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

Eric Morand. *Monash University, Melbourne, Australia*

10.1136/lupus-2023-la.6

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.

REFERENCES

1. Morand EF, *et al.* Efficacy of anifrolumab across organ domains in patients with moderate-to-severe systemic lupus erythematosus: a post-hoc analysis of pooled data from the TULIP-1 and TULIP-2 trials. *Lancet Rheumatol*. 2022;**4**(4): E282-E292. doi: 10.1016/S2665-9913(21)00317-9.
2. Bruce IN, *et al.* Sustained glucocorticoid tapering in the phase 3 trials of anifrolumab: a post hoc analysis of the TULIP-1 and TULIP-2 trials. *Rheumatology (Oxford)*. 2023 Apr 3;**62**(4):1526–1534. doi: 10.1093/rheumatology/keac491.
3. Morand EF, *et al*. Lupus low disease activity state attainment in the phase 3 TULIP trials of anifrolumab in active systemic lupus erythematosus. *Ann Rheum Dis*. 2023 May;**82**(5):639–645. doi: 10.1136/ard-2022-222748.
4. Kalunian KC, *et al*. A randomized, placebo-controlled phase iii extension trial of the long-term safety and tolerability of anifrolumab in active systemic lupus erythematosus. *Arthritis Rheumatol*. 2023 Feb;**75**(2):253–265. doi: 10.1002/art.42392.

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

Doruk Erkan. *Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, 10021*

10.1136/lupus-2023-la.7

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.

REFERENCES

1. Wilson WA, *et al*. International consensus statement on preliminary classification criteria for definite antiphospholipid syndrome: report of an international workshop. *Arthritis Rheum*. 1999 Jul;**42**(7):1309–11. doi: 10.1002/1529-0131(199907)42:7<1309::AID-ANR1>3.0.CO;2-F.
2. Miyakis S, *et al*. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006 Feb;**4**(2):295–306. doi: 10.1111/j.1538-7836.2006.01753.x.
3. Barbhaiya M, *et al*. Development of a new international antiphospholipid syndrome classification criteria phase I/II report: generation and reduction of candidate criteria. *Arthritis Care Res (Hoboken)*. 2021 Oct;**73**(10):1490–1501. doi: 10.1002/acr.24520. Epub 2021 Sep 2.
4. Johnson SR, *et al*. Classification criteria in rheumatic diseases: a review of methodologic properties. *Arthritis Rheum*. 2007 Oct 15;**57**(7):1119–33. doi: 10.1002/art.23018. Erratum in: *Arthritis Rheum*. 2007 Dec 15;**57**(8):1574.
5. Barbhaiya M, *et al.* 2023 ACR/EULAR antiphospholipid syndrome classification criteria. *Arthritis Rheumtol* 2023 (in press).

Learning Objectives

- Discuss the merits of the new APS classification system
- Describe the presentation of heterogenous aPL-related clinical and laboratory manifestations and how these reflect current thinking about APS
- Explain how the criteria provide an improved foundation for APS research

08 DISRUPTION POINTS IN LUPUS PATIENT PATHWAYS

Laurent Arnaud. *Department of Rheumatology, National Reference Center for Autoimmune Diseases (RESO), Hôpitaux Universitaires de Strasbourg, France*

10.1136/lupus-2023-la.8

A **patient pathway** is the patient experience from the first symptom through the initial referral for diagnosis, treatment and follow-up, and includes diverse aspects of disease management, such as holistic support and prevention of complications. Among the most significant **challenges in systemic lupus erythematosus (SLE)**[1] are the excessive **diagnosis delay** and the **lack of coordinated care**. At our national reference center in Strasbourg (France), we have conducted a series of focus groups with healthcare professionals and SLE patients. Based on the collected data, the most impactful disruption points in SLE patient pathways were identified.[2] A novel framework to improve individual patient pathways in SLE was developed, discussed and validated during a consensus meeting with representative stakeholders. Six main disruptions in optimal SLE patient pathways were identified: (1) appropriate and timely **referral strategy for SLE** diagnosis; (2) the **need for a dedicated consultation** during which the diagnosis of SLE would be communicated, and following which clarifications and psychological support offered; (3) individualized patient pathways with **coordinated care** based on organ involvement, disease severity and patient preference; (4) improved **therapeutic patient education**; (5) **prevention of complications** such as infections, osteoporosis and cancer; (6) and additional **patient support. These disruption points are valuable knowledge, which may be used to improve individual patient pathways in SLE.** These data may be of valuable interest to patients with SLE, their physicians, health organizations and policy makers.

