drugs in this category, methotrexate eventually was established as the main DMARD for RA.

In the other diseases, the concept of disease modification was defined differently, based on the characteristics of that disease. Therefore, it was of interest to investigate the commonalities between these definitions, with a view to develop an evidence- and consensus-based definition of disease modification for treatments in lupus.[1]

Based on a systematic review of the literature and extensive discussions, an international task force arrived at such a definition, the main ingredients of which are demonstrated efficacy with respect to established disease activity indices, as well as with respect to organ damage outcomes.

The task force believes that establishing a definition of disease modification in systemic lupus erythematosus will help to clarify which treatments can be considered disease modifying. This will help to harmonise future clinical trial outcomes and enable comparison between therapies, all of which could ultimately help to improve patient outcomes.

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Learning Objectives

- Explain the concept of disease modification as they are applied to other diseases
- Discuss the proposed definition of disease modification in SLE
- Describe the potential utility of a definition of disease modification in SLE

26 OPTIMIZING STEROID-SPARING DRUGS IN SLE

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10.1136/lupus-2023-la.26

Glucocorticoids (GC) have long been one of the cornerstones of the treatment of systemic lupus erythematosus (SLE). However, it is now a well-established fact that GC are a major cause of irreversible damage.[1] Therefore, strategies to decrease GC load without compromising the adequate control of disease activity are essential in the management of SLE.

Hydroxychloroquine (HCQ) should be considered the main GC-sparing drug in lupus. Its continued use has been associated to a myriad of beneficial effects, including the prevention of damage accrual and the improvement of survival, but also to a better control of lupus activity and, thus, a reduced need for GC use. Also, immunosuppressive drugs such as cyclophosphamide, azathioprine and methotrexate, have been extensively used throughout different clinical scenarios in order to decrease GC doses.[2] Although clinical trials with this group of drugs are few, their use has long been validated by clinical practice. More recently, biologic agents approved for SLE such as belimumab and anifrolumab have also been shown to allow a good control of disease activity whilst reducing the dose of GCs.[3 4]

However, it is my view that the best GC-sparing drugs are…GCs. Pulses of methyl-prednisolone (MP), 125–500 mg/d, given for short periods of time (usually 3 days) have been shown to be the most effective way of rapidly controlling lupus flares through the activation of the non-genomic pathway.[5 6] Therefore, the use of MP in the induction of remission, not only in life-threatening scenarios, combination therapy with HCQ and immunosuppressive drugs and a rapid tapering with a slow withdrawal of prednisone is our proposal for the successful management of SLE. In cases in which this scheme fails to adequately control lupus activity, the addition of biologic drugs should be considered.

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Learning Objectives

- Describe the concept and the need for sparing GC
- Describe different drugs used to treat SLE with a GC-sparing effect
- Discuss results from recent studies on the efficacy and toxicity of therapeutic schemes using methyl-prednisolone pulses followed by lower doses of prednisone in active lupus
- Describe practical guidelines for using glucocorticoid-sparing drugs in the different settings of active lupus

27 DISEASE MODIFICATION IN LUPUS NEPHRITIS

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10.1136/lupus-2023-la.27

The treatment of lupus nephritis (LN) in recent decades has relied on combined treatment with corticosteroids and either mycophenolate mofetil (MMF) or intravenous boluses of cyclophosphamide. In recent years the therapeutic possibilities for LN have expanded remarkably, thanks to the completion of several landmark randomised controlled trials (RCT) that have demonstrated the efficacy of new drugs. Drugs that have shown efficacy in the initial treatment of LN include calcineurin inhibitors (CNI). Several small local trials with cyclosporine and tacrolimus showed that these CNI increase the achievement of remission and have a strong antiproteinuric effect. Recently, the AURORA-1 study confirmed that voclosporin, a new CNI, added to corticosteroids and MMF was superior to placebo in obtaining complete remission with a good safety profile.[1] Longer-term follow-up of patients suggests that voclosporin does not share the nephrotoxic effect of

other CNIs. Belimumab, a drug that blocks BLyS (a stimulator of B lymphocyte proliferation), had shown efficacy in improving different extrarenal manifestations of systemic lupus erythematosus (SLE) and decrease immunological activity. The BLYS-LN study demonstrated that belimumab, added to corticosteroids and MMF, induces a significantly higher number of LN remission than placebo, with a satisfactory safety profile.[2] Obinutuzumab, a newer anti-CD20 drug, has also shown encouraging preliminary data as initial therapy for NL. It is important to highlight that all these recent RCT compare triple therapy (corticosteroids plus MMF and the new drug under evaluation) with double therapy (corticosteroids plus MMF and placebo), so the addition of a CNI or belimumab for refractory cases or the use of triple therapy regimens from the onset for patients with high-risk profiles are recommended in recent guidelines.[3] Conversely, new renoprotective and cardioprotective drugs, such as SGLT2 inhibitors, are starting to show their importance in the non-immunosuppressive treatment of LN.[4] Despite these important successes in improving the initial treatment of LN, more studies are needed to determine the optimal maintenance treatment and criteria to personalize treatment duration in patients who achieve remission.

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Learning Objectives

- Describe studies about the use of calcineurin inhibitors in LN
- Describe the use of belimumab in LN
- Discuss the option of triple versus double therapy as initial treatment in LN
- Discuss different treatment options according to a patient´s disease profile
- Discuss newer non-immunosuppressive treatments for renal and cardioprotection in LN

Sunday 10th September 2023

Plenary II: pipeline and potential SLE therapies

28 JAK-STAT INHIBITORS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Janus kinase (JAK) inhibitors have enriched our armamentarium to treat autoimmune rheumatic diseases, with their approval in inflammatory arthritides (rheumatoid arthritis, spondyloarthritides). The rationale supporting a role for inhibition of the JAK/STAT pathway in the management of systemic lupus erythematosus (SLE) was provided by two fundamental facts: first, interferons (IFN) type I (α/β) and II (γ) are well-established and important players in SLE pathophysiology; second, the JAK/STAT signalling pathway has been identified as the cascade responsible for the signal transduction from the activated IFN receptor to the nucleus. Subsequently, evidence from *in vitro* studies and animal models supported a role for JAK inhibitors targeted against different JAKs in the treatment of cutaneous and systemic lupus erythematosus, including amelioration of lupus nephritis.[1]

Contrary to these encouraging preclinical data, clinical trials of JAK inhibitors in SLE were recently marked by the recent discontinuation of the development program of baricitinib (a selective JAK1/JAK2 inhibitor) for SLE, after the discordant results of the two identical SLE-BRAVE phase 3 trials, and following a very successful phase 2 trial.[2 3] Post-hoc analyses of the two studies are eagerly awaited to clarify the reasons behind these results. Regarding other JAK inhibitors, only a phase 1 study of tofacitinib has been published with reassuring safety results, and more data are needed.[4]

Notwithstanding these setbacks, evidence from case series and case reports still support a role for JAK inhibitors in SLE, particularly in patients with skin and joint disease. This is further supported by the fact that baricitinib and upadacitinib are also indicated for autoimmune dermatologic diseases, like alopecia areata (baricitinib) and atopic dermatitis (baricitinib and upadacitinib).

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Learning Objectives

- Explain the scientific rationale for testing JAK inhibitors in SLE
- Discuss preclinical data that provided proof-of-concept for clinical trials of JAK inhibitors in SLE
- Discuss the main results and conclusion from clinical trials of JAK inhibitors in SLE, with a focus on baricitinib
- Provide potential insight into the future of JAK-STAT inhibition of SLE following the failure of baricitinib and halting of its clinical programme in SLE