events identified in every clinical trial pose hazard to quality and quantity of life.

The unmet needs evident in these trials are:

1. Earlier diagnosis and treatment
2. Strategies to identify responders early
3. Strategies to anticipate flares before they are clinically apparent
4. Optimization of background therapies
5. Even better new treatments or combination therapies
6. Reduction of risk for damage and death

In LN, delaying renal biopsy by 3 months increases risk of poor outcomes and delaying by 6 months increases risk of end-stage kidney disease by 9-fold.^{1, 2} In a California study of LN patients with government insurance (Medicaid), only 31% were treated with immunosuppressive approaches 1 year after diagnosis.³ Added to these disturbing delays are problems with patients' treatment compliance, which is well less than 60% in many populations. It is also important to identify responders early, with LN there is a strong association between good outcome and decline in proteinuria, with the goal of $\leq 0.7/24$ hours at one year associated with better outcomes.⁴ Several laboratories are reporting panels of cytokines/chemokines and other proteins in serum or urine that predict lupus flare; none are yet widely available for clinical use. Regarding background therapies, all SLE patients that can tolerate it should receive hydroxychloroquine, since it reduces mortality by 35% (over 12 years). Reducing prednisone to the lowest dose possible is also a major goal, whilst finding the balance between damage from active disease and that caused by prednisone and other treatments. Some of the interesting new treatments in clinical trials include inhibition of plasmacytoid dendritic cell activation (a major source of interferon type 1), antibodies to CD20 that are more depleting and less immunogenic than rituximab, and inhibitors of pathways activated by cytokines and receptors in and on B and T cells. Finally, close attention to preventing damage (in addition to reducing immunosuppression) will improve quality and quantity of life, including prevention of infections (COVID vaccination is recommended for SLE patients), accelerated atherosclerosis and osteoporosis with fractures.

In conclusion, the recent advances are transformative in that we can suppress disease activity to protect from organ damage in increasingly higher proportions of patients with SLE, but there is a long way to go and much hard thinking lies ahead.

Learning Objectives

- Describe the efficacy of novel treatment interventions and combinations in improving outcomes in patients with SLE/LN
- Discuss current unmet needs in the management of SLE/LN and how novel treatments may overcome these
- Explain the need for the improving fast access to treatment, whilst minimizing costs and adverse treatment effects, and the importance of educating patients and caregivers about these

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Plenary II: Treatment challenges

29 TREATMENT OF CAPS: WHICH DRUGS AND IN WHICH ORDER?

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Antiphospholipid syndrome (APS) may be complicated by a 'thrombotic storm' called catastrophic antiphospholipid syndrome (CAPS), which can lead to multiple organ failure and admission of patients to the intensive care unit. An international consensus statement defined CAPS as the occurrence of: at least three organ/tissue/vessel involvement, occurring in less than a week, with biopsy-proven small vessel occlusion, in patients with defined APS.¹ The prognosis of CAPS is severe but has drastically improved in the last two decades from a 58% mortality in 1996 to a 23% in-hospital death in 2020.² The CAPS classification criteria do not encompass the full spectrum of severe thrombotic APS and patients with pre-CAPS or near-CAPS share the same prognosis as CAPS patients and should probably be treated identically.³ Several treatments have been tested, reported and recommended in the management of CAPS, but all these recommendations rely on a very low level of evidence and are mainly based on the publications from the a single group, the CAPS Registry.⁴ Anticoagulation is the cornerstone treatment of CAPS as it is the only one associated with better outcome in several cohorts.⁵ Heparin (unfractionated or low-molecular-weight) is the treatment of choice and its efficacy must be monitored with heparinemia. The combination of anticoagulation and corticosteroids (i.e. double-therapy) should be provided for every CAPS patient and triple-therapy (double-therapy plus plasma exchange or intravenous immunoglobulins) in patients with life-threatening involvement. In patients with CAPS associated with systemic lupus erythematosus, cyclophosphamide should probably be associated to triple-therapy. When triple-therapy has failed, antiplatelet agents can be added to the standard regimen. Successful use of rituximab and eculizumab have been reported in some refractory patients, however the level of evidence supporting their use is extremely low.

