Successful treatment of active systemic lupus erythematosus with belimumab

Gary Reynolds [1], Bridget Griffiths[1]

(1) Freeman Hospital, Newcastle-Upon-Tyne

Background:

Belimumab is a monoclonal antibody targeting soluble B-cell activating factor (BAFF)/B-lymphocyte stimulator (BLyS). In June 2016 NICE published guidance (TA397) supporting the use of belimumab as add-on therapy in patients with active, autoantibody-positive systemic lupus erythematosus (SLE) following results from two phase III trials in which it demonstrated efficacy[1,2]. However, the clinical effect seen was less impressive than in trials of biologics in other diseases[3]. In the BLISS-76 trial the SLE responder index was 33.5% for placebo vs 43.2% for belimumab. This relatively subtle difference may reflect the heterogeneity of the disease and the limitations of current outcome measures to adequately capture clinical improvements. In their decision NICE, while referencing the high incremental cost effectiveness ratio of belimumab (£64,410), recommended ongoing data collection to better characterise which patients may benefit from treatment. To highlight the importance of this process and to counter some of the pessimism around the use of biologics in SLE we present the case of a patient under our care with active SLE who had failed to respond to standard therapy but had an excellent response to belimumab.

Case report:

We present the case of a 41 year old woman with SLE who initially presented in 2001 with mouth ulcers, arthralgia, malar rash, bullous LE, lymphadenopathy, significant proteinuria (1.9g/day), an ANA titre of 1:640 and dsDNA 300IU/ml (normal range <4IU/ml). A renal biopsy showed class IV lupus nephritis and, following induction therapy with cyclophosphamide and rituximab, she achieved good disease control and was maintained on azathioprine alone. In 2013 her disease deteriorated with increasing arthralgia, mouth ulcers, malar rash and worsening proteinuria. This time treatment with rituximab produced only a partial response and her prednisolone requirements increased (6mg OD to 20mg OD). In 2016 rituximab treatment was stopped after she developed severe angioedema during her infusion. In 2017 following MDT discussion, belimumab 10mg/kg was added to methotrexate, hydroxychloroquine and prednisolone. Following three months of treatment this has had a positive effect with reduction in SLEDAI score from 14 to 6, BILAG-2004 disease activity score reduced to 2Cs, a reduction in dsDNA (180IU/ml to 114IU/ml), resolution of proteinuria, improvement in complement levels and a corticosteroid-sparing effect.

Conclusion:

The heterogeneity of SLE makes clinical trials difficult and responses less impressive than in other rheumatological diseases. Furthermore it may obscure a subpopulation who would benefit and even the rejection of potentially effective treatments.

References:

1 Navarra S V, Guzmán RM, Gallacher AE, *et al.* Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;**377**:721–31.

2 Furie R, Petri M, Zamani O, *et al.* A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. *Arthritis Rheum* 2011;**63**:3918–30.

3 Aytan J, Bukhari MAS. Use of biologics in SLE: a review of the evidence from a clinical perspective. *Rheumatology (Oxford)* 2016;**55**:775–9.