

SUPPLEMENTARY MATERIALS

Table S1. Baseline demographics and patient characteristics of the SPOCS population by country

	Australia (n=51)	Canada (n=81)	USA (n=308)	France (n=64)	Germany (n=74)	Italy (n=52)	Spain (n=97)	UK (n=96)	Nominal <i>p</i> -value
Age, years	n=51	n=81	n=308	n=64	n=74	n=52	n=97	n=96	0.1062
Mean ± SD	43.7 ± 13.6	46.1 ± 15.2	45.9 ± 14.9	42.8 ± 13.5	47.8 ± 12.5	41.3 ± 13.3	45.4 ± 12.0	45.1 ± 12.7	
Median (IQR)	45.0 (34.0, 52.0)	45.0 (33.0, 57.0)	45.0 (33.0, 56.5)	42.0 (32.0, 52.0)	50.5 (36.0, 56.0)	42.0 (30.5, 49.0)	44.0 (38.0, 53.0)	45.0 (35.0, 54.5)	
Age >40 years, n (%)	29 (56.9)	47 (58.0)	194 (63.0)	36 (56.2)	48 (64.9)	30 (57.7)	63 (64.9)	56 (58.3)	0.845
Male, n (%)	7 (13.7)	6 (7.4)	14 (4.6)	7 (10.9)	9 (12.2)	3 (5.8)	8 (8.2)	2 (2.1)	0.0331
Race, n (%)	n=50	n=81	n=293	n=41	n=74	n=51	n=96	n=93	<0.001
Asian	16 (32.0)	21 (25.9)	20 (6.8)	0 (0.0)	2 (2.7)	1 (2.0)	0 (0.0)	11 (11.8)	
Black	1 (2.0)	6 (7.4)	92 (31.4)	11 (26.8)	2 (2.7)	0 (0.0)	2 (2.1)	14 (15.1)	
White	29 (58.0)	44 (54.3)	168 (57.3)	29 (70.7)	70 (96.4)	49 (96.1)	90 (93.8)	62 (66.7)	
Other	4 (8.0)	10 (12.3)	13 (4.4)	1 (2.4)	0 (0.0)	1 (2.0)	4 (4.2)	6 (6.5)	
Ethnicity, n (%)	n=1	n=81	n=304	n=25	n=72	n=52	n=96	n=91	<0.001
Hispanic or Latino	0 (0)	3 (3.7)	49 (16.1)	3 (12.0)	1 (1.4)	6 (11.5)	49 (51.0)	2 (2.2)	
BMI kg/m²	n=31	n=74	n=283	n=63	n=73	n=47	n=87	n=69	<0.001
Mean ± SD	28.7 ± 5.3	25.9 ± 5.5	29.3 ± 7.5	24.8 ± 6.3	26.0 ± 5.2	23.3 ± 4.8	25.0 ± 5.5	27.4 ± 6.6	
Median (IQR)	28.4 (24.9, 32.1)	24.9 (21.9, 28.0)	27.8 (24.2, 32.9)	22.7 (20.0, 28.4)	25.3 (22.0, 28.3)	21.8 (19.9, 26.0)	24.0 (21.0, 27.3)	26.5 (22.0, 31.6)	
BMI category, n (%)	n=31	n=74	n=283	n=63	n=73	n=47	n=87	n=69	<0.001
Underweight	1 (3.2)	3 (4.1)	9 (3.2)	8 (12.7)	3 (4.1)	4 (8.5)	3 (3.4)	2 (2.9)	
Normal	7 (22.6)	34 (45.9)	77 (27.2)	29 (46.0)	31 (42.5)	29 (61.7)	50 (57.5)	27 (39.1)	
Overweight	9 (29.0)	24 (32.4)	90 (31.8)	15 (23.8)	27 (37.0)	10 (21.3)	19 (21.8)	18 (26.1)	
Obese	14 (45.2)	13 (17.6)	107 (37.8)	11 (17.5)	12 (16.4)	4 (8.5)	15 (17.2)	22 (31.9)	

All *p*-values are nominal; there have been no adjustments for multiplicity. Subgroups do not total overall population n due to missing data.

BMI, body mass index; IQR, interquartile range; SD, standard deviation; SLE, systemic lupus erythematosus; SPOCS, SLE

Prospective Observational Cohort Study; UK, United Kingdom; USA, United States of America.

