

## Response to: 'Remission in systemic lupus erythematosus: durable remission is rare' by Wilhelm *et al*

We read with interest the article by Wilhelm *et al*, reporting the frequency, durability and predictors of four definitions of remission, agreed upon by an international group of experts (Definition of Remission in Systemic Lupus Erythematosus (SLE); DORIS, in the Baltimore lupus cohort).<sup>1</sup>

As the premise of defining remission is to provide a therapeutic target to guide the management of SLE, we question the value of having four definitions. We further argue that the complete absence of clinical disease activity off of all treatment may simply identify a small group of patients who inherently have a less severe disease phenotype. While a definition that allows immunosuppressive treatment is more realistic, it could be argued that any patient requiring long-term prednisone, even at a very low dose, may not be truly in remission.<sup>2</sup> The allowance of some disease activity on the physician's global assessment (PGA), which may be a more sensitive, although less specific measure of overall disease activity than SLE disease activity index (SLEDAI), may speak to a state of minimal or low disease activity rather than true remission. The inclusion of serologic criteria in the definition of remission remains contentious and may ultimately depend on whether the patient has a disease profile that is seroconcordant or serodiscordant. For these reasons, we believe that a more thorough conceptual base that encapsulates the entity of 'remission' is needed to guide the definition of operational criteria.

We propose that a singular definition of remission be derived using rigorous methodology that begins with consensus, followed by demonstration of criterion validity against meaningful endpoints such as damage accrual and mortality. Demonstrations of construct validity, discriminant capacity, responsiveness to change and feasibility are also required to complete validation before widespread use. Such an approach could be used to reduce the current multiple definitions of remission to a single definition that has maximum usefulness.

The lupus low disease activity state (LLDAS) was recently defined by the Asia Pacific Lupus Collaboration using consensus methods (Delphi survey and nominal group discussion) and validated against the end-point of damage accrual using prospectively acquired cohort data.<sup>3</sup> Given the rarity of sustained zero

disease activity, LLDAS allows minimal disease activity and places limits on treatment, allowing a prednisone dose of  $\leq 7.5$  mg daily and standard well-tolerated doses of immunosuppressives. In a prospective study, we have shown that LLDAS criteria are fulfilled by 44% of patients at cohort entry, and that being in LLDAS is associated with better health-related quality of life (Golder *et al*; submitted for publication). Further validation studies are currently under way.

Given the difficulty in achieving consensus regarding the definition of remission in SLE and the questionable feasibility of such definitions that are fulfilled by so few patients, we propose that LLDAS is a viable treatment target in SLE, representing an attainable state that is associated with good long-term outcomes.

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- 3 Franklyn K, Lau CS, Navarra SV, *et al*. Definition and initial validation of a Lupus Low Disease Activity State (LLDAS). *Ann Rheum Dis* 2016;**75**:1615–21.