In chronic inflammatory diseases such as rheumatoid arthritis, attainment of a specific cut-off of low (or even absent) disease activity has been associated with favourable long-term disease outcomes. Systemic lupus erythematosus (SLE) is a complex, systemic disease where prognosis is determined by a variety of factors including disease activity and exposure to potentially toxic drugs particularly glucocorticoids. To this end, both increased activity (either persistent or exacerbations following a period of inactivity) and continuous intake of prednisone at doses above 5–7.5 mg/day have been correlated with accrual of irreversible dysfunction or damage in a variety of organs.

Delineation of the optimal therapeutic goal in SLE is challenging, which is in part due to the inherent limitations of the available clinical instruments for monitoring the disease. Nonetheless, through an evidence- and consensus-based approach, an international expert panel has recently introduced various definitions of remission in SLE 1 namely: (a) complete remission (with normal serological markers); (b) clinical remission (irrespective of serological markers); (c) complete remission on-treatment (allowing intake of stable maintenance immunosuppressives and/or ≤5 mg/day of prednisone); and (d) clinical remission on-treatment. In the aforementioned definitions, remission is established by combination of absent disease activity (typically, SLEDAI=0 and physician-rated global activity [physician global assessment-PhGA] ≤0.5). In addition, an Asia-Pacific collaborative group has proposed lupus low disease activity state (LLDAS) 2 as minimally acceptable disease activity (including serological markers and allowing intake of stable maintenance immunosuppressives and/or ≤7.5 mg/day of prednisone) in patients with SLE. A SLEDAI cut-off of ≤4 with PhGA of ≤1 are included in this definition. Accordingly, a number of observational studies have shown that attainment of either remission or LLDAS is associated with improved patient outcomes such as prevention of flares and organ damage accrual.3 4

However, a number of issues pertaining to the definition of therapeutic target in SLE require clarification. First, although PhGA is useful in monitoring the disease by acting as a ‘safety net’ against the drawbacks of SLEDAI, it is still subject to inter-rater variability.5 Second, existing definitions of remission and LLDAS comprise of a combination of features such as an objective activity index, physician-rated activity and dose of glucocorticoids. The extent to which all these components are prognostically important is not clear and recent studies suggest that SLEDAI=0 alone may suffice for the definition of remission in SLE.6 Finally, it has been a matter of debate whether serology (serum C3/C4, anti-dsDNA) should be included in the definition of treatment targets (remission, LLDAS) or whether the latter should be based on the clinical parameters of SLE activity. This is due to the lack of absolute concordance between clinical and serological activity and the fact, that most patients with stable abnormal serology have favourable long-term prognosis. Further studies in large, well-characterised patient registries will be required to address the abovementioned issues, thus defining the optimal treatment goal in the disease.

Learning Objectives
• Identify factors with an adverse impact on organ damage accrual in patients with SLE
• Demonstrate understanding of the existing definitions of remission and low disease activity state in SLE
• Discuss unresolved issues related to the definitions of remission and low disease activity and their implementations in clinical practice

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prednisone intake ≤7.5 mg, and negative predictors of remission and LDA were number of flares in the 3 years before belimumab treatment initiation and baseline renal involvement. Notably, patients spending at least 50% of follow-up in LDA (66%) or at least 25% of follow-up in remission (42.9%) accumulated less damage at the end of the follow-up.

Consequently, this study provided novel evidence that an earlier use of belimumab in patients with active SLE and low damage may maximise its efficacy in clinical practice.

Learning Objectives
- Explain the importance of achieving remission or LDA in SLE management
- Describe the role of belimumab in achieving remission or LDA in post-hoc analysis of the randomised control trials
- Discuss the best use of belimumab in clinical practice settings

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CAN WE WITHDRAW LOW-DOSE PREDNISONE IN REMITTED PATIENTS?
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Maintenance of remission has become central in the management of systemic lupus erythematosus (SLE). However, an active disease-free state is generally maintained only when patients are on medication, which often leads to treatment-related complications. Therefore, once remission has been achieved, prolonged maintenance treatment inevitably requires a regimen of drug de-escalation. The recent EULAR recommendations for the treatment of SLE during chronic maintenance treatment advocate that glucocorticoids (GC) should be, when possible, withdrawn.1 However, in routine practice a significant proportion of treating physicians prefers to continue a low dose GC regimen, despite clinical remission, which is most likely due to the fear that withdrawal of low-dose GCs may lead to a severe flare, even after very long intervals of remission.2 In a recent prospective randomised controlled trial, we showed that, in SLE patients in remission and with stable treatment regimen for at least 1 year, withdrawal of 5 mg of prednisone was associated with a fourfold increase (i.e. 27%), in the risk of flare, as defined by the SFI or the BILAG index.3 Other SLE treatments remained unmodified during this study. In particular, at study entry 91% and 27% of the patients were also treated with hydroxychloroquine and an immunosuppressant, respectively. The 27% relapse rate observed in the withdrawal group in our study is in line with the ones recently reported in two recent cohorts.4,5 Tani et al described the longitudinal study of a cohort of 91 SLE Italian patients who attempted stopping GC treatment.4 A total of 77 patients successfully stopped GC. For those patients who were successfully withdrawn from GC, 18 flares (23%) were recorded after a median follow-up period of about 2 years. As in our study, 72% of flares were mild. The time period since the last flare was the sole determinant predictor of disease flare identified. A recent observational study, performed by Goswami et al in India, reported that 21% of patients in remission undergo exacerbation of the disease after GC withdrawal with most of the flares occurring in the first year of follow-up. Therefore, until the availability of effective drugs with little or no toxicity, it is recommended to not abandon the option of using very low doses of GCs (i.e. ≤5 mg prednisone) given their potential benefits in SLE patients in remission, especially those at low cardiovascular risk.

Learning Objectives
- Define remission in SLE patients
- Discuss drug de-escalation in SLE patients in remission

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