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Steroid-sparing effect of belimumab: results from a retrospective observational study of real-world data

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ABSTRACT

Objective Comparison of oral corticosteroid (OCS) use in patients with SLE in a US rheumatology network pre- and post-belimumab initiation.

Methods This retrospective cohort study (GSK Study 214140) used data from the Patient-Important Outcomes Data Repository (PIONEER)-Rheumatology database. Eligible adults with SLE initiated belimumab between 1 January 2012 and 30 June 2021, and had available data for >180 days pre- and >360 days post-belimumab initiation. The index was the date of belimumab initiation. Changes in OCS use were measured by: proportion of patients receiving OCS; mean total OCS dose/patient; mean total number of OCS days supplied/patient; mean daily OCS dose for days supplied/patient; the proportion of patients with OCS doses of ≤5 mg/day and ≤7.5 mg/day for days supplied. These changes were assessed between period (P)1 (6 months pre-index) and P2 (first 6 months post-index) and P3 (second 6 months post-index) in patients with OCS use in P1 who persisted with belimumab at each assessed period.

Results Overall, 608 patients received belimumab for 180 days (full analysis set (FAS)) and 492 for 360 days. Most patients were female (92.8%); 70.4% had moderate SLE. In P1, 56.3% of FAS patients and 54.5% of patients who persisted with belimumab for 360 days received OCS.

Among patients receiving OCS in P1, significantly fewer patients received OCS in P2 (78.4%) and P3 (64.9%) vs P1 (100.0%). Significant reductions from P1 were observed in P2 and P3 in the mean total OCS dose/patient, the mean OCS daily dose for days supplied and the proportions of patients with OCS dose of ≤5 mg/day and ≤7.5 mg/day, and the mean total OCS days supplied/patient in P3 only.

Conclusions This analysis showed significant reductions in OCS dose and use in patients with SLE who persisted with belimumab, providing more real-world evidence for belimumab's steroid-sparing effect.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The beneficial effect of belimumab on the reduction of oral corticosteroid use (OCS) in patients with SLE was previously shown in clinical trials and real-world analyses.

WHAT THIS STUDY ADDS

⇒ This study brings an additional perspective from a large real-world US database of community rheumatologists on OCS use patterns before and during belimumab treatment.

⇒ Patients initiating belimumab under the care of US rheumatologists significantly decreased use of OCS, with greater reductions observed with increasing duration of belimumab administration.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study suggests that increased adoption of belimumab among rheumatologists may be a step forward in reducing the deleterious effects of OCS use in patients with SLE.

INTRODUCTION

SLE is a chronic, inflammatory, autoimmune disease characterised by periods of flares and remission.[1] In addition to antimalarials, corticosteroids and non-targeted immunosuppressants are the mainstay of therapy for SLE.[2] However, the prolonged use of corticosteroids is associated with an increased risk of organ damage and early mortality.[3 4] Even short-term use of corticosteroids has been associated with adverse events (AEs).[5] Previous studies in patients with SLE showed that a prolonged, cumulative corticosteroid exposure was linked to the development of AEs such as infections, hypertension and type 2 diabetes mellitus, as well as more serious damage, including osteoporotic fractures and avascular necrosis.[3 6–8] Therefore, minimising the use of corticosteroids is among SLE treatment goals.

Furthermore, previous claims-based studies in patients with SLE have demonstrated that patients with prevalent corticosteroid use, in addition to having greater odds of experiencing corticosteroid-related AEs, have significantly higher healthcare costs and healthcare resource utilisation (HCRU) compared with patients receiving lower doses or those with no corticosteroid use.[9 10] It has been reported that these health and economic burdens increase with increasing duration of oral corticosteroid (OCS) use and dose.[9]

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Belimumab, a recombinant human immunoglobulin G1λ monoclonal antibody that specifically targets and inhibits the biological activity of soluble B-lymphocyte stimulator (BLyS), is approved as an add-on to standard therapy for the treatment of SLE and lupus nephritis (LN).[11 12] In a large, pooled analysis of five randomised, placebo-controlled clinical trials, as well as pooled analysis of BLISS-52 and BLISS-76 clinical trials, belimumab-treated patients had significantly greater corticosteroid dose reductions compared with placebo-treated patients.[13 14] A corticosteroid-sparing effect of belimumab was also shown in a post hoc pooled analysis of six real-world, retrospective OBSErve studies.[15] In their systematic review and meta-analysis, Huang *et al* demonstrated the overall effectiveness of belimumab in SLE in the real-world context, including a reduction of corticosteroid dose.[16]

