Evolving Strategies in Lupus Care: Is Earlier Sustained Remission Now Within Reach?

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Interview Summary

Systemic lupus erythematosus (SLE) is a complex autoimmune disease that remains challenging to diagnose and treat. In this interview, rheumatologist and clinical epidemiologist Zahi Touma, Associate Professor of Medicine, Clinician Scientist, University of Toronto, Canada, highlights the need for a shift from traditional symptom suppression to early and proactive treat-to-target approaches. Despite the availability of more advanced SLE-targeted therapies offering the potential to reduce glucocorticoid (GC) dependency and improve disease control, many patients continue to rely on long-term GC use, placing them at increased risk of irreversible organ damage, poor health-related quality of life, and even mortality. Touma emphasises the importance of proactive, individualised care to achieve sustained remission and improve long-term outcomes for a greater proportion of patients.

INTRODUCTION

SLE is a chronic, complex autoimmune condition affecting over 3.4 million people globally, and is among the leading causes of death in young women in the USA.[1-3] It disproportionately affects those of Asian, Black, or Hispanic racial/ethnical background, and its heterogeneous symptoms can often delay diagnosis, exposing these untreated patients to a higher risk of unpredictable flares, disease progression, and early damage accrual in different organs.[1,4,5] Beyond physical symptoms, SLE can have a profound impact on patients' health-related quality of life and financial well-being, placing a high burden on patients, their families, and health systems.[1,6,7]

However, with targeted therapies and recommendations supporting a treat-to-target approach with sustained remission as the primary goal,[6,8,9] there is an opportunity to improve long-term patient outcomes, reduce high-dose GC use, and achieve sustained clinical remission. In this expert discussion, Touma addresses key questions on the importance of taking a more proactive treat-to-target approach to disease management in order to reduce long-term risk and improve outcomes for patients living with SLE.

WHAT IS THE BIGGEST CHALLENGE IN SYSTEMIC LUPUS ERYTHEMATOSUS TREATMENT TODAY?

One of the greatest challenges we face in managing SLE today is controlling disease activity without over reliance on GCs.[1,10] This requires a treat-to-target approach that prioritises long-term disease control and timely treatment adjustments once, or if, the desired goal is not met.[8,9]

While GC treatments are still recommended for short-term use in SLE management and play a key role in providing rapid symptom relief and flare control, they do not provide optimal control on causal disease mechanisms or offer continuous disease control.[10,11] To manage SLE symptoms, GCs are often given at high doses and over a long period, alongside antimalarials and/or immunosuppressants.[12,13] However, long-term use of GCs can leave patients open to the risks of cumulative harm, which can include organ damage, infections, cardiovascular disease, osteoporosis, and cataracts.[7,11,14-16] It also resulted in few patients achieving lasting disease control and remission.[17]

WHY IS NOW A PIVOTAL MOMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS TREATMENT?

Until relatively recently, we did not have the therapeutic medications to directly target and address the underlying drivers of disease. While remission has always been a possibility for some patients on standard-of-care therapies, recent scientific advances have led to the development of treatment strategies that make achieving lasting remission a more attainable goal, without relying on long-term use of GCs.[6,12] This growing research demonstrates how using early intervention with targeted biological therapies can lead to better patient outcomes, and mirrors treatment strategies in other autoimmune diseases.[18] For example, in rheumatoid arthritis, we have seen patients reach remission or lower disease activity sooner, reducing the risk of organ damage accrual and leading a better quality of life for longer.[19,20]

We now have more advanced therapies and validated treatment endpoints such as Definitions of Remission in SLE (DORIS; defined as a clinical SLE Disease Activity Index [SLEDAI] score of 0; a Physician Global Assessment [PGA] score of <0.5; stable doses of antimalarials and/or immunosuppressives [including biologics], and on ≤5 mg/day prednisolone [or equivalent]),[21] providing measurable goals that allow us to assess and optimise patient outcomes more effectively.[18] The value of achieving DORIS-defined remission is affirmed by the 2023 European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of SLE, which provide us with evidence and guidance to refine treatment goals

and enhance patient outcomes.[18] The recommendations underscore the need for timely and individualised management strategies, focusing on tailored treatment plans that prevent disease flares and maximise treatment adherence.[18]

HOW HAVE RECENT ADVANCEMENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS RESEARCH AND CLINICAL RECOMMENDATIONS INFLUENCED YOUR APPROACH TO PATIENT CARE?

