

Treat-to-Target in SLE: Balancing Burden, Benefit, and Risk

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Managing Systemic Lupus Erythematosus (SLE) presents a persistent clinical dilemma: how to achieve sustained disease remission while mitigating treatment-related adverse events and patient burden. The treat-to-target approach, widely adopted in other rheumatological conditions, seeks to standardise therapeutic goals in SLE, yet its implementation requires careful consideration of the multifaceted impact on patients and healthcare systems.

KEY TAKEAWAYS

- **The Pivot:** Treat-to-target strategies in SLE aim to standardise disease control, moving beyond symptom management to objective targets.
- **The Data:** While aiming for low disease activity or remission, the approach necessitates frequent monitoring and potentially intensified immunosuppression.
- **The Action:** Clinicians must balance the potential for improved long-term outcomes against the increased treatment burden, risk of adverse events, and impact on patient quality of life.

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterised by heterogeneous clinical manifestations and unpredictable flares, leading to cumulative organ damage and reduced quality of life. Traditional management has often been reactive, responding to flares or severe symptoms. The treat-to-target (T2T) concept, successfully implemented in conditions such as rheumatoid arthritis, proposes a proactive strategy where treatment is escalated or adjusted until a predefined target of disease activity is achieved and maintained. For SLE, common targets include a Lupus Low Disease Activity State (LLDAS) or clinical remission, often defined by indices such as the SLE Disease Activity Index (SLEDAI) or British Isles Lupus Assessment Group (BILAG) index, alongside corticosteroid tapering.¹ The rationale for T2T in SLE is to minimise disease activity, prevent organ damage, and improve long-term outcomes.² However, the complexity of SLE, with its diverse organ involvement and fluctuating activity, makes defining and consistently achieving a universal target challenging. SLE affects an estimated 5 million people worldwide, with a higher prevalence in women and individuals of non-European descent. The disease can manifest at any age, but typically presents between the ages of 15 and 44. Its varied presentation, ranging from mild skin and joint involvement to severe organ-threatening manifestations like lupus nephritis or neuropsychiatric lupus, necessitates highly individualised treatment approaches.

The Treat-to-Target Balancing Act

The implementation of a treat-to-target strategy in SLE necessitates frequent and comprehensive disease activity assessments. This typically involves regular clinical evaluations, laboratory testing for inflammatory markers, autoantibodies, and complement levels, and potentially imaging studies. The increased frequency of clinic visits and diagnostic procedures can impose a significant burden on patients, affecting their daily lives, work, and financial stability.³ Furthermore, achieving and maintaining low disease activity or remission often requires the use of immunosuppressive medications, including corticosteroids, antimalarials, and various biologics. While these therapies are effective in controlling disease activity, they carry inherent risks of adverse events, such as infections, metabolic complications, and malignancy.⁴ The selection of specific therapeutic agents often depends on the predominant organ involvement and disease severity. For instance, antimalarials like hydroxychloroquine are foundational for most SLE patients due to their immunomodulatory effects and ability to reduce flares, while more potent immunosuppressants such as mycophenolate mofetil or cyclophosphamide are reserved for severe organ-threatening disease.

The potential benefits of a T2T approach include reduced flare rates, prevention of irreversible organ damage, and improved survival. Studies in other autoimmune diseases have demonstrated that T2T strategies lead to better long-term outcomes compared to conventional care.⁵ For SLE, the evidence specifically supporting a T2T approach is evolving. Achieving LLDAS has been associated with a reduced risk of damage accrual and improved quality of life.⁶ However, the intensity of treatment required to reach these targets, particularly in patients with severe or refractory disease, must be weighed against the potential for treatment-related toxicity. For instance, prolonged or high-dose corticosteroid use, while effective in acute flares, contributes significantly to cumulative damage, including osteoporosis, cardiovascular disease, and diabetes.⁷ The long-term impact of these adverse events can sometimes outweigh the benefits of aggressive disease control, particularly in patient populations with pre-existing comorbidities or those who are more susceptible to medication side effects.

Patient adherence to complex medication regimens and frequent monitoring schedules is another critical factor influencing the success of T2T. Non-adherence can lead to suboptimal disease control, increased flare risk, and progression of organ damage.⁸ Effective patient education and shared decision-making are essential to ensure patients understand the rationale for T2T, the importance of adherence, and the potential benefits and risks associated with treatment escalation. The psychological impact of living with a chronic, unpredictable disease like SLE, coupled with the demands of a T2T strategy, also warrants consideration. Patients may experience anxiety, depression, and fatigue, which can be exacerbated by intensive treatment protocols.⁹ These psychological burdens can further complicate adherence and overall treatment success, highlighting the need for a holistic approach that addresses both physical and mental health.

The economic implications of a T2T strategy are also substantial. Increased clinic visits, laboratory tests, and the use of often expensive biologic therapies contribute to higher healthcare costs.¹⁰ Health economic analyses are crucial to determine the cost-effectiveness of T2T in SLE, balancing the upfront investment in intensive management against the long-term savings from preventing organ damage and reducing hospitalisations. The EULAR 2026 discussion on the treat-to-target balancing act in SLE underscores the need for a nuanced approach, integrating evidence-based targets with individual patient circumstances, preferences, and tolerance for treatment burden and risk. This includes careful consideration of patient-reported outcomes and quality of life measures, ensuring that the pursuit of disease control does not unduly diminish a patient's overall well-being.

CLINICAL IMPLICATIONS

The push for treat-to-target in SLE, while conceptually sound, risks oversimplifying a highly complex disease. Clinicians are now tasked with not just managing symptoms, but actively pursuing objective targets like LLDAS or remission. This shift, while laudable for its ambition to prevent organ damage, places a significant burden on both the patient and the healthcare system. The increased frequency of monitoring and the potential for intensified immunosuppression demand a level of patient engagement and adherence that is often challenging to sustain in chronic illness.

From an industry perspective, the emphasis on treat-to-target naturally drives demand for more precise diagnostic tools and, crucially, more potent and targeted therapies. Pharmaceutical companies developing biologics for SLE will undoubtedly leverage this framework, positioning their products as essential for achieving and maintaining these stringent targets. However, the cost-effectiveness of these advanced therapies within a T2T paradigm, especially when considering the cumulative burden of monitoring and potential adverse events, remains a critical area for ongoing evaluation. Guidelines, such as those from EULAR, will need to provide clear, actionable recommendations that balance therapeutic ambition with practical realities and patient quality of life.

Ultimately, the success of treat-to-target in SLE will hinge not just on achieving numerical targets, but on how well it integrates into the patient's life. If the pursuit of LLDAS leads to an unbearable schedule of appointments, blood tests, and medication side effects, the benefit may be negated by the burden. The discussion at EULAR 2026 serves as a timely reminder that while precision medicine aims for optimal outcomes, it must never lose sight of the human element. A truly effective strategy will be one that is both clinically robust and patient-centric, acknowledging that for many, a good quality of life with manageable disease activity may be a more realistic and desirable target than absolute remission at any cost.

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