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

Rheumatology key message

- Of UK SLE patients with disease requiring biologic therapy, 13% are eligible for belimumab.

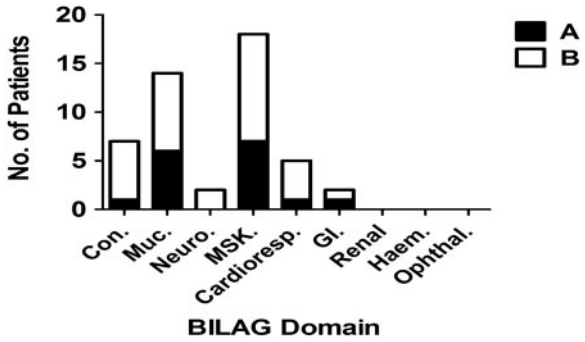
SIR, Belimumab, an anti-B lymphocyte stimulator mAb, has proven efficacy for the treatment of SLE [1, 2]. The European licence is based on *post hoc* analysis of randomized trials showing that predictors of better response include elevated antibodies to dsDNA, low complement and higher Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) scores [3, 4]. Patients with severe active LN or CNS lupus were excluded from these trials and do not form part of the patient population assessed as part of the marketing authorization [1, 2]. In June 2016, The National Institute for Health and Care Excellence 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 $\geqslant 10$, despite standard treatment [5].

Since 2010, patients commencing biologic therapy for SLE in the UK have been registered in the BILAG-BR, the initial results of which are presented in a paper currently under review (McCarthy *et al.*, manuscript under review). 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 November 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 four (4.9%) had a SLEDAI score <10. Thus, from 2010 to 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; Fig. 1). Seventeen (53%) patients had a history of renal disease. The median [interquartile range (IQR)] baseline SLEDAI was 12.5 (12–15.75).

FIG. 1 BILAG-2004 organ systems with active disease in SLE patients eligible for belimumab



Number of individual patients scoring either an A or B on BILAG-2004 scoring system across the systems assessed.

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 15 mg (10–20 mg). The median (IQR) number of prior standard immunosupressant agents was 2 (1–3). MMF was the most frequently prescribed therapy (n = 23), followed by AZA (n = 15) and CYC (n = 11).

When we assessed response to Rituximab (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 CS dose was also noted from 15 mg (10–20 mg) to 6 mg (5–10 mg) at 6 months ($P < 0.001$).

Improved access to biologic therapies will enhance physicians' ability to control disease activity while facilitating CS tapering and preventing damage [6]. Given that the response rate to most biologic therapies in SLE is ~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. MUC and MSK were the systems most likely to have active disease requiring belimumab. A history of renal involvement was, however, noted in ~50% of cases, emphasizing that previous renal involvement does not exclude patients from belimumab; indeed, both the Belimumab in Subjects With Systemic Lupus Erythematosus (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 suggest 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, CS dose reduction and improved long-term outcomes for these patients.

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Statin-associated autoimmune myopathy

Rheumatology key message

- Statin-associated autoimmune myopathy is a rare complication of statins that can involve oropharyngeal and respiratory muscles.

Sir, Statins are widely used lipid-lowering drugs with protective cardiovascular properties. Well-established musculoskeletal side effects include elevations of creatinine kinase (CK), myalgias and rhabdomyolysis. Statin-associated autoimmune myopathy (SAAM) is an extremely rare and serious complication of therapy characterized by proximal symmetric muscle weakness, elevation of CK levels and antibodies to 3-hydroxy-3-methylglutaryl coenzyme A (HMGCR). Symptoms typically persist or worsen after discontinuation of the offending statin. Incidence is estimated at two cases per million per year. Immunosuppressive therapy is utilized to treat SAAM [1–3]. We report a severe case of SAAM with respiratory and oropharyngeal muscle weakness with patient demise despite immunosuppressive therapy.

A 71-year-old male presented with 4 weeks of progressive proximal muscle weakness. He was started on atorvastatin for hyperlipidaemia 2 months prior but discontinued the statin after 1 month prior to presentation when he began to notice muscle weakness. The weakness involved the proximal upper and proximal lower extremities bilaterally. His past medical history was also significant for well-controlled diabetes mellitus and hypertension. He was a non-smoker, consumed alcohol socially and did not use any illicit drugs. On examination his skin revealed no rashes and lungs were clear to auscultation. Muscle strength was 3/5 in bilateral proximal upper and lower extremities. Laboratory values were remarkable for a peak CK of 9648 U/l (normal 25–250 U/l), peak aspartate aminotransferase of 706 U/l (normal 10–42 U/l) and alanine amiontransferase of 742 U/l (normal 7–55 U/l). ANA, anti-DNA, anti-Sm, anti-RNP, anti-Jo-1 and anti-signal recognition particle antibodies were negative. IgG antibodies to HMGCR were elevated at >200 U (normal 0–19) using ELISA. Electromyography demonstrated increased insertional activity with myotonic discharges, sharp waves and fibrillations. Muscle biopsy showed neurogenic and necrotizing myopathy without associated inflammatory infiltrates (Fig. 1). A diagnosis of SAAM was established on the basis of clinical symptoms, muscle biopsy findings