STRATEGIES FOR MINIMIZING CORTICOSTEROID EXPOSURE IN SLE

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Glucocorticoids (GCs) play a central role in the treatment of active systemic lupus erythematosus (SLE). Long-term GC-related side effects (i.e., infections, diabetes mellitus, cataract, osteoporosis, gastrointestinal bleeding and cardiovascular disease), leading to the development of irreversible organ damage, mean that clinicians must develop strategies for minimizing GC exposure in SLE.¹ Initiation of oral GC should be avoided, especially when there are effective therapeutic alternatives as for cutaneous and articular manifestations. In patients with lupus nephritis, starting GC with a medium prednisone dose (0.5 mg/kg/day) is as effective as high-dose dose (1 mg/kg/day) prednisone.¹ Use of intravenous methylprednisolone (MP) pulses (usually 250–1000 mg/day for 3 days) may allow for a lower starting dose and faster tapering of oral GC.^{2–3} Early initiation of immunosuppressive drugs can facilitate a more rapid GC tapering and may prevent SLE flares.⁴ Long-term GC administration with doses of ≤5 mg/day prednisone produces an acceptably low level of harm, with the exception of patients at high cardiovascular risk who may require preventive measures.⁵ Withdrawal of low dose prednisone is also recommended by EULAR, when possible,¹ but recent data suggest that this exposes SLE patients to an increased risk of flare, whereas its long-term maintenance is not associated with increased damage scores.⁶

Learning Objectives

- Describe strategies for minimizing corticosteroid dose at treatment initiation for lupus nephritis, cutaneous lupus and lupus arthritis
- Describe strategies for minimizing corticosteroid exposure when SLE remission has been reached

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TARGETING REMISSION AND LOW DISEASE ACTIVITY IN SLE

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Remission and low disease activity (LDA) are the most important targets to achieve in systemic lupus erythematosus (SLE) management.^{1–5} In this process, the first target we should try to achieve is remission and when remission cannot be achieved we should aim for clinical LDS.³ Nowadays, achieving remission or LDA is not uncommon in SLE; however maintaining remission over time is more difficult, since SLE relapses are very common. We should make every effort to achieve and maintain these targets, in fact we know that the longer the remission or the LDA, the lower the damage accrual.^{1–2–5–6} In patients with lupus nephritis (LN) the lack of achievement of EULAR/ERA-EDTA response at 1 year is predictive of a poor renal outcome⁷ and, again, the longer the duration of LN remission the lower the proportion of patients who develop chronic kidney disease.⁸

The second step in the treat-to-target (T2T) strategy should be to minimize or even withdrawal glucocorticoids (GC). The short- and long-term side-effects of GC are very well known. We evaluated the increase in damage progression according to the level of remission in our patients: complete remission, clinical remission off GC, and clinical remission on prednisone ≤5 mg/day.² Interestingly, no differences in damage progression were observed among the different levels of remission in patients who achieve <5 consecutive years remission, by contrast a significant difference was observed in those who achieve ≥5 years remission: i.e. patients in clinical remission on prednisone accumulated more damage than those in clinical remission off prednisone or in complete remission.² Thus, to achieve clinical remission is more important than to take a small daily dosage of prednisone in the short term, but in the long term even a small daily dosage of prednisone can contribute to damage progression.²

The third step in the T2T strategy is to reduce and to withdraw immunosuppressants (IS) where possible. In a recent study carried out in the Toronto lupus cohort, univariate and multivariate analysis showed IS as well as GC and other factors were predictors of damage progression within 5 years. We have recently analysed prevalence and predictors of flare after IS discontinuation in SLE patients in remission: Out of 319 patients ever treated with IS, 139 discontinued IS, 105 due to remission and 34 due to poor adherence/intolerance. Twenty-six patients developed a flare, and the flare-free survival was higher in patients who discontinued due to remission than in those who discontinued IS due to poor adherence/intolerance.⁶ The longer the remission before discontinuation and hydroxychloroquine intake were the most significant protective factors.

T2T strategy through the achievement of remission/LDA can improve disease outcomes, especially halting damage accrual. The proportion of patients who can achieve remission and LDA largely depends on the definition used, and in any case is higher in a clinical practice setting than in randomised controlled trials (RCTs). Notably, biologics can help attain remission and LDA and, in turn, dampen damage progression.⁹

Learning Objectives

- Discuss the major targets in SLE management and their timing in a sequential strategy
- Explain the importance of achieving remission or LDA in SLE
- Describe the role of biologics in achieving remission or LDA in post-hoc analysis of RCTs and in clinical practice setting