

Pre-meeting session I: old drugs on the stage

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

Guillermo Ruiz-Irastorza. Autoimmune Research Unit, Cruces University Hospital, Bizkaia, Spain

10.1136/lupus-2022-1a.1

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}

REFERENCES

- Buttgereit F, et al. Glucocorticoids in the treatment of rheumatic diseases: an update on the mechanisms of action. *Arthritis Rheum* 2004 Nov;**50**(11):3408–3417.
- Ugarte-Gil MF, et al. Impact of glucocorticoids on the incidence of lupus-related major organ damage: a systematic literature review and meta-regression analysis of longitudinal observational studies. *Lupus Sci Med* 2021 Dec;**8**(1):e000590.
- Ji L, Xie W, Zhang Z. Low-dose glucocorticoids should be withdrawn or continued in systemic lupus erythematosus? A systematic review and meta-analysis on risk of flare and damage accrual. *Rheumatology (Oxford)* 2021 Dec 1;**60**(12):5517–5526.
- Ruiz-Irastorza G. Prednisone in systemic lupus erythematosus: taper quickly, withdraw slowly. *Rheumatology (Oxford)* 2021 Dec 1;**60**(12):5489–5490.
- Ruiz-Irastorza G, Bertsias G. Treating systemic lupus erythematosus in the 21st century: new drugs and new perspectives on old drugs. *Rheumatology (Oxford)* 2020 Dec 5;**59**(Suppl5):v69–v81.

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?

Liz Lightstone. Imperial College London, UK

10.1136/lupus-2022-1a.2

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.

REFERENCES

- Chan TM, et al. Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. Hong Kong-Guangzhou Nephrology Study Group. *N Engl J Med* 2000 Oct 19;**343**(16):1156–1162.