While previous research has evaluated data from randomised trials, retrospective claims and prospective chart reviews, the present study is unique in that it brings the perspective of community rheumatologists by leveraging real-world data from a large US rheumatology network. It seeks to evaluate patterns of OCS use before and during treatment with belimumab.

METHODS

Study design

This was a retrospective cohort study (GSK Study 214140) that used data from the Patient-Important Outcomes Data Repository (PIONEER)-Rheumatology database.[17] The database is fully de-identified and Health Insurance Portability and Accountability Act–compliant, and contains the electronic medical data on patient diagnoses, prescription, laboratory, procedure, infusion and medical claims generated in care of patients in the American Rheumatology Network (ARN). The ARN network has over 38 community-based physician practices with >300 providers in 82 locations across 22 US states and over 300 000 patients.

The data were extracted during the observation period from 1 July 2011 to 25 June 2022. The index was defined as the date of first belimumab initiation, occurring between 1 January 2012 and 30 June 2021.

The study comprised three periods: period 1 (baseline) was defined as 180 days pre-index (not including index); period 2 was defined as the first 6 months post-index (0–180 days); and period 3 was defined as the second 6 months post-index (181–360 days).

Study population

The current analysis included patients in the care of ARN who met the following eligibility criteria (full analysis set (FAS)): patients ≥18 years of age at index who were diagnosed with SLE at any time pre-index, with ≥1 diagnosis code of SLE (International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM): 710.0x; ICD-10-CM: M32, M32.1x, M32.8, M32.9) recorded on two different occasions ≥30 days apart, who initiated belimumab between 1 January 2012 and 30 June 2021, and had available data >180 days pre- and >360 days post-belimumab initiation. Patients were excluded if they discontinued belimumab in the first 6 months after belimumab initiation, had a diagnosis of drug-induced lupus at any point during the observation period or if there was a lack of OCS prescription data available >180 days pre-index.

As inflammatory and connective tissue disorder comorbidities are common in patients with SLE in real-world practice, patients with Sjögren's syndrome, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, osteoarthritis, osteoporosis/osteopenia or other similar disorders were included in the study analysis.

Eligible patients were stratified into the following subsets: patients who were on OCS during period 1 and patients who continued/increased or decreased OCS during periods 2 and 3.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination of this research.

Assessments

The primary objective was to evaluate the change in OCS use from period 1 to periods 2 and 3, as measured by: proportion of patients receiving any OCS, mean total prednisone-equivalent dose per patient, mean total number of OCS days supplied per patient, mean daily OCS dose for days supplied per patient among those who had an OCS prescription in the period and proportion of patients with OCS of ≤5 mg/day and ≤7.5 mg/day for days supplied.

The secondary objective was to describe laboratory measures (complement component (C)3 and C4) and clinical characteristics (SLE Disease Activity Index (SLEDAI)) at period 1, period 2 and period 3.

Statistical analysis

Changes in OCS use were assessed between period 1 and periods 2 and 3 in patients with OCS use in period 1 who persisted on belimumab therapy at each assessed period. P values were generated for comparisons of continuous variables via the Wilcoxon signed-rank test and for categorical variables using McNemar's χ^2 test (or Fisher's exact test for cell sizes of five or less).

Changes in OCS use were also evaluated in the overall population (ie, FAS) as an exploratory analysis. When summarising OCS dose values, measures that involved 'days supplied' were limited to patients receiving OCS in the period.

