Comments on: Increased serum soluble interleukin-2 receptor concentrations are linked to high-sensitivity troponin T and disease progression in systemic sclerosis

Sir,

We read with great interest the recent publication by Schumacher *et al*. in your esteemed journal (1). The study explores the association between serum soluble interleukin-2 receptor (sIL-2R) levels and disease progression in systemic sclerosis (SSc), providing valuable insights. However, several critical limitations warrant attention to enhance the clinical relevance of the findings.

Firstly, the study acknowledges the use of various immunosuppressive therapies, including rituximab (RTX), but lacks details on standardized treatment protocols, such as dosing, duration, and criteria for therapy escalation. This inconsistency hampers the interpretation of sIL-2R dynamics during treatment, as evidenced by the finding that RTX did not significantly reduce sIL-2R levels, which contradicts the 2023 EULAR recommendations. These recommendations advocate for the use of RTX in treating skin and lung fibrosis in SSc, emphasising the necessity of standardised regimens (2). Therefore, we recommend further research to evaluate changes in sIL-2R levels during RTX treatment to assess its utility in tracking treatment efficacy.

Secondly, SSc is characterised by multiorgan involvement; however, this study primarily focuses on cardiac, pulmonary, and cutaneous manifestations, with minimal attention given to gastrointestinal (GI) and renal damage. GI involvement, such as oesophageal dysfunction and intestinal hypomotility, affects over 40% of SSc patients (3). The study notes that sIL-2R concentrations did not correlate with gastrointestinal involvement but failed to explore specific GI complications. Similarly, scleroderma renal crisis (SRC) is a life-threatening complication occurring in approximately 2-5% of SSc cases (3); however, the study does not analyse sIL-2R levels in patients with SRC or chronic kidney disease. This gap is significant, as the 2023 EULAR guidelines highlight GI and renal involvement as key determinants of SSc prognosis.

Thirdly, autoantibodies play a crucial role in the classification of SSc; however, the research did not analyse the relationships between sIL-2R levels and antinuclear antibody (ANA) profiles. While the authors report the prevalence of antibodies such as anti-centromere antibodies (ACA) and anti-topoisomerase I antibodies (anti-Scl-70), they do not investigate whether sIL-2R levels differ across these subsets. Autoantibodies are pivotal for both the classification and prognosis of SSc. Notably, patients who are positive for anti-Scl-70 often exhibit more severe organ involvement, whereas ACA is associated with limited cutaneous subsets (2, 3). Nevertheless, the study fails to explore the associations between sIL-2R and these antibody profiles. This lack of analysis hampers our understanding of whether sIL-2R serves as a surrogate marker for antibody-driven pathogenesis, thereby limiting its utility in subtype-specific risk stratification. Investigating how sIL-2R correlates with ANA subtypes could enhance its role as a biomarker, facilitating more precise risk stratification in accordance with the British Society for Rheumatology guidelines that emphasise personalised medicine.

Lastly, the study primarily focuses on limited cutaneous systemic sclerosis (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc), but it does not explicitly address systemic sclerosis sine scleroderma (ssSSc), a subtype characterised by the absence of skin fibrosis (4). The authors note that sIL-2R correlates with skin involvement; however, ssSSc patients, who may still exhibit severe visceral involvement (*e.g.*, interstitial lung disease in 49.8%), were not analysed separately. Given that ssSSc accounts for approximately 8.8% of SSc cases and possesses distinct prognostic features (5), the exclusion of this subgroup may limit the generalisability of sIL-2R as a universal biomarker.

This study enhances our understanding of sIL-2R in SSc. However, it is crucial to address its limitations for effective clinical translation. Standardising treatment protocols, expanding analyses to encompass GI and renal involvement, and exploring correlations with ANA profiles will be essential in validating sIL-2R as a clinically useful biomarker.

G. Chen, *MD*
L.M. Zhang, *MD*
Y. Zhang, *MD*

Department of Rheumatology and Immunology, Sichuan Tianfu New Area People's Hospital, Chengdu, Sichuan, China.

Please address correspondence to:
Yu Zhang
Department of Rheumatology and Immunology, Sichuan Tianfu New Area People's Hospital, 610213 Chengdu, Sichuan, China.
E-mail: 624292631@qq.com

Competing interests: none declared.

References

1. Schumacher L, Müller A, Koch A *et al.*: Increased serum solubleinterleukin-2 receptor concentrations are linked to high-sensitivity troponin T and disease progression in systemic sclerosis. *Clin Exp Rheumatol* 2025; 43(8): 1446-54. https://doi.org/10.55563/clinexprheumatol/re755k
2. Del Galdo F, Lescoat A, Conaghan PG *et al.*: EULAR recommendations for the treatment of systemic sclerosis: 2023 update. *Ann Rheum Dis* 2025; 84(1): 29-40. https://doi.org/10.1136/ard-2024-226430
3. Denton CP, De Lorenzis E, Roblin E *et al.*: The 2024 British Society for Rheumatology guideline for management of systemic sclerosis. *Rheumatology* (Oxford) 2024; 63(11): 2956-75. https://doi.org/10.1093/rheumatology/keae394
4. van den Hoogen F, Khanna D, Fransen J *et al.*: 2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative. *Ann Rheum Dis* 2013; 72(11): 1747-55. https://doi.org/10.1136/annrheumdis-2013-204424
5. Lescoat A, Huang S, Carreira PE *et al.*: Cutaneous Manifestations, Clinical Characteristics, and Prognosis of Patients with Systemic Sclerosis Sine Scleroderma: Data from the International EUSTAR Database. *JAMA Dermatol* 2023; 159(8): 837-847. https://doi.org/10.1001/jamadermatol.2023.1729