

## 15 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.<sup>1</sup> 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.<sup>1</sup> 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.<sup>2–3</sup> Early initiation of immunosuppressive drugs can facilitate a more rapid GC tapering and may prevent SLE flares.<sup>4</sup> Long-term GC administration with doses of  $\leq 5$  mg/day prednisone produces an acceptably low level of harm, with the exception of patients at high cardiovascular risk who may require preventive measures.<sup>5</sup> Withdrawal of low dose prednisone is also recommended by EULAR, when possible,<sup>1</sup> 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.<sup>6</sup>

### 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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## 16 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.<sup>1–5</sup> 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.<sup>3</sup> 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.<sup>1–2–5–6</sup> In patients with lupus nephritis (LN) the lack of achievement of EULAR/ERA-EDTA response at 1 year is predictive of a poor renal outcome<sup>7</sup> and, again, the longer the duration of LN remission the lower the proportion of patients who develop chronic kidney disease.<sup>8</sup>

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  $\leq 5$  mg/day.<sup>2</sup> 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  $\geq 5$  years remission: i.e. patients in clinical remission on prednisone accumulated more damage than those in clinical remission off prednisone or in complete remission.<sup>2</sup> 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.<sup>2</sup>

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.<sup>6</sup> 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.<sup>9</sup>

### 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

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## LUPUS TREATMENT IN THE NEXT DECADE: THE NEXT DECADE IS UPON US

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There is little question that our colleagues in rheumatology who treat patients with rheumatoid or psoriatic arthritis have outdone us ‘lupologists’ in bringing new therapies to the community. Biologics have truly been transformative for those patients with inflammatory arthritis. We are now starting to see the same successes in lupus. As we celebrate the 10th anniversary of the FDA approval of belimumab, the lupus community recently witnessed the approval of two drugs, belimumab and voclosporin, for the treatment of lupus nephritis. In addition, several Phase 2 studies yielded favorable results and will be progressing to Phase 3.<sup>1–5</sup> Drug development activity is currently unprecedented, and there is no doubt that research advances will improve outcomes and ensure brighter futures for our patients with systemic lupus.

## Learning Objectives

- Describe unmet needs in SLE treatment
- Discuss biologic targets for SLE drug development
- Explain recent clinical trial results

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## Workshop

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## CUTANEOUS LUPUS

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## Case 1: 35-year-old Mestizo female

## Bernardo Pons-Estel

A 35-year-old Mestizo female was diagnosed with systemic lupus erythematosus (SLE) in 2005 based on polyarthritis, malar rash, photosensitivity, mucosal ulcerations, positive ANA and anti-dsDNA, and low complement. She was treated with prednisone 20–30 mg/day and hydroxychloroquine (HCQ) 400 mg/day. In June 2010, lupus pneumonitis was diagnosed.

In July 2018, she was first admitted to our hospital. She was cushingoid and had fever, fatigue, malar rash, oral ulcers, alopecia, polyarthritis, oedema, multiple purplish-red streaks, and active erythematous, palpable and painful subcutaneous indurated nodules/plaques located on her face, proximal lower extremities and abdomen; some were ulcerated.

Laboratory tests RBC 3.8 ( $\times 10^{12}/L$ ), hemoglobin 11.8 g/dl, WBC 2.3 ( $\times 10^9/L$ ), platelets 62 ( $\times 10^9/L$ ), ESR 8 mm, CRP 0.8 mg/L, serum ferritin 1,487 ng/ml, ALAT 70 UI/ml, ASAT 26 UI/ml, GGT 64 U/L, BUN 43 mg/dl, serum creatinine 1.54 mg/dl, GFR 67 mL/min, cholesterol 186 mg/dL, triglycerides 149 mg/dl, proteinuria 210 mg/24 h, ANA 1/320, speckled pattern, anti-Sm (+) and anti-dsDNA, anti-U1RNP, anti-Ro and anti-La all (-). C3 75 mg/dl, C4 10, Coombs test (-), procalcitonin 0.29 ng/ml (<0.5). VDRL and viral serologies were negative. A cutaneous ulcer culture showed proteus mirabilis. Her SLEDAI was 19. Three skin biopsies of indurated lesions all showed lobular panniculitis.

She was treated with IV methylprednisolone (500 mg/day/3 days), and high-dose intravenous immunoglobulin, and discharged with mycophenolate mofetil 1 g/day, HCQ 400 mg/day, prednisone 20 mg/day and TMS-SMX 860/160 BID for 5 days. A week later she was re-admitted with fever, pancytopenia, hepatosplenomegaly, lymphadenopathy and several painful, indurated erythematous lesions. Her SLEDAI was 13. A bone marrow aspiration and biopsy was interpreted as a macrophage activated syndrome in the context of SLE exacerbation and treated with IV dexamethasone, colony stimulating factor, and rituximab 1000 mg. Despite treatment, she remained severely ill with fever, asthenia, petechiae and purpura on her abdomen and thighs, and pancytopenia. Due to disease severity, treatment with etoposide was indicated. Finally, the patient presented an acute episode of respiratory distress followed by death.

## Discussion Points

- Interpreting the different skin manifestations in a patient with SLE
- Analyzing complications and differential diagnoses with other associated diseases

## Case 2: 28-year-old Caucasian female

## Annegret Kuhn

A 28-year-old Caucasian female was diagnosed with systemic lupus erythematosus (SLE) in 1996 and presented with severe, erythematous, scarring discoid lesions on the scalp,