06 APPROVED BIOLOGICS FOR SLE: WHICH TO TRY FIRST AND IN WHICH PATIENTS? – THE CASE FOR ANIFROLUMAB

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Unlike many other autoimmune diseases, in systemic lupus erythematosus (SLE) there are only two targeted biological therapies approved to choose between, namely belimumab and anifrolumab. Each is approved for the treatment of moderate to severe active SLE, and the 2023 European Alliance of Associations for Rheumatology (EULAR), guidelines recommend consideration of biological therapy in first line treatment. But how are we to choose which one to use first in each patient? Assuming equal access and cost, our decisions are based largely on clinical trial and long-term extension data, with some additional information from investigator-initiated studies.

The case for using anifrolumab as first line biologic in SLE rests on several points of difference from belimumab. First, the available data suggest the potential for a fast onset of action for anifrolumab, with pooled data from the phase 3 trials showing separation between placebo and anifrolumab as early as 4 weeks in some domains.[1] Secondly, anifrolumab was efficacious in mucocutaneous, musculoskeletal, and haematological domains, suggesting the potential for broad effects in SLE; importantly, efficacy in lupus nephritis has not yet been demonstrated.[1] Thirdly, glucocorticoid sparing effects of anifrolumab were robustly demonstrated.[2] Fourthly, anifrolumab is the only drug shown to increase attainment of remission in SLE; increased LLDAS was also demonstrated.[3] Finally, the long-term extension study of anifrolumab, the first in SLE to include a long term placebo-control group, showed good tolerance, low rates of serious adverse events, and prolonged reduction in disease activity and glucocorticoid use; prolonged attainment of LLDAS has been reported in abstract form.[4]

Together these data suggest that anifrolumab treatment can induce broad, deep, and lasting effects on SLE disease activity and achieve steroid sparing.

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Learning Objectives

- Increased understanding of the efficacy and safety data for anifrolumab in SLE clinical trials and long-term extension
- Increased awareness of key points of difference between anifrolumab and belimumab, potentially including onset of action and attainment of remission

Keynotes

07 NEW (ACR/EULAR) ANTIPHOSPHOLIPID SYNDROME CLASSIFICATION CRITERIA

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Until recently, classification of antiphospholipid syndrome (APS) for clinical trials and studies was based on clinical and laboratory criteria described in the Sapporo classification criteria published in 1999,[1] and revised in 2006.[2]

Given the limitations of the Sapporo criteria,[3] and new data-driven and expert-based methodology available to develop classification criteria,[4] an international effort jointly supported by the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR), was initiated. The goal was to develop a new APS classification system, based on a more modern disease understanding, allowing for the weighting of individual criterion, and demonstrating excellent operating characteristics with the highest possible specificity. This international multidisciplinary effort included four phases: (1) criteria generation; (2) criteria reduction; (3) criteria definition, further reduction, and weighting via consensus-based multi-criteria decision analysis, and threshold identification; and (4) validation using independent adjudicators' consensus as the 'gold standard'.[3 5]

Novel clinical features of the new criteria include: (a) risk stratification of macrovascular events by traditional thrombosis risk factors; (b) well-defined microvascular domain items; (c) re-defined pregnancy morbidity definitions; and (d) the addition of cardiac valve disease and thrombocytopenia, to capture and quantify the magnitude of heterogeneous aPL manifestations. Novel laboratory features include: (a) quantifying single-, double-, and triple- antiphospholipid antibody (aPL) positivity based on different domains and weights; (b) separating anticardiolipin antibody (aCL)/anti-β_2-Glycoprotein-I ($a\beta_2$GPI) IgG and IgM isotypes; and (c) defining two levels of aCL/$a\beta_2$GPI positivity that will be interpreted as clinically relevant by most investigators.[5]

In summary, the new (ACR/EULAR) APS classification criteria incorporate heterogenous aPL-related clinical and laboratory manifestations into a hierarchically clustered, weighted, and risk-stratified criteria reflecting current thinking about APS, providing high specificity and an improved foundation for APS research.

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