

Pre-meeting session I: old drugs on the stage

01 GLUCOCORTICOIDS FOR SLE: WHAT ARE THE CURRENT QUESTIONS AND ISSUES?

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Glucocorticoids (GCs) have long been one of the cornerstones of the treatment of systemic lupus erythematosus (SLE). However, for many years, recommendations for GC therapy have been more based on custom than on true evidence.

It is now a well-established fact that GCs are a major cause of irreversible damage. This association is dose dependent and has a close relationship with the progressive saturation of the genomic way with increasing doses over 7.5 mg/d of prednisone.^{1 2} On the contrary, pulses of methylprednisolone (MP), 125–500 mg/d for short periods of time (usually 3 days) have been consistently free from secondary damage in observational studies and a recent meta-analysis.²

Considering these thresholds, the use of MP in the induction phase followed by a rapid tapering of prednisone to reach maintenance doses of 2.5–5 mg/d is the safest and most effective approach to treat lupus flares, always in combination with hydroxychloroquine and, when necessary, immunosuppressive drugs.

The complete withdrawal of prednisone has been aimed as a main objective in recent recommendations. Recent studies and meta-analysis have shown that this is possible in about 80% of cases, however, the remaining patients would experience flares when GCs are completely stopped.³ A slowly gradual tapering from 5 mg/d when SLE is in longstanding remission maximises the chance of a successful withdrawal of the drug.⁴ If this is not possible, long-term maintenance doses of 2.5–5 mg/d are a reasonably safe option, much better than facing recurrent flares with the subsequent use of higher doses of GCs.

Therefore, combination therapy with hydroxychloroquine and immunosuppressive drugs, the use of MP in the induction of remission, not only in life-threatening scenarios, and a rapid tapering with a slow withdrawal of prednisone is our proposal for the successful management of SLE.^{4 5}

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Learning Objectives

- Describe the role of the genomic and non-genomic ways in the therapeutic and toxic effects of GCs

- Discuss the association of different doses of GCs with side effects including damage
- Explain the results from recent studies on the efficacy and toxicity of therapeutic schemes using MP pulses followed by lower doses of prednisone in active lupus
- Discuss practical guidelines for using GCs in the different settings of active lupus

02 CYCLOPHOSPHAMIDE: WHAT IS ITS ROLE IN THE TREATMENT OF LUPUS NEPHRITIS AND THE NEW TREATMENT PARADIGM?

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Cyclophosphamide (CyP) is perhaps the most venerable of immunosuppressants used to treat lupus nephritis (LN). Its use was established in the so-called NIH regimen in the 1980s and high-dose monthly injections for at least 6 months along with high-dose steroids became standard of care, globally. The issue became, not that it isn't an effective treatment, but the 'cost' to the patients was too high.

It was recognised that the main issues were using a drug in doses associated with premature ovarian failure and teratogenicity to treat a disease that mostly affects women of child-bearing age. There was also the very real risk of neutropenic sepsis associated with the high doses and infection has always been a major cause of death in patients with LN. Most clinicians were therefore relieved when an alternative immunosuppressant, mycophenolate mofetil (MMF) – albeit one which is teratogenic but has no impact on fertility – was shown to be effective in treating LN. Although the original study by Chan et al was small and only in Chinese population,¹ many clinicians rapidly switched to using MMF instead of CyP.

The next challenge came from a paper by Contreras et al² showing that prolonged courses were less effective than switching to maintenance with mycophenolate (MMF) or azathioprine. However, CyP has been rehabilitated by the EuroLupus trial (ELNT) – a small, underpowered study but which has shown benefit in long term outcomes and in multiple ethnic groups.³ The ELNT regimen, whilst still steroid heavy, uses very low doses of CyP and has been shown, as a one-off course, unlikely to reduce fertility and have low rates of infectious complications. Most recent trials, however, have not included CyP as standard of care (SOC) – the exception being the BLISS-LN study,⁴ where 1/3 of the patients received CyP as SOC induction therapy and there was no apparent benefit when belimumab added, despite the overall positive outcome of the trial.

Does this mean CyP has no role in the modern management of LN? Almost certainly not. From a very practical perspective, it is a very cheap drug and therefore highly suitable to use low-dose regimens in resource poor countries. Importantly, it is effective, it has the advantage of being given intravenously, which overcomes issues with adherence and is still favoured by many for more severe disease.

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Learning Objectives

- Describe the evidence base for current cyclophosphamide-based regimens
- Discuss the advantages and disadvantages of using cyclophosphamide-based regimens
- Explain how cyclophosphamide might be used in combination with newer therapies

03 TOP 10 TIPS REGARDING PATIENT ADHERENCE TO HYDROXYCHLOROQUINE

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Adherence is defined as ‘the extent to which a person’s behaviour coincides with medical or health advice’. Non-adherence to therapeutic regimens is a common and expensive problem in patients with chronic diseases including systemic lupus erythematosus (SLE) and is associated with a higher risk of flares, morbidity, hospitalisations and poor renal outcomes.^{1 2} Non-adherence is also very difficult to evaluate.^{3–5}

Hydroxychloroquine (HCQ), an important medication in SLE with an excellent benefit:risk ratio, has a long half-life and it can be measured in blood. Undetectable or very low levels of blood HCQ is then a simple, objective and reliable marker of non-adherence in SLE patients.^{1 4 5}

Levels of HCQ and then HCQ non-adherence should be routinely and repeatedly assessed. If severe non-adherence is unmasked, a non-judgmental and open discussion must take place to improve adherence as much as possible. This task is not simple, but particularly important and some tips will be discussed (table 1).⁵

Abstract 02 Table 1 Addressing medication non-adherence in clinical practice

Remember that non-adherence is the rule and perfect adherence the exception.

Improve your diagnostic skills to unmask non-adherence.

Always ask open questions.

Use objective methods to detect non-adherence, such as measurement of blood hydroxychloroquine levels.

Try to understand the reasons for non-adherence.

Explain but listen first.

Set-up a tailored-management plan.

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Learning Objectives

- Recognise the frequency and consequences of non-adherence
- Describe methods to evaluate non-adherence
- Analyse blood hydroxychloroquine levels
- Improve the way we discuss non-adherence with our patients

Opening session (live-streamed with external Q&A)

Debate

04 THE MATTER OF THE DEBATE: LLDAS IS AN EXCELLENT OUTCOME MEASURE, BUT DOES IT REALLY CAPTURE PATIENTS WITH TRUE LDA?

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Accurate definitions of disease states can be very helpful in care, education and research. During recent years, definitions of low disease activity and remission in systemic lupus erythematosus (SLE) have been developed, tested and published. The definition Low Lupus Disease Activity State (LLDAS) was extensively validated and has already been utilized in several studies and clinical trials. However, some uncertainties remain. Does this definition define patients whose disease does truly have a low level of activity? Or conversely, can patients whose disease activity really is low be ‘missed’ by this definition? And if so, what would the consequences of that be. These questions will be addressed in this year’s debate at the 11th Annual Meeting of the Lupus Academy.

Learning Objectives

- Explain the importance of having definitions of lupus disease states
- Describe the recent development of the LLDAS
- Demonstrate understanding that some questions remain around the LLDAS

05 LLDAS IS AN EXCELLENT OUTCOME MEASURE, BUT DOES IT REALLY CAPTURE PATIENTS WITH TRUE LDA?

YES

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The deployment of treat-to-target approaches requires the identification of feasible, attainable endpoints, that are empirically associated with improved patient outcomes. While remission is the goal of care, the AsiaPacific Lupus