REFERENCES

1. Felten R, *et al*. 10 most important contemporary challenges in the management of SLE. *Lupus Sci Med*. 2019 Jan 10;**6**(1):e000303. doi: 10.1136/lupus-2018-000303.
2. Schlencker A, *et al*. Improving patient pathways for systemic lupus erythematosus: a multistakeholder pathway optimisation study. *Lupus Sci Med*. 2022 May;**9**(1): e000700. doi: 10.1136/lupus-2022-000700.

Learning Objectives

- Explain the key concept of patient pathways
- Describe how patient pathways can be mapped in systemic lupus
- Identify the main disruption points in lupus patient pathways
- Describe how to improve lupus patient pathways

Plenary I: infections in SLE

09 HERPES ZOSTER PREVALENCE AND RECOMMENDATIONS FROM CLINICAL TRIAL SAFETY DATA

Richard Furie. *Zucker School of Medicine at Hofstra/Northwell, New York, USA*

10.1136/lupus-2023-la.9

The importance of interferons as a component of human antiviral host defense was first suggested by Isaacs and Lindenmann in 1957.[1] It was not until the 1970s that a pathogenic role of interferons in systemic lupus erythematosus (SLE) was suspected.[2] While it was recognized long ago that patients with systemic lupus were at increased risk of Herpes zoster reactivation (shingles), it was the phase 2 studies of sifalimumab and anifrolumab that highlighted the importance of this complication.[3 4] Given the mechanism of action of sifalimumab and anifrolumab, namely their ability to dampen type I interferon pathway activation, it was no surprise that the incidence of Herpes zoster was as much as 8-fold higher in the treatment arms than in the placebo groups of the phase 2 and 3 SLE trials.[4–6] In a post-hoc analysis of the phase II and the two phase III trials of anifrolumab, Tummala *et al* reported exposure-adjusted incidence rates (EAIR) per 100 patient-years of 6.9 and 1.5 in the 300 mg anifrolumab and placebo groups, respectively.[7] Even higher frequencies of Herpes zoster were observed in the phase II anifrolumab trial in lupus nephritis with frequencies over the course of the study of 13.7% and 20.0% in the two treatment groups compared to 8.2% in the placebo group.[8]

Other drugs in development in SLE, such as litifilimab, daxdilimab, and deucravacitinib, also impact type I interferons. However, Herpes zoster was infrequent in these studies suggesting that the degree of inhibition of type I interferon pathway activation correlates with the risk of Herpes zoster. Despite a low basal incidence rate of Herpes zoster, vaccination with Zoster Vaccine Recombinant, Adjuvanted, is now recommended for adults aged ≥18 years who are or will be at increased risk for shingles because of immunodeficiency or immunosuppression caused by their underlying disease or therapy.

REFERENCES

1. Isaacs A, Lindenmann J. Proceedings of the Royal Society of London. Series B, Biological Sciences 1957.
2. Hooks JJ, *et al*. Immune interferon in the circulation of patients with autoimmune disease. *N Engl J Med*. 1979 Jul 5;**301**(1):5–8. doi: 10.1056/NEJM197907053010102.
3. Khamashta M, *et al*. Sifalimumab, an anti-interferon-α monoclonal antibody, in moderate to severe systemic lupus erythematosus: a randomised, double-blind, placebo-controlled study. *Ann Rheum Dis*. 2016 Nov;**75**(11):1909–1916. doi: 10.1136/annrheumdis-2015-208562.
4. Furie R, *et al*. Anifrolumab, an anti-Interferon-α receptor monoclonal antibody, in moderate-to-severe systemic lupus erythematosus. *Arthritis Rheumatol*. 2017 Feb;**69**(2):376–386. doi: 10.1002/art.39962.
5. Furie RA, *et al*. Type I interferon inhibitor anifrolumab in active systemic lupus erythematosus (TULIP-1): a randomised, controlled, phase 3 trial. *Lancet Rheumatol*. 2019, **1**(4), e208–e219.
6. Morand EF, *et al*. Trial of anifrolumab in active systemic lupus erythematosus. *N Engl J Med*. 2020 Jan 16;**382**(3):211–221. doi: 10.1056/NEJMoa1912196.
7. Tummala R, *et al*. Safety profile of anifrolumab in patients with active SLE: an integrated analysis of phase II and III trials. *Lupus Sci Med*. 2021 Feb;**8**(1): e000464. doi: 10.1136/lupus-2020-000464.