations in UBA1, which encodes the E1 ubiquitin-activating enzyme. This impairment leads to the accumulation of ubiquitylated proteins and activation of inflammatory pathways, contributing to the systemic inflammation and hematological abnormalities observed in affected individuals. The X-linked nature of the gene explains the predominant male involvement, although rare cases in females have been reported, often with skewed X-chromosome inactivation. The average age of onset typically ranges from the sixth to eighth decade of life, highlighting its presentation as a disorder of older adults.2,3

Multidisciplinary Expert Perspectives at EULAR 2026

At EULAR 2026, a panel of experts from rheumatology, hematology, dermatology, and pulmonology convened to discuss optimal strategies for VEXAS syndrome patient care. The consensus highlighted several key areas for improving diagnosis and management. Early recognition was emphasized as paramount, particularly in older male patients presenting with unexplained systemic inflammation, cytopenias, and features such as vacuolization of myeloid and erythroid precursors in bone marrow biopsies.6

The diagnostic pathway recommended by the panel involves a high index of suspicion in patients with refractory inflammatory conditions not responding to conventional immunosuppressive therapies. Genetic testing for somatic UBA1 mutations in myeloid cells is the definitive diagnostic tool.7 The panel noted that while bone marrow biopsy findings of cytoplasmic vacuoles in myeloid and erythroid precursors are highly suggestive, they are not pathognomonic and require confirmation via genetic analysis.8 The experts further elaborated on the importance of considering VEXAS syndrome in the differential diagnosis for conditions such as relapsing polychondritis, polyarteritis nodosa, Sweet's syndrome, and myelodysplastic syndromes, especially when these conditions present with atypical features or resistance to standard treatments. This broader consideration can significantly reduce diagnostic timelines.7,8

Management strategies discussed focused on symptom control and disease modification. Corticosteroids are frequently used for acute symptom management, often at high doses, but long-term use is associated with significant side effects and disease recurrence upon tapering.9 Immunosuppressive agents, including methotrexate, azathioprine, and TNF inhibitors, have shown variable efficacy, with many patients demonstrating refractoriness.10 The panel highlighted the emerging role of targeted therapies. JAK inhibitors, particularly ruxolitinib, have demonstrated promising results in some cohorts, leading to clinical improvement and reduction in corticosteroid dependence.11 Interleukin-1 (IL-1) inhibitors, such as anakinra, have also been explored, with some patients experiencing a reduction in inflammatory markers and symptoms.12

Hematopoietic stem cell transplantation (HSCT) was presented as the only potentially curative treatment option for VEXAS syndrome.13 However, HSCT is associated with significant risks and is typically reserved for younger, fitter patients with severe, refractory disease. The panel stressed the importance of careful patient selection and pre-transplant conditioning regimens.14

The experts underscored the necessity of a coordinated multidisciplinary team (MDT) approach. This involves regular communication between rheumatologists, hematologists, dermatologists, pulmonologists, and geneticists to ensure comprehensive patient assessment, timely diagnosis, and individualized treatment plans.15 The MDT should also address supportive care, including infection prophylaxis, management of cytopenias, and monitoring for disease complications.16

Limitations in current knowledge include the lack of large-scale randomized controlled trials for specific VEXAS treatments due to the rarity of the disease. Most evidence is derived from case series and observational studies.

Future research directions include identifying novel therapeutic targets, developing standardized diagnostic criteria, and establishing international registries to collect more comprehensive data on treatment efficacy and long-term outcomes. The panel also called for increased awareness among clinicians to reduce diagnostic delays and improve access to specialized care.17

For deeper insights into this and other complex rheumatological conditions, consult the comprehensive Oxford Handbook of Rheumatology for specialised clinical guidance.

CLINICAL IMPLICATIONS

The EULAR 2026 discussions on VEXAS syndrome underscore a critical need for a paradigm shift in how clinicians approach unexplained systemic inflammatory conditions, particularly in older male patients. The emphasis on early genetic testing for UBA1 mutations is not merely an academic point; it is a call to action that could significantly reduce diagnostic odysseys that often span years and multiple specialties. GPs and specialists alike must integrate VEXAS into their differential diagnoses for patients presenting with refractory fevers, cytopenias, and dermatological or pulmonary involvement, even if the symptoms appear to fit other, more common conditions. The cost-effectiveness of delayed diagnosis, both in terms of patient morbidity and healthcare resource utilization, far outweighs the cost of appropriate genetic screening.

For the pharmaceutical industry, the focus on targeted therapies, particularly JAK inhibitors and IL-1 inhibitors, suggests a nascent but growing market for orphan drug development. While current evidence is largely anecdotal or from small cohorts, the high mortality rate and refractory nature of VEXAS syndrome create a compelling need for effective treatments. Companies with existing portfolios in inflammation and hematology should be actively exploring repurposing or developing novel agents. The challenge will be designing clinical trials for such a rare disease, likely necessitating international collaborations and adaptive trial designs to generate robust evidence. The potential for hematopoietic stem cell transplantation as a curative option also highlights the need for improved patient selection criteria and supportive care protocols to maximize its benefit.

Ultimately, the patient experience is at the heart of these discussions. A VEXAS diagnosis often follows years of debilitating symptoms, misdiagnoses, and ineffective treatments. A coordinated multidisciplinary approach, as advocated by the EULAR experts, promises to streamline care, reduce patient suffering, and potentially extend lives. This requires not only better clinical pathways but also enhanced communication between specialists and primary care, ensuring that patients receive consistent, evidence-based care from the moment VEXAS is suspected. The medical community must move beyond isolated specialty consultations towards truly integrated care models for complex rare diseases like VEXAS syndrome.

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