

CAR T Cell Therapy Shows Promise in SLE and SSc Immune Reset

Written by The Life Science Feed Editorial Team · Published 3 June 2026 · Edited by Mara Voss

Systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) present significant challenges in management, often progressing despite conventional immunosuppressive therapies. The concept of immune reset, aiming for deep and sustained remission by eliminating autoreactive immune cells, represents a critical area of unmet need. Chimeric antigen receptor (CAR) T cell therapy is now being explored as a novel approach to achieve this reset in refractory autoimmune diseases.¹

KEY TAKEAWAYS

- ° The Pivot: CAR T cell therapy, traditionally an oncology treatment, is being repurposed for severe autoimmune diseases like SLE and SSc to induce immune reset.
- ° The Data: Early phase trials indicate high rates of disease remission, often allowing for discontinuation of prior immunosuppressive regimens, though specific HR/p-values are pending larger studies.
- ° The Action: Clinicians should monitor ongoing trials and consider CAR T cell therapy as a future option for patients with refractory SLE and SSc, understanding its current experimental status and associated risks.

The EULAR 2026 conference highlighted emerging data on CAR T cell therapy for severe, refractory autoimmune diseases, specifically systemic lupus erythematosus (SLE) and systemic sclerosis (SSc). These conditions are characterized by chronic inflammation and organ damage driven by aberrant immune responses, often necessitating long-term immunosuppression with variable efficacy and significant side effects. The therapeutic goal of an immune reset, involving the profound depletion of autoreactive B cells and subsequent immune system reconstitution, has gained traction as a strategy to achieve sustained, drug-free remission.¹

CAR T Cell Therapy in Autoimmunity

CAR T cell therapy involves genetically modifying a patient's own T cells to express a chimeric antigen receptor that targets a specific antigen on diseased cells. In the context of autoimmune diseases, the primary target has been the CD19 antigen, expressed on B cells. The rationale is that depleting CD19-positive B cells, which are central to autoantibody production and antigen presentation in diseases like SLE and SSc, can interrupt the autoimmune cascade and allow for the regeneration of a new, tolerant immune repertoire.²

Early phase clinical investigations have focused on patients with severe, refractory SLE and SSc who have failed multiple lines of conventional immunosuppressive therapy, including high-dose corticosteroids, mycophenolate mofetil, cyclophosphamide, and biologics such as rituximab. The treatment protocol typically involves leukapheresis to collect autologous T cells, ex vivo genetic modification with a lentiviral vector to express the anti-CD19 CAR, expansion of the

CAR T cells, and subsequent reinfusion into the patient following lymphodepleting chemotherapy.³

Initial reports from small cohorts of patients with SLE have demonstrated rapid and profound depletion of B cells, leading to significant improvements in disease activity scores. For example, patients with severe SLE, including those with lupus nephritis and neuropsychiatric lupus, have shown complete or partial remission, often allowing for the discontinuation of all immunosuppressive medications. The safety profile observed in these autoimmune cohorts appears consistent with that seen in oncology settings, with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) being the most common acute toxicities. These are generally manageable with established protocols, including tocilizumab for CRS and corticosteroids for ICANS.⁴

Similarly, in severe SSc, particularly those with rapidly progressive skin fibrosis and interstitial lung disease, CAR T cell therapy has shown encouraging preliminary results. Patients have experienced improvements in skin scores (e.g., modified Rodnan skin score) and stabilization or improvement in lung function parameters. The mechanism is thought to involve the depletion of pathogenic B cells that contribute to fibrosis and inflammation, followed by a potential reset of the immune system. The long-term durability of these responses and the precise mechanisms of immune reconstitution remain areas of active investigation.⁵

The concept of immune reset implies not just transient disease control, but a sustained state of remission where the immune system no longer targets self-antigens. Post-CAR T cell therapy, B cell aplasia is typically observed for several months, followed by B cell reconstitution. The emerging B cell population is hypothesized to be less autoreactive, potentially due to the elimination of memory B cells and the generation of new naive B cells from the bone marrow. This 'reset' could offer a disease-modifying effect beyond mere immunosuppression.⁶

Limitations of current data include the small sample sizes of the initial trials, the lack of long-term follow-up, and the absence of randomized controlled trials comparing CAR T cell therapy to standard of care. The high cost and specialized infrastructure required for CAR T cell therapy also present significant barriers to widespread implementation. Future research will need to address optimal patient selection, refine conditioning regimens, mitigate toxicities, and establish the long-term safety and efficacy in larger, diverse patient populations. Comparative effectiveness studies are essential to position CAR T cell therapy within the existing treatment algorithms for SLE and SSc.⁷

Gain foundational insights into rheumatological conditions, including SLE and SSc, with the authoritative Oxford Handbook of Rheumatology for further reading.

CLINICAL IMPLICATIONS

The prospect of CAR T cell therapy for autoimmune diseases, particularly severe SLE and SSc, represents a significant conceptual shift. For clinicians managing these often intractable conditions, the idea of an immune reset, rather than continuous immunosuppression, offers a compelling vision. While the data are still nascent and largely from single-arm studies, the observed rates of deep remission, allowing for the cessation of other immunosuppressants, are striking. This could fundamentally alter the treatment paradigm for patients who have exhausted conventional options, moving from chronic disease management to a potential cure, or at least a prolonged drug-free remission.

However, the practicalities are formidable. The infrastructure required for CAR T cell therapy, including specialized apheresis units, cell processing facilities, and intensive care support for managing acute toxicities

like cytokine release syndrome, means this will remain a highly specialized treatment. The cost, currently exorbitant in oncology, will also be a major hurdle for broader adoption in autoimmune diseases, which affect a much larger patient population. Payers and health systems will need to grapple with the economic implications, and pharmaceutical companies developing these therapies will face pressure to demonstrate not just efficacy, but also cost-effectiveness and long-term durability to justify the investment.

For patients, the promise of drug-free remission is undoubtedly appealing, but it comes with significant risks and logistical burdens. The acute toxicities, while manageable, are serious. The long-term effects on immune function, including the risk of hypogammaglobulinemia and infection, require careful monitoring. It is imperative that patient selection is meticulous, focusing on those with truly refractory disease where the potential benefits clearly outweigh the risks. As more data emerge, particularly from larger, controlled trials, we will gain a clearer understanding of where CAR T cell therapy fits into the complex landscape of autoimmune disease management, and whether it can transition from a niche experimental treatment to a more widely accessible therapeutic option.

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