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

Sir,

We thank Chen *et al*. (1) for their interest in our study on soluble interleukin-2 receptor (sIL-2R) concentrations reflecting disease severity, particularly cardiac damage, and disease progression suggestive of a potential role for sIL-2R in assessing disease extent and for monitoring response to therapy in systemic sclerosis (SSc) (2). This monocentric retrospective longitudinal cross-sectional study reports real-world data under different immunosuppressive therapies. Of note, SSc patients with severe interstitial lung disease received either cyclophosphamide at 600 mg/m^2 body surface area or rituximab at 1000 mg on day 0 and 13 intravenously for induction therapy based on the RECITAL trial (3), also referred to in the EULAR 2023 recommendations (4). As described, baseline sIL-2R concentrations were similar across treatment subgroups in our study (2). A decrease in sIL-2R concentration upon follow-up was associated with remission, except in the rituximab (RTX) group (Supplementary Fig. S2). This finding can, with all caution, also be interpreted as an indication of a more severe disease course or persistence of disease activity in those patients treated with rituximab or may be due to other causes. As stated in our article (2), the use of sIL-2R as a biomarker should be further investigated in a prospective study. Nonetheless, biomarker findings per se cannot "contradict the 2023 EULAR recommendations", as the authors put it (1). Biomarker findings cannot be predicted based on therapy recommendations. As noted by Chen *et al*. (1), gastrointestinal involvement can present with a range of different manifestations (5). To address changes of sIL-2R concentrations related to gastrointestinal involvement, this subgroup was not further subdivided regarding different gastrointestinal manifestations in our study (2). Other than stated by Chen *et al*., patients with renal involvement were included in our study showing a higher frequency of chronic kidney disease and scleroderma renal crisis in patients with a sIL-2R concentration above 900 U/ml (Table I and II). By contrast, subgroup analysis showed no association between sIL-2R concentrations and antinuclear antibody profiles (2). And as final note, 315 SSc patients with either lcSSc or dcSSc were included in this study (2). There were only a few patients with systemic sclerosis sine scleroderma (ssSSc) seen during the observation period, making this subgroup too small for comparative analysis.

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Competing interests: none declared.

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