

Lupus Management: Progress and Persistent Challenges at EULAR 2026

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Systemic lupus erythematosus (SLE) presents a persistent clinical dilemma for rheumatologists, marked by heterogeneous disease manifestations and a high burden of organ damage and morbidity. While therapeutic options have expanded, a substantial proportion of patients continue to experience inadequate disease control and treatment-related toxicities. The upcoming EULAR 2026 congress is anticipated to consolidate recent advancements and highlight areas requiring further research and clinical innovation.

KEY TAKEAWAYS

- **The Pivot:** Biologic therapies have expanded treatment options for SLE, moving beyond traditional immunosuppressants.
- **The Data:** While specific trial data are not provided, the overall landscape indicates that complete and sustained remission remains elusive for a significant patient cohort.
- **The Action:** Clinicians should continue to individualize treatment, integrating newer biologics where appropriate, while closely monitoring for both disease activity and adverse events.

Systemic lupus erythematosus (SLE) is a chronic, autoimmune inflammatory disease affecting multiple organ systems, with a global prevalence estimated between 20 and 150 cases per 100,000 individuals.¹ The disease course is highly variable, ranging from mild cutaneous and articular involvement to severe, life-threatening manifestations such as lupus nephritis, neuropsychiatric lupus, and cardiovascular complications.² Historically, treatment has relied on corticosteroids, antimalarials, and broad-spectrum immunosuppressants like azathioprine, methotrexate, and cyclophosphamide.³ While these agents have improved survival rates, they are associated with significant long-term toxicities and often fail to achieve sustained remission, leaving many patients with ongoing disease activity and cumulative organ damage.⁴

The development of targeted biologic therapies represents a significant evolution in SLE management. Belimumab, a B-lymphocyte stimulator (BLyS)-specific inhibitor, was the first biologic approved for SLE, demonstrating efficacy in reducing disease activity and corticosteroid use in patients with active, autoantibody-positive SLE.⁵ Subsequent trials have further elucidated its role, particularly in patients with non-renal and non-neuropsychiatric manifestations.⁶ Anifrolumab, a type I interferon receptor antagonist, has also shown efficacy in reducing disease activity across various organ systems, including skin and joints, and in lowering oral corticosteroid dosage.⁷ These agents offer more specific immunomodulation compared to conventional immunosuppressants, aiming to disrupt key pathogenic pathways in SLE.⁸

The pathogenesis of SLE involves a complex interplay of genetic predisposition, environmental triggers, and

dysregulation of both innate and adaptive immune responses. Key immunological abnormalities include overactive B cells, aberrant T cell function, and increased production of autoantibodies and inflammatory cytokines, particularly type I interferons. These mechanisms contribute to systemic inflammation and subsequent organ damage. Understanding these pathways has been crucial for identifying novel therapeutic targets and developing more precise interventions. The clinical presentation of SLE is highly heterogeneous, making diagnosis challenging and often delayed. Patients frequently experience fatigue, arthralgia, skin rashes, and serositis, alongside more severe manifestations affecting the kidneys, central nervous system, and hematologic system. The impact on quality of life is substantial, and the chronic nature of the disease necessitates long-term management strategies. Regular monitoring of disease activity, organ involvement, and treatment-related adverse events is essential for optimizing patient outcomes.

Current Therapeutic Landscape and Unmet Needs

Despite these advancements, a substantial proportion of patients with SLE continue to experience persistent disease activity, flares, and accumulation of irreversible organ damage.⁹ For example, while belimumab and anifrolumab have demonstrated statistically significant improvements in composite endpoints such as the SLE Responder Index (SRI-4) and British Isles Lupus Assessment Group (BILAG) scores, complete and sustained remission remains an infrequent outcome.¹⁰ Furthermore, specific patient populations, such as those with severe lupus nephritis or neuropsychiatric lupus, often require more aggressive or alternative treatment strategies, highlighting ongoing unmet needs.¹¹ The optimal sequencing and combination of conventional and biologic therapies are still subjects of active investigation, with current guidelines often recommending individualized approaches based on disease severity, organ involvement, and patient comorbidities.¹²

The EULAR 2026 congress is expected to feature updates on ongoing clinical trials investigating novel therapeutic targets and strategies. These include therapies targeting other immune pathways, such as Janus kinase (JAK) inhibitors, Bruton's tyrosine kinase (BTK) inhibitors, and complement pathway inhibitors.¹³ Data on long-term safety and efficacy of currently approved biologics, as well as real-world evidence studies, will also be critical for informing clinical practice.¹⁴ Furthermore, research into precision medicine approaches, including biomarker identification for predicting treatment response and stratifying patients, is anticipated to be a key theme.¹⁵ The goal is to move beyond a 'one-size-fits-all' approach to more tailored therapies that can achieve deeper and more durable remission while minimizing adverse effects.¹⁶

Limitations in current SLE management include the challenge of accurately measuring disease activity and damage, the heterogeneity of patient responses to treatment, and the persistent need for corticosteroids in many patients.¹⁷ Corticosteroid-sparing strategies remain a high priority due to the well-documented long-term adverse effects of these drugs.¹⁸ Future directions will likely focus on combination therapies, earlier intervention, and the development of therapies that can prevent or reverse organ damage.¹⁹ The integration of patient-reported outcomes (PROs) and quality of life measures into clinical trial design and routine care is also gaining prominence, reflecting a more holistic approach to patient management.²⁰

For an authoritative and practical guide to lupus and broader rheumatological practice, we recommend the extensive Oxford Handbook of Rheumatology.

CLINICAL IMPLICATIONS

The evolution of lupus therapeutics, particularly with the introduction of biologics like belimumab and anifrolumab, has undeniably expanded the rheumatologist's toolkit. However, the persistent reliance on corticosteroids and the elusive nature of sustained, drug-free remission underscore that these advancements, while welcome, are incremental rather than transformative. Clinicians are now faced with a more complex decision-making process, requiring careful consideration of patient phenotypes, prior treatment responses, and the specific risk-benefit profiles of newer agents. The notion that a single biologic will universally address the multifaceted pathology of SLE is proving to be overly optimistic; combination strategies and personalized medicine approaches are becoming increasingly essential.

From an industry perspective, the focus on novel targets beyond B-cell and interferon pathways is a logical next step, yet the commercial viability of highly niche therapies for specific SLE subsets remains a challenge. The development of robust biomarkers that can reliably predict response to these targeted agents is not merely academic; it is critical for guiding prescribing decisions and ensuring that expensive therapies are directed to those most likely to benefit. Without such precision, the economic burden on healthcare systems will continue to escalate, potentially limiting access to these innovations. Regulatory bodies like the EMA and FDA will need to adapt their frameworks to evaluate therapies designed for increasingly narrow patient populations, balancing efficacy in specific subgroups against broader population needs.

For patients, the expanding therapeutic landscape offers hope, but also potential confusion and the burden of navigating complex treatment regimens. While the reduction in corticosteroid use is a significant patient-centric outcome, the long-term safety data for many newer biologics are still maturing. Patients and their clinicians must engage in shared decision-making, weighing the potential for improved disease control against the risks of novel immunosuppression. The ultimate goal remains a treatment that not only suppresses disease activity but also preserves organ function, minimizes side effects, and significantly improves quality of life, allowing individuals with SLE to live full and productive lives without the constant shadow of their condition.

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