

The potential overlapping populations for treatment with belimumab and rituximab using current NHS England and National Institute for Clinical Excellence Guidelines in England and Wales

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Sir,

Belimumab, an anti B Lymphocyte Stimulator (BLyS) monoclonal antibody, has proven efficacy for the treatment of SLE [1, 2]. The European licence is based on post hoc analysis of randomised trials showing that predictors of better response include elevated antibodies to double-stranded DNA (dsDNA), low complement and higher SELENA-SLEDAI scores [3, 4]. Patients with severe active lupus nephritis or central nervous system lupus were excluded from these trials and do not form part of the patient population assessed as part of the marketing authorisation [1,2]. In June 2016 The National Institute for Clinical Excellence (NICE) recommended the use of belimumab as add-on therapy for patients with active auto-antibody positive SLE, who have serological activity (defined as positive anti-dsDNA and low complement) and a SELENA-SLEDAI score ≥ 10 , despite standard treatment [5].

Since 2010 patients commencing biologic therapy for SLE in the UK have been registered in the British Isles Lupus Assessment Group Biologics Register (BILAG-BR), the initial results of which are presented elsewhere in this journal (ref).

We sought to investigate the number of patients and the clinical characteristics of patients treated with a biologic in the BILAG-BR who would potentially have been eligible for belimumab using this guidance[5]

Of the 270 patients registered for biologic use to Nov 2015, 82 (33%) had evidence of both low complement and elevated anti-dsDNA antibodies at enrolment. Of these, 46 (56.1%) patients had a BILAG A in the renal (n=29) or neuropsychiatric system (n=17) making them ineligible for therapy. An additional 4 (4.9%) had a SLEDAI score < 10 . Thus from 2010-2015 32 patients (13%) enrolled in the BILAG-BR would have been eligible for belimumab.

Amongst these 32 patients the BILAG mucocutaneous (MUC) and musculoskeletal (MSK) systems had the most frequent A (MSK=7, MUC=6) and B scores (MSK=11, MUC=8) (Figure 1). 17 (53%) patients had a history of renal disease. The median (IQR) baseline SLEDAI was 12.5 (12 -15.75).

Regarding medication use 28 (87.5%) and 27 (84.4%) patients were on an anti-malarial or oral prednisolone respectively. The median (IQR) baseline prednisolone dose was 15mg (10mg-20mg). The median (IQR) number of prior standard immunosuppressant agents was 2 (1-3). Mycophenolate mofetil was the most frequently prescribed therapy (n=23) followed by azathioprine (n=15) and cyclophosphamide (n=11).

When we assessed response to RTX in this cohort who would now be eligible for belimumab, the median (IQR) SLEDAI improved from 12.5 (12-15.75) at baseline to 4 (0-8) at 6 months ($p < 0.0001$). The total number of BILAG A scores reduced from 16 to 2 and B scores from 33 to 9. A corresponding reduction in corticosteroid dose was also noted from 15mg (10mg-20mg) to 6mg (5mg-10mg) at 6 months ($p < 0.001$).

Improved access to biologic therapies will enhance physician's ability to control disease activity whilst facilitating corticosteroid tapering and preventing damage [6]. Given the response rate to most biologic therapies in SLE is approximately 50%, the addition of belimumab to UK physicians' armamentarium is to be welcomed, especially for those patients who have not responded to conventional therapy. Our data will help inform clinicians and planners about the expected rates of usage and the clinical characteristics of patients requiring belimumab in the UK. Mucocutaneous and musculoskeletal were the systems most likely to have active disease requiring belimumab. A history of renal involvement was however noted in approximately 50% of cases, emphasising that previous

renal involvement does not exclude patients from belimumab, indeed both the BLISS-52 and 76 trials included patients with active renal disease and a post hoc analysis suggested favourable renal outcomes in this population [7]. Our data also suggests that RTX remains a realistic therapeutic option for patients who fail to respond to belimumab.

In summary, between 2010 and 2015 13% of patients who commenced biologic therapy for SLE in the UK would have been eligible for belimumab. Access to such treatment offers the potential of improved disease control, corticosteroid dose reduction and improved long term outcomes for these patients.

Key messages

13% of UK SLE patients with disease requiring biologic therapy are eligible for belimumab.

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BILAG-BR collaborators – to be indexed by The National Library of Medicine (NLM)

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Conflict of Interest Statement

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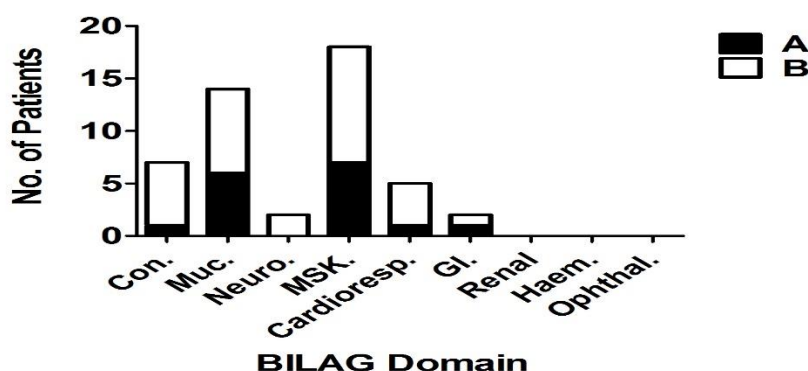


Figure 1. BILAG-2004 organ systems with active disease in SLE patients eligible for belimumab. (A) Number of individual patients scoring either an A or B on BILAG-2004 scoring system across the systems assessed