Learning Objectives

- Describe CAPS as a rare and severe complication of antiphospholipid syndrome
- Explain the importance of early treatment, even in pre-CAPS/near-CAPS patients
- Describe why combination of anticoagulation and corticosteroids is the cornerstone treatment of CAPS and that life-threatening CAPS episodes should be treated with a triple-therapy including anticoagulation, corticosteroids and intravenous immunoglobulins or plasma exchange
- Discuss the importance of continued anticoagulation in CAPS-related severe thrombocytopenia
- Explain why rituximab and eculizumab may be useful in refractory CAPS patients

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REFRACTORY CUTANEOUS LUPUS: USE OF THALIDOMIDE OR LENALIDOMIDE FOR REFRACTORY LUPUS SKIN DISEASE

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Cutaneous lupus erythematosus (CLE) may cause extensive skin damage leading to aesthetic prejudice and poor quality of life. Antimalarial agents are recommended as first-line systemic therapy for CLE patients with moderate-to-severe skin lesions. In case of failure of antimalarial agents, a European expert consensus for CLE treatment and EULAR recommendation for systemic lupus erythematosus (SLE) recommend adding quinine, methotrexate, retinoids, dapsone or mycophenolate mofetil.¹ However, the overall efficacy of these second-line treatments is approximately 50% depending on CLE subtypes and may be associated with potential toxicity. Thalidomide (α-N-phthalimidoglutarimide) is currently recommended as a ‘rescue’ therapy in patients with severe and refractory CLE treatment. However, in France, a ‘Temporary Recommendations for Use’ has been granted for thalidomide in CLE after failure of antimalarials as second-line agent.^{1–2} Moreover, in a systematic literature review including 21 observational studies and 548 patients the pooled rate of response to thalidomide 50–100mg/day was 90% (95% CI, 85–94), with similar response rates between CLE subtypes.³ The clinical benefits need to be balanced against potential adverse events with a pooled rate of thalidomide withdrawal related to adverse events of 24% (95% CI 14–35) including high teratogenicity, peripheral neuropathy 16% (95% CI 9–25), thromboembolic events in 2% (95% CI 1–3). Moreover, the efficacy of thalidomide is only suppressive with a rate of relapse of 71% (95% CI 65–77) after thalidomide withdrawal which supports the use of a minimal maintenance dose.³ In case of failure of thalidomide, lenalidomide 5 mg/day a 4-amino-glutamyl analogue of thalidomide has shown promising results with partial response of 88% in a retrospective study of 40 patients.⁴ Importantly, no cases of new or worsening peripheral thalidomide-induced neuropathy was reported with lenalidomide.⁴ A case of progression to SLE with renal involvement was reported in a patient with isolated CLE after starting lenalidomide.⁵ Recent data did not confirm this finding but suggested that lenalidomide has little or no effect on global SLE activity.

Learning Objectives

- Describe the therapeutic strategy in CLE
- Explain when to prescribe thalidomide and lenalidomide
- Discuss the safety profile of thalidomide and lenalidomide

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OSTEONECROSIS: PREVENTION AND TREATMENT

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Osteonecrosis (ON) is a well-known component of damage accrual in patients with systemic lupus erythematosus (SLE), it frequently causes disability and considerably affects patients’ quality of life.

The increased incidence of ON in SLE patients as compared to the general population, patients with other autoimmune diseases, or diseases requiring high doses of corticosteroids (CS) suggest that the disease itself and/or the underlying genetic background of the patients might dictate the susceptibility in its occurrence.^{1–5} Several modifiable risk factors have been associated with an increased risk of ON, such as alcohol intake, cigarette smoking, high triglyceride levels, and heavy physical work. The use of CS has been recognized as a major risk factor for the development of ON. The average daily dose of CS, its highest dose, and the total cumulative CS dose, as well as the use of pulse therapy, and the presence of Cushingoid appearance have all been associated with ON. The prevalence of ON in patients with SLE ranges between 5–15% but it may be as high as 40% when patients with silent patterns are included. The clinical presentation of ON is variable, being related to the size and location of the affected bone(s). The hip and knee are the most frequently affected joints followed by ankle and shoulder. Multifocal ON has been reported in up to half of patients with SLE.

The early diagnosis of ON is challenging because it frequently occurs silently; there is often a time lag between the development of ON and the onset of symptoms. Preventing ON involves controlling modifiable risk factors. Corticosteroids, if needed, should be prescribed at the lowest possible dose and for the shortest period of time, regardless of patient’s disease manifestations. Anticoagulant therapy, and statins/lipid-lowering drugs, may reduce the incidence of CS-induced ON.

The therapeutic approach depends largely on the joint involved and the extent of the injury. Immobilization has a role for small lesions that will spontaneously heal. Various medications have been used anecdotally with some benefit, including lipid-lowering drugs, anticoagulants, vasodilators, and bisphosphonates. Stem cell treatment of femoral head ON has