RESULTS

Patient baseline characteristics

Overall, 608 patients met the eligibility criteria and were included in the FAS population. The majority of patients were female (92.8%) and white (61.3%; table 1). During period 1, most patients had moderate SLE disease severity

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Table 1 Baseline patient characteristics during period 1 (pre-index)

	FAS, n=608
Female, n (%)	564 (92.8)
Ethnicity, n (%)	
Hispanic or Latino	47 (7.7)
Not Hispanic or Latino	445 (73.2)
Unmapped	116 (19.1)
Race, n (%)	
American Indian or Alaska Native	2 (0.3)
Asian	15 (2.5)
Black or African-American	110 (18.1)
Native Hawaiian or other Pacific Islander	2 (0.3)
Other	25 (4.1)
Unmapped	81 (13.3)
White	373 (61.3)
Census region, n (%)	
Midwest	4 (0.7)
South	387 (63.7)
West	217 (35.7)
Payer, n (%)	
Commercial	361 (59.4)
Govt/Veterans Affairs	22 (3.6)
Medicaid	39 (6.4)
Medicare	161 (26.5)
Unspecified	18 (3.0)
SLE severity*, n (%)	
Mild	98 (16.1)
Moderate	428 (70.4)
Severe	82 (13.5)
Current therapy, n (%)	
Monotherapy (belimumab only)	231 (38.0)
Antimalarials	201 (33.1)
Antimalarials+immunosuppressants	123 (20.2)
Immunosuppressants	53 (8.7)
Current therapy route of administration, n (%)	
Intravenous	406 (79.9)
Subcutaneous	56 (11.0)
Mixed	46 (9.1)
Condition present prior to index, n (%)	
Ankylosing spondylitis	7 (1.2)
Osteoarthritis/Osteopenia/Osteoporosis	187 (30.8)
Psoriatic arthritis	18 (3.0)
Rheumatoid arthritis	169 (27.8)
Sjögren's disease	156 (25.7)
Lupus nephritis	112 (18.4)

*SLE severity was assigned based on diagnosis codes (ICD-9/ICD-10) and treatments observed prior to index as described in previous research.[26]
FAS, full analysis set; ICD-9, International Classification of Diseases-9th Revision; ICD-10, International Classification of Diseases-10th Revision.

(70.4%). For the FAS, 56.3% (n=342) of patients had OCS use during period 1 (online supplemental table 1). Among patients who persisted with belimumab treatment for 360 days (n=492), 54.5% (n=268) had OCS use during period 1. Patients with OCS use in period 1 (n=342) vs those without OCS use (n=266) were slightly younger (mean age 47.9 vs 50.1 years, respectively; p=0.066) and had lower mean body mass index (29.1 vs 30.8 kg/m^2, respectively; p=0.017).

Baseline characteristics were generally similar between patients with no change/gain in OCS use and those who had a decrease in OCS use from period 1 to period 3, except for cardiovascular and pulmonary Systemic Lupus International Collaborating Clinics/American College of Rheumatology Systemic Damage Index organ damage, with higher proportions of patients observed with organ damage among those with no change/gain in OCS use (p<0.05; table 2). No statistically significant differences were observed in baseline characteristics between patients who continued belimumab treatment for 360 days and those who discontinued the treatment earlier (data not shown).

From the start of period 2, approximately 3.0% of patients discontinued belimumab treatment each month; 80.9% of patients remained on treatment through period 3. For patients who discontinued belimumab treatment before the end of period 3 (n=116), the main reasons documented for discontinuation included lack or loss of efficacy (27.6%) and non-clinical reason (17.2%); no reason was specified for 38.8% of patients. The reasons for belimumab discontinuation were indicated in visit notes for each patient.

Change in OCS use among patients receiving OCS in period 1

For patients who persisted with belimumab treatment for 180 days and who were receiving OCS in period 1 (n=342), the proportion of patients receiving OCS significantly decreased by 22% (p<0.001) from period 1 to period 2 (table 3). Overall, mean total OCS dose per patient significantly decreased by 20% (p<0.001) from period 1 to period 2, and the mean OCS daily dose for days supplied significantly decreased by 15% (p<0.001) from period 1 to period 2.

