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**Learning Objectives**

- Recognize the potential of a universal SLE patient charter to address lupus care
- Identify significant barriers in developing and implementing the charter, including stakeholder consensus and defining key elements
- Appreciate the need to accommodate the heterogeneity of SLE and address barriers to access and equity in care
- Understand the importance of patient education and empowerment and the practical challenges of implementing and enforcing the charter across healthcare systems and jurisdictions

## 03 DISEASE MODIFICATION AND PREVENTION OF DAMAGE

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Although there is currently a need to adopt a treat to target approach in systemic lupus erythematosus (SLE), there are no clear descriptions of disease modifications to guide this approach. Recently van Vollenhoven *et al* reported a conceptual framework for defining disease modification in SLE in three epochs, year 1, years 2–5, and ≥5 years.[1] They suggested criteria to define disease modification for each epoch including minimizing disease activity and slowing or preventing organ damage progression.[1] Failure to achieve these disease modifications results in damage accrual either due to the disease or its treatment. Furthermore, damage accrual predicts increasing damage and mortality.[2 3] Very few of the therapeutic agents currently available to treat SLE have been successful in disease modification in all three epochs either because their therapeutic effect is short lived, or they have not yet been used for ≥5 years or toxicity has precluded long term use.

Four medications merit mention at this time: corticosteroids, antimalarials, belimumab and anifrolumab. Corticosteroids are very effective anti-inflammatory/anti-immunologic agents, but should not be used long term because of their significant toxicities. One should use a dose required to achieve suppression of the acute inflammatory clinical disease BUT strive to wean to a dose of ≤5 mg prednisone by 3 months. Time to achieve the clinical response desired may vary depending on disease manifestations, but rapid weaning should remain the desired target. With complete remission weaning the last 5 mg prednisone is possible, using a slow taper schedule.[4] Antimalarials used early and consistently have been shown to protect against damage accrual and mortality.[2 3] Belimumab, the first biologic developed for the treatment of SLE, was first approved in 2011 and has now been shown to be disease modifying in each of the three epochs with minimal toxicity. Belimumab's long term use has demonstrated a reduction in organ damage progression, a slowed rate of organ damage progression and reduction in the magnitude of year-to-year organ damage.[5] Anifrolumab was approved by the FDA in 2021 but has data for 3 years of follow-up in an extension study that show the initial therapeutic responses persist. There is a lower cumulative corticosteroid dose in patients and there was no safety issue signal.[6]

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**Learning Objectives**

- Describe a definition of disease modification in SLE
- Describe that failure of disease modification results in significant damage
- Explain how managing corticosteroids, antimalarials and two newer biologics may aid damage prevention

## 04 BIOLOGIC DISEASE MODIFYING DRUGS IN SLE

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Although the concept of disease modification is well-established in several immune-mediated diseases, there is no widely accepted definition of disease modification in systemic lupus erythematosus (SLE). A group of international lupus experts recently proposed a framework for the definition of disease modification in SLE that includes minimizing disease activity with the fewest treatment associated toxicities and slowing/preventing organ damage progression.[1] Achieving this goal in SLE will require a multifaceted approach including the use of therapies that target key immunologic pathways important to disease pathogenesis and shared decision making between patients and physicians to encourage therapeutic adherence.

The successful development and approval of two targeted biologic agents, belimumab and anifrolumab, will hopefully accelerate our ability to achieve disease modification in SLE. Both agents target key mechanisms that contribute to ongoing SLE disease activity and damage. Belimumab is a fully human IgG1l antibody against soluble B cell activating factor (BAFF) and anifrolumab is a fully human IgG1k against subunit 1 of the Type I Interferon receptor. In large scale international phase III trials of participants with SLE, both agents reduced disease activity across multiple organ domains and enabled tapering of glucocorticoids.[2–5] The agents differ in kinetics of response, with anifrolumab demonstrating a faster time to response, particularly in people with cutaneous lupus manifestations. The availability of belimumab over the past decade has enabled studies demonstrating reduction in damage

progression with belimumab compared to matched controls receiving conventional therapies. Such long-term studies are not yet available with anifrolumab. In terms of the critical issue of predictors of response, serologic activity predicts response to belimumab and to anifrolumab compared to conventional therapies. As a result of the distinct effects on pathways involved with host defence, the safety profile between belimumab and anifrolumab is quite distinct. Belimumab has consistently demonstrated a reassuring safety profile in comparison to conventional therapies with one exception being the increased risk of depression-related adverse events. In contrast, anifrolumab has been associated with an increased risk of mild-moderate infections, including herpes zoster and influenza. Thus, all patients should be strongly encouraged to receive appropriate vaccinations prior to start of therapy.

The pipeline of therapies for the treatment of SLE is full of promising agents targeting a variety of important immunologic pathways. An ongoing area of active investigation is learning how to select the right therapy for the right patient at the right stage of their disease. In this way, we will continue to make significant progress towards disease modification in SLE.

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### Learning Objectives

- Describe the evolving framework for disease modification in SLE
- Distinguish the mechanisms of action of belimumab and anifrolumab
- Explain the key differences in efficacy and safety between belimumab and anifrolumab

# Lupus academy 12th annual meeting

# Opening session (hybrid)

# Hot topic: new era of treatments for SLE

## 05 APPROVED BIOLOGICS FOR SLE: WHICH TO TRY FIRST AND IN WHICH PATIENTS? – THE CASE FOR BELIMUMAB

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The monoclonal anti-Blys antibody belimumab was approved for the treatment of systemic lupus erythematosus more than ten years ago, based on findings in two large, randomized trials demonstrating clinical efficacy and safety.[1] [2] A further analysis of these two trials clarified that patients with anti-DNA and low complement had the highest likelihood of benefitting from the treatment.[3] In subsequent years, many additional studies have further defined the efficacy of belimumab: it was shown to be effective in a subcutaneous formulation as well as intravenously, to reduce flares, maintain responses for many years, allow glucocorticoid dose reductions, reduce the accrual of damage, and last but not least, as an add-on to conventional treatment, to improve the renal response in patients with lupus nephritis – leading to approval for this indication as well.[4–6] Belimumab has an excellent safety profile, and is associated with slight increases in infections and an increase in certain psychiatric adverse events.

For the clinician, the main reasons to consider belimumab are:

- Proven efficacy both for general lupus and for lupus nephritis
- Biomarkers for higher likelihood of response
- More than a decade of experience
- Safety
- Flexibility in administration: subcutaneous or intravenous

As with all treatments available today, response in the individual patient is impossible to predict. Therefore, a trial of belimumab may reasonably be considered for any patients who are not responding sufficiently to conventional therapy.

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### Learning Objectives

- Describe the demonstrated efficacy and safety of belimumab in the treatment of SLE
- Explain the established biomarker combination anti-DNA and low complement for identifying patients at higher likelihood to benefit from belimumab
- Discuss the evidence base for use of belimumab in practice, both for general SLE and lupus nephritis
- Recognize the features of belimumab that may, in practice, help choose this therapeutic option for the patient