De novo lupus nephritis following the introduction of Belimumab

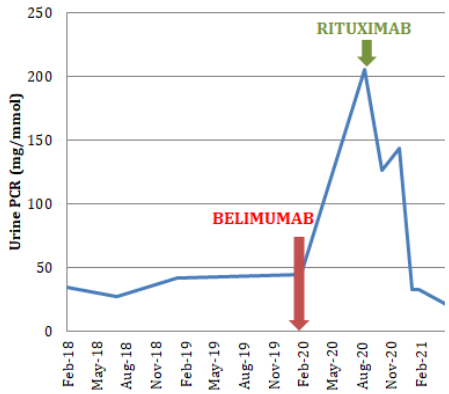
Mark Ford [1], Jonathan Pinnell [1], Sofia Tosounidou [1]
1. Rheumatology, Birmingham City Hospital, Birmingham, United Kingdom

Sandwell and West Birmingham Hospitals NHS Trust

We present three patients with a background of systemic lupus erythematosus (SLE) who developed lupus nephritis (LN) shortly after commencing Belimumab. None of the patients had pre-existing renal disease.

Case 1: 59 year old Afro-Caribbean female

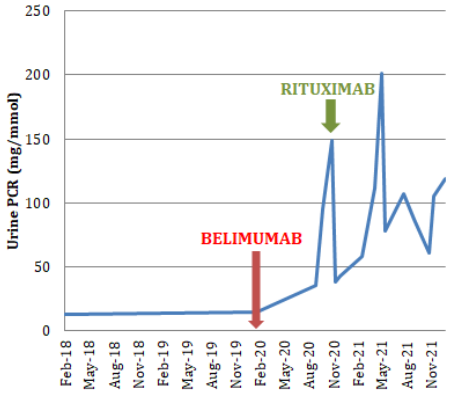
Clinical diagnosis	Presenting serology
Neuropsychiatric	Anti-nuclear antibody (ANA) Anti-dsDNA Anti-U1-RNP Anti-Sm Anti- SS-A/Ro
SLE treatment prior to Belimumab	Belimumab started Feb 2020
Hydroxychloroquine Mycophenolate Azathioprine Cyclophosphamide	Arthritis, Serositis, Mucocutaneous Raised anti-dsDNA Low complement SLEDAI 13



Biopsy: Class IV and V Lupus Nephritis

Case 2: 37 year old Afro-Caribbean female

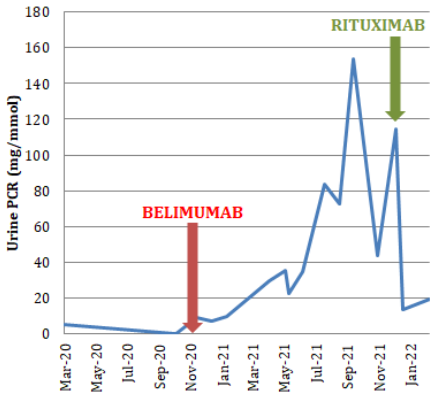
Clinical diagnosis	Presenting serology
Arthritis Mucocutaneous Haematological	Anti-nuclear antibody (ANA) Anti-dsDNA Anti-U1-RNP Anti-Sm Anti- SS-A/Ro
SLE treatment prior to Belimumab	Belimumab started Feb 2020
Hydroxychloroquine Mycophenolate Azathioprine	Arthritis, Mucocutaneous Raised anti-dsDNA Low complement SLEDAI 12



Biopsy: Class III Lupus Nephritis

Case 3: 22 year old Afro-Caribbean female

Clinical diagnosis	Presenting serology
Chilblain vasculitis Arthralgia	Anti-nuclear antibody (ANA) Anti-dsDNA Anti-U1-RNP Anti-Sm Anti- SS-A/Ro
SLE treatment prior to Belimumab	Belimumab started Nov 2020
Hydroxychloroquine Methotrexate	Arthritis, Mucocutaneous Raised anti-dsDNA Low complement SLEDAI 16



Biopsy: Class V Lupus Nephritis

Discussion

Belimumab inhibits the activity of the soluble cytokine BLyS (B lymphocyte stimulator) and is currently recommended for use in moderate refractory SLE. Following results of a recent randomised controlled trial, BLISS LN, Belimumab has been approved in LN following induction with Mycophenolate or Cyclophosphamide (1). This study showed no benefits of using Belimumab in pure Class V LN and in patients of African ancestry.

Case reports that Belimumab may be associated with the development of new onset LN are concerning and our cases add to these (2,3). A recent prospective observational study also reported significantly increased rates of new LN in patients receiving Belimumab in addition to standard care compared to those receiving standard treatment (4). A causative association between Belimumab and the development of de novo LN is not established and Belimumab may not be strong enough to prevent LN in susceptible patients. Current evidence supports a role for Belimumab as a maintenance therapy in LN, but not for induction.

In these cases, belimumab did not protect from de novo LN. Despite its role, **we recommend caution when using Belimumab and we recommend the active monitoring of renal parameters during treatment.**

References
(1) Furie R, Rovin BH, Houssiau F, et al. Two-year, randomized, controlled trial of belimumab in lupus nephritis. N Engl J Med. 2020; 383(12):1117-28. (2) Sjöwall C, Cöster L. Belimumab may not prevent lupus nephritis in serologically active patients with ongoing non-renal disease activity. Scand J Rheumatol. 2014; 43(5):428-30. (3) Staveri C, Karokis D, Liossis SN. New onset of lupus nephritis in two patients with SLE shortly after initiation of treatment with belimumab. Semin Arthritis Rheum. 2017; 46(6):788-790. (4) Parodis I, Vital EM, Hassan SU, et al. De novo lupus nephritis during treatment with belimumab. Rheumatology. 2020; keaa796