Among patients who persisted with belimumab treatment for 360 days and who were receiving OCS in period 1 (n=268), the proportion of patients receiving OCS significantly decreased by 35% (p<0.001) from period 1 to period 3. Overall, mean total OCS dose per patient significantly decreased by 39% (p<0.001) from period 1 to period 3. The mean OCS daily dose for days supplied significantly decreased by 20% (p<0.001) from period 1 to period 3. The proportion of patients with an OCS dose ≤7.5 mg/day increased significantly from 37.3% in period 1 to 57.5% (p<0.001; data not shown) in period 2 and 68.3% (p<0.001) in period 3 (table 3), demonstrating an increased number of patients lowering their steroid dose. Similarly, the proportion of patients receiving an OCS dose ≤5 mg/day significantly increased from 25.4% in period 1 to 48.9% (p<0.001; data not shown) in period 2 and 60.1% (p<0.001) in period 3 (table 3).

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Table 2 Patient baseline characteristics stratified by patients with no change or gain in OCS use and patients with a decrease in OCS use from P1 to P3 (among patients who remained on belimumab for >360 days and who had an OCS prescription during P1, N=268)

	Patients with no change or gain in OCS use from P1 to P3 (n=87)	Patients with a decrease in OCS use from P1 to P3 (n=181)	Total (N=268)	P value
Gender, n (%)				
Female	80 (92.0)	171 (94.5)	251 (93.7)	0.428
Male	7 (8.0)	10 (5.5)	17 (6.3)	
Age				
Mean (SD)	49.0 (14.91)	47.3 (14.94)	47.8 (14.93)	0.375
Median (IQR)	48.0 (38.00, 61.00)	46.0 (37.00, 58.00)	47.0 (37.50, 59.00)	
BMI				
Mean (SD)	27.7 (7.27)	29.6 (7.36)	29.0 (7.38)	0.051
Median (IQR)	25.6 (22.28, 31.89)	28.8 (24.19, 34.55)	28.1 (23.28, 33.95)	
Charlson Comorbidity Index				
Mean (SD)	1.3 (0.6)	1.3 (0.9)	1.3 (0.8)	0.448
Median (IQR)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	
Ethnicity, n (%)				
Hispanic or Latino	8 (9.2)	15 (8.3)	23 (8.6)	0.929
Not Hispanic or Latino	63 (72.4)	135 (74.6)	198 (73.9)	
Unmapped	16 (18.4)	31 (17.1)	47 (17.5)	
Race, n (%)				
American Indian or Alaska Native	1 (1.1)	1 (0.6)	2 (0.7)	0.780
Asian	3 (3.4)	3 (1.7)	6 (2.2)	
Black or African-American	18 (20.7)	38 (21.0)	56 (20.9)	
Native Hawaiian or other Pacific Islander	0 (0.0)	1 (0.6)	1 (0.4)	
Other	3 (3.4)	6 (3.3)	9 (3.4)	
Unmapped	14 (16.1)	20 (11.0)	34 (12.7)	
White	48 (55.2)	112 (61.9)	160 (59.7)	
Census region, n (%)				
Midwest	1 (1.1)	1 (0.6)	2 (0.7)	0.855
South	54 (62.1)	111 (61.3)	165 (61.6)	
West	32 (36.8)	69 (38.1)	101 (37.7)	
Payer, n (%)				
Commercial	51 (58.6)	114 (63.0)	165 (61.6)	0.176
Copay/Drug assistance	1 (1.1)	1 (0.6)	2 (0.7)	
Govt/Veterans Affairs	2 (2.3)	5 (2.8)	7 (2.6)	
Medicaid	5 (5.7)	12 (6.6)	17 (6.3)	
Medicare	23 (26.4)	48 (26.5)	71 (26.5)	
Unspecified	5 (5.7)	1 (0.6)	6 (2.2)	
SLE severity, n (%)				
Mild	11 (12.6)	11 (6.1)	22 (8.2)	0.098
Moderate	67 (77.0)	140 (77.3)	207 (77.2)	
Severe	9 (10.3)	30 (16.6)	39 (14.6)	
SDI organ damage, n (%)				
Cardiovascular	5 (5.7)	2 (1.1)	7 (2.6)	0.026
Diabetes	3 (3.4)	12 (6.6)	15 (5.6)	0.289
Gastrointestinal	0 (0.0)	2 (1.1)	2 (0.7)	0.325
Gonadal	2 (2.3)	5 (2.8)	7 (2.6)	0.824
Malignancy (excluding dysplasia)	2 (2.3)	6 (3.3)	8 (3.0)	0.647
Musculoskeletal	3 (3.4)	8 (4.4)	11 (4.1)	0.707
Neuropsychiatric	9 (10.3)	29 (16.0)	38 (14.2)	0.212