Ultimately, the 2023 EULAR recommendations encourage us to adopt a more targeted approach that prioritises sustained remission or low disease activity as treatment targets.[18] From Touma's clinical experience, these updates are a transformative step forward. Instead of focusing solely on active disease or managing flares, we are able to prevent disease progression wherever possible when treat-to-target strategies are implemented.[18,22] By establishing targets based on an individual patient's needs, and monitoring for this, we can take steps to introduce targeted therapies earlier and optimise our strategy for care.[8]

Effective management of SLE also goes beyond pharmacological treatment with non-pharmacological management strategies, including sun protection, smoking cessation, and maintaining a healthy diet, playing a crucial role in encouraging adherence and enhancing patient's quality of life.[18] These approaches are supported by a growing body of evidence and the recent EULAR recommendations that stress the importance of incorporating non-pharmacological interventions alongside pharmacotherapy to enhance patient care.[18]

Collaboration between patients, healthcare professionals (HCP), multidisciplinary teams, and policymakers is essential for improving understanding of available treatments, addressing misconceptions regarding newer therapies, and implementing recommendations into clinical practice.[23] Ensuring optimised and consistent approaches to early diagnosis and proactive, goal-directed treatment will enable more people living with this complex disease to achieve meaningful disease control, giving them more of their lives back.[8,24,25]

HOW DOES CUMULATIVE ORGAN DAMAGE IMPACT LONG-TERM PATIENT OUTCOMES?

Around 40% of all SLE patients may develop early organ damage in the first year of diagnosis, and 28–56% of patients can experience this within 5 years of diagnosis.[26] This is a result of uncontrolled disease activity, flares, and side effects associated with treatment options such as GCs and immunosuppressants.[7,8,10-13] Patients who accumulate early organ damage face a higher risk of early- and long-term complications,[7] and as a result, uncontrolled disease activity results in significant physical, economic and social costs.[1,10] Early and sustained control of SLE activity can prevent organ damage, ultimately leading to better outcomes and reduced financial strain on healthcare systems.[1,6,7]

Even a small reduction in daily steroid use (for example 1 mg/day) can lower the risk of organ damage, with GC tapering in patients with SLE associated with lower risk.[27] Promptly initiating treat-to-target strategies in patients with SLE may prevent organ damage accrual by controlling disease activity and reducing GC exposure through tapering/withdrawal strategies.[6,8,9,18] Moreover, the EULAR recommendations support this and emphasise cautious use of GCs in SLE management due to their long-term risks and the earlier use of new agents with GC-sparing effects.[18]

HOW DOES EARLY INTERVENTION WORK IN THE REAL WORLD TO REDUCE THE RISK OF ORGAN INVOLVEMENT?

Patient A

A 26-year-old woman was diagnosed early with SLE and initiated promptly on a targeted treatment plan that included adding a biologic shortly after diagnosis, for optimal control of ongoing disease activity despite the use of standard-of-care therapy, in-line with recommendations. The treatment goal was remission and improved health-related quality of life. This approach enabled suppression of her symptoms, achieving a treat-to-target goal and rapid GC tapering, while maintaining long-term remission, with no major flares or organ damage, allowing her to lead an active, full-time working life.

Patient B

A 30-year-old woman diagnosed with severe SLE and initially treated with multiple immunosuppressants and high-dose steroids. However, due to multiple disease flares, by the time she was initiated on a biologic, 18 months after diagnosis, she had already accrued significant kidney damage and osteoporosis.

These cases underscore the result of an early proactive, treat-to-target approach and the difference of working towards a goal of sustained remission.

WHAT IS THE MOST IMPORTANT TAKEAWAY FOR HEALTHCARE PROFESSIONALS MANAGING SYSTEMIC LUPUS ERYTHEMATOSUS TODAY?

We are at a pivotal moment for SLE, where effective disease management is no longer just about enduring the next flare, but rather ensuring that patients live full, active lives with minimal disease burden.[28] While traditional approaches have played a crucial role, continuous improvement is essential and we can do this by:

- Recognising the importance of early intervention to prevent irreversible damage and improve patient outcomes;[24]
- Minimising prolonged GC exposure through timely use of immunosuppressives or biologics,[6] and pursuing a treatment target, ideally long-term remission, as a realistic goal in SLE;[6,18] and
- Collaborating across disciplines to implement evolving clinical recommendations and engage patients in shared decision-making that benefits long-term health.[18,22,23]

We must seize this moment to break the cycle. By advocating for earlier intervention and treatment escalation, treat-to-target strategies, and steroid reduction, we can help patients live better for longer.

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