Continued

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Table 2 Continued

	Patients with no change or gain in OCS use from P1 to P3 (n=87)	Patients with a decrease in OCS use from P1 to P3 (n=181)	Total (N=268)	P value
Ocular	0 (0.0)	0 (0.0)	0 (0.0)	–
Peripheral vascular	2 (2.3)	1 (0.6)	3 (1.1)	0.203
Pulmonary	6 (6.9)	3 (1.7)	9 (3.4)	0.026
Renal	2 (2.3)	2 (1.1)	4 (1.5)	0.450
Skin	4 (4.6)	6 (3.3)	10 (3.7)	0.604
Current therapy, n (%)				
Belimumab monotherapy	28 (32.2)	67 (37.0)	95 (35.4)	0.258
Belimumab+antimalarials	23 (26.4)	61 (33.7)	84 (31.3)	
Belimumab+antimalarials+immunosuppressants	26 (29.9)	37 (20.4)	63 (23.5)	
Belimumab+immunosuppressants	10 (11.5)	16 (8.8)	26 (9.7)	

BMI, body mass index; IQR, interquartile range; OCS, oral corticosteroid; P, period; SD, standard deviation; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Systemic Damage Index.

Changes in OCS use among the FAS population

For patients who persisted with belimumab treatment for 180 days (N=608), 2% fewer patients overall were receiving OCS at period 2 compared with period 1, but the decrease was not statistically significant (p=0.613; table 4). The mean total OCS dose per patient decreased by 7% (p=0.260) from period 1 to period 2, and the mean OCS daily dose for days supplied decreased by 11% (p<0.001) from period 1 to period 2.

Among patients who persisted with belimumab treatment for 360 days (N=492), a significant decrease of 12% in the proportion of patients receiving OCS was observed from period 1 to period 3 (p=0.013). The mean total OCS dose per patient decreased by 23% (p=0.004) from period 1 to period 3. The mean OCS daily dose for days supplied decreased by 12% from period 1 to period 3 (p<0.001). Overall, 65.9% of patients had an OCS dose ≤7.5 mg/day in period 1, which increased to 69.9% in period 2 (p=0.088; data not shown) and 74.8% in period 3 (p=0.001; table 4), demonstrating an overall increase in the number of patients lowering their OCS dose. The proportion of patients tapering to a lower dose of OCS also increased when using a threshold of 5 mg/day, as 59.3% of patients had a dose ≤5 mg/day in period 1, 63.8% in period 2 (p=0.063; data not shown) and 68.5% in period 3 (p=0.001; table 4).

Table 3 Change from P1 to P2 and P3 in OCS use among patients who persisted with belimumab treatment for 180 days (P1 vs P2) and 360 days (P1 vs P3) and who were receiving OCS in P1

	Change from P1 to P2 in OCS use among patients who persisted with belimumab treatment for 180 days and who were receiving OCS in P1				Change from P1 to P3 in OCS use among patients who persisted with belimumab treatment for 360 days and who were receiving OCS in P1			
	P1, N=342	P2, N=342	P1 vs P2 difference, %	P1 vs P2 p value	P1, N=268	P3, N=268	P1 vs P3 difference, %	P1 vs P3 p value
Proportion of patients receiving OCS, n (%)	342 (100.0)	268 (78.4)	–22	<0.001	268 (100.0)	174 (64.9)	–35	<0.001
Mean total OCS dose per patient (mg)	718.8	572.8	–20	<0.001	695.1	426.6	–39	<0.001
Mean total OCS days supplied per patient	64.1	59.6	–7	0.084	62.7	51.9	–17	<0.001
Mean OCS daily dose for days supplied (mg)	12.3	10.4	–15	<0.001	11.7	9.4	–20	<0.001
Proportion of patients with prednisone-equivalent dose of ≤5 mg/day for days supplied, n (%)	85 (24.9)	163 (47.7)	92	<0.001	68 (25.4)	161 (60.1)	137	<0.001
Proportion of patients with prednisone-equivalent dose of ≤7.5 mg/day for days supplied, n (%)	121 (35.4)	196 (57.3)	62	<0.001	100 (37.3)	183 (68.3)	83	<0.001

Percentages for differences are shown after rounding up to the nearest whole number.
OCS, oral corticosteroid; P, period.

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Table 4 Change from P1 to P2 and P3 in OCS use among patients who persisted with belimumab treatment for 180 days (P1 vs P2) and 360 days (P1 vs P3)

	Change from P1 to P2 in OCS use among patients who persisted with belimumab treatment for 180 days				Change from P1 to P3 in OCS use among patients who persisted with belimumab treatment for 360 days			
	P1, N=608	P2, N=608	P1 vs P2 difference, %	P1 vs P2 p value	P1, N=492	P3, N=492	P1 vs P3 difference, %	P1 vs P3 p value
Proportion of patients receiving OCS, n (%)	342 (56.3)	335 (55.1)	–2	0.613	268 (54.5)	236 (48.0)	–12	0.013
Mean total OCS dose per patient (mg)	404.3	377.1	–7	0.260	378.7	292.2	–23	0.004
Mean total OCS days supplied per patient	36.0	38.6	7	0.220	34.1	34.2	0	0.775
Mean OCS daily dose for days supplied (mg)	12.3	11.0	–11	<0.001	11.7	10.4	–12	<0.001
Proportion of patients with prednisone-equivalent dose of ≤5 mg/day for days supplied, n (%)	351 (57.7)	377 (62.0)	7	0.048	292 (59.3)	337 (68.5)	15	0.001
Proportion of patients with prednisone-equivalent dose of ≤7.5 mg/day for days supplied, n (%)	387 (63.7)	417 (68.6)	8	0.022	324 (65.9)	368 (74.8)	14	0.001

Percentages for differences are shown after rounding up to the nearest whole number.
OCS, oral corticosteroids; P, period.

Changes in patient laboratory measures and clinical characteristics from period 1 to periods 2 and 3

Changes in laboratory measures and clinical characteristics were recorded among patients who persisted on belimumab for 180 days (N=608; period 2) and 360 days (N=492; period 3); however, the data included may not be from the same patients in each period. Mean (SD) C3 levels increased slightly from 113.9 (34.70) mg/dL in period 1 to 120.6 (33.29) mg/dL in period 2 (table 5). Similarly, mean (SD) C4 levels increased slightly from 25.7 (8.88) mg/dL in period 1 to 26.9 (9.40) mg/dL in period 2. Similar results were observed for the change in C3 and C4 levels from period 1 to period 3 (N=492; table 5). Slight decreases from period 1 in mean SLEDAI score were observed in both groups; however, the SLEDAI data were available for only a small number of patients.

DISCUSSION

This observational, retrospective study is the first to specifically look at the relationship between belimumab and OCS use in a US database of community rheumatology care. The results demonstrated statistically significant reductions in OCS use in periods 2 and 3 among patients with OCS use during period 1 and who persisted with belimumab therapy for each period. Statistically significant reductions were also observed in the mean total OCS dose per patient in period 3 and in the mean total daily

Table 5 Changes from P1 to P2 and P3 in patient clinical characteristics among patients who persisted with belimumab treatment for 180 days (P1 vs P2) and 360 days (P1 vs P3)

	P1, N=608	P2, N=608	P1, N=492	P3, N=492
C3				
N	326	323	259	255
Mean (SD), mg/dL	113.9 (34.70)	120.6 (33.29)	113.1 (34.78)	120.7 (33.25)
Median (IQR), mg/dL	113.0 (86.00, 136.00)	119.0 (99.00, 145.00)	112.0 (85.00, 136.00)	117.0 (97.00, 146.00)
C4				
N	240	260	189	211
Mean (SD), mg/dL	25.7 (8.88)	26.9 (9.40)	25.7 (8.93)	27.3 (9.94)
Median (IQR), mg/dL	24.0 (19.00, 31.15)	25.0 (20.00, 31.85)	24.0 (19.00, 31.30)	25.6 (20.00, 31.50)
SLEDAI				
N	34	30	28	23
Mean (SD)	12.5 (6.34)	9.6 (6.44)	12.7 (5.72)	11.6 (9.35)
Median (IQR)	11.5 (8.00, 16.00)	8.50 (6.00, 16.00)	12.0 (8.00, 16.50)	8.0 (4.00, 17.00)

IQR, interquartile range; P, period; SD, standard deviation; SLEDAI, SLE Disease Activity Index.

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OCS dose for days supplied in periods 2 and 3. There was also an increase in the proportions of patients tapering to a lower OCS dose ≤7.5 mg/day and ≤5 mg/day. Similarly, statistically significant reductions in OCS use were observed across the entire population of patients who received belimumab 12 months following belimumab initiation, except for the mean total OCS days supplied per patient.

Our results are consistent with those observed in randomised clinical trials as well as previous real-world observational studies, demonstrating that belimumab-treated patients either reduced or eliminated OCS use.[14 15 18–22] For example, a previous claims-based study in a large sample of US patients with SLE demonstrated that OCS use was significantly lower in the 6 months post-belimumab initiation than in the 6 months pre-belimumab initiation.[23]

The International Task Force for SLE recommends using the lowest corticosteroid dosage needed to control disease and that, if possible, corticosteroids should be withdrawn completely to minimise risks.[24] Low-dose OCS use has also been associated with significantly lower HCRU and costs compared with high-dose OCS use.[10] Therefore, the results of this study suggest that belimumab could potentially reduce the health and economic burden in patients with SLE through its OCS-sparing effect.

In addition to the OCS reduction results observed in this study, there were also slight increases in the mean C3 and C4 levels and slight decreases in the mean SLEDAI score from period 1 to periods 2 and 3. Although these results are consistent with those observed in previous real-world belimumab studies,[16 25] they should be interpreted with caution as the data may not be from the same patients assessed in each period. Also, the SLEDAI scores were analysed in a small patient number.

Some limitations of this study should be considered, including those that are inherent to non-interventional, observational studies such as lack of source data verification, limited control of confounding effects or possible issues with availability and comparability of diagnostic data. The accuracy and completeness of data input are dependent on data collection methods at the individual and practice levels; some providers did not conduct laboratory or disease assessments as regularly as others, or at all. In addition, the database only includes patients seen in rheumatology clinics that are part of the ARN and, thus, may not be representative of all patients in US community rheumatology care or of all patients with SLE in the USA. Treatment occurring outside of the ARN may not be present in the data included in this study; for instance, any OCS prescriptions written by non-ARN physicians may be missing. Furthermore, corticosteroids administered by non-oral routes were not assessed; as such, changes in OCS use may not reflect overall changes in corticosteroid use. Some OCS prescriptions may have been missing from the dataset, based on the low proportion of patients (56.3%) in the FAS with OCS use in period 1. Sensitivity analyses were performed to evaluate the likelihood of missing prior OCS data from the dataset, demonstrating that the missing data had a limited effect on the observed overall OCS use reductions. Reductions in proportions of patients receiving OCS, total OCS use and mean daily dose for patients remaining on OCS approximated the group of patients who remained on belimumab for 360 days not limited by evidence of OCS history. Sensitivity analyses performed in patients whose observation periods concluded pre-COVID-19 demonstrated little impact of COVID-19-related treatment practices on changes in OCS use. Despite these limitations, the results of this study provide further evidence of the effect of belimumab on OCS use reduction.

In conclusion, the results of this study demonstrate a lower proportion of patients rely on OCS for disease management after initiating belimumab, as well as a reduction in daily dose of OCS among those who persist with belimumab over time. This study suggests that long-term use of belimumab in a community rheumatology practice may allow for a reduction in overall OCS use and its associated deleterious effects in patients with SLE.

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Competing interests KW and BR are employees of GSK and hold stocks and shares in the company. SM is an employee of Trio Health Analytics, which has received research support from AbbVie, Actelion Pharmaceuticals, AstraZeneca, Gilead Sciences, GSK, Horizon Pharma, JNJ, Merck, Pharming Healthcare, Sanofi, Takeda, UCB Biosciences and ViiV Healthcare.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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Ethics approval No direct patient contact or primary collection of individual patient data were performed and, thus, informed consent, ethics committee or Institutional Review Board approval was not required for this study.

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