Table S2. Clinical characteristics of the SPOCS population at baseline, by country

	Australia (n=51)	Canada (n=81)	USA (n=308)	France (n=64)	Germany (n=74)	Italy (n=52)	Spain (n=97)	UK (n=96)	Nominal p-value
Years since diagnosis of SLE	n=51	n=81	n=300	n=63	n=74	n=52	n=97	n=96	0.337
Mean ± SD	13.0 ± 10.5	11.5 ± 9.8	11.0 ± 9.3	8.7 ± 7.3	11.4 ± 8.0	10.2 ± 9.1	11.9 ± 10.0	11.4 ± 8.8	
Median (IQR)	12.0 (5.0, 18.0)	10.0 (3.0, 18.0)	8.0 (4.0, 17.0)	7.0 (1.5, 15.5)	10.5 (5.0, 15.8)	8.0 (1.8, 17.2)	9.0 (3.0, 18.0)	10.0 (3.5, 19.0)	
Age at first SLE manifestation	n=50	n=73	n=283	n=63	n=40	n=49	n=86	n=88	0.554
Mean ± SD	29.0 ± 13.1	33.2 ± 13.5	32.6 ± 14.3	31.2 ± 13.6	34.1 ± 14.3	30.0 ± 14.3	32.4 ± 13.3	31.1 ± 13.4	
Median (IQR)	26.5 (18.2, 37.8)	31.0 (26.0, 41.0)	30.0 (22.0, 43.0)	30.0 (23.0, 39.0)	32.0 (22.8, 41.8)	27.0 (20.0, 38.0)	32.0 (22.2, 41.8)	28.0 (21.0, 41.0)	
SLE diagnosis age (years), n (%)	n=51	n=81	n=300	n=64	n=74	n=52	n=97	n=96	0.041
<18	9 (17.6)	15 (18.5)	38 (12.7)	11 (17.2)	3 (4.1)	9 (17.3)	13 (13.4)	16 (16.7)	
18–29	20 (39.2)	11 (13.6)	86 (28.7)	16 (25.0)	25 (33.8)	21 (40.4)	26 (26.8)	26 (27.1)	
30–49	16 (31.4)	43 (53.1)	129 (43.0)	27 (42.2)	31 (41.9)	15 (28.8)	50 (51.5)	39 (40.6)	
50+	6 (11.8)	12 (14.8)	47 (15.7)	10 (15.6)	15 (20.3)	7 (13.5)	8 (8.2)	15 (15.6)	
SLEDAI-2K	n=49	n=72	n=192	n=54	n=41	n=39	n=79	n=58	<0.001
Mean ± SD	8.4 ± 3.4	11.0 ± 5.6	8.7 ± 3.7	9.8 ± 4.8	10.6 ± 4.6	11.1 ± 5.0	10.6 ± 5.5	10.1 ± 4.5	
Median (IQR)	8.0 (6.0, 9.0)	9.0 (7.0, 13.2)	8.0 (6.0, 10.0)	8.0 (6.0, 12.0)	10.0 (8.0, 12.0)	10.0 (8.0, 12.0)	8.0 (7.0, 12.0)	8.0 (8.0, 12.0)	
SLEDAI-2K ≥10, n (%)	12 (24.5)	35 (48.6)	68 (35.2)	22 (40.7)	22 (53.7)	21 (53.8)	36 (45.6)	25 (43.1)	0.031
Modified SLEDAI-2K^a	n=50	n=81	n=308	n=63	n=74	n=51	n=96	n=94	0.016
Mean ± SD	4.9 ± 3.3	6.6 ± 3.6	6.5 ± 2.9	6.1 ± 3.1	6.6 ± 3.9	5.9 ± 3.4	6.6 ± 4.4	7.2 ± 3.4	
Median (IQR)	4.0 (2.0, 6.0)	6.0 (4.0, 8.0)	6.0 (4.0, 8.0)	4.0 (4.0, 8.0)	6.0 (4.0, 8.0)	4.0 (4.0, 8.0)	6.0 (4.0, 8.0)	6.0 (4.0, 8.0)	
Physician Global Assessment	n=50	n=81	n=306	n=64	n=74	n=52	n=97	n=96	<0.001
Mean ± SD	1.1 ± 0.6	1.3 ± 0.6	1.5 ± 0.5	1.5 ± 0.7	1.7 ± 0.5	1.6 ± 0.5	1.8 ± 0.5	1.7 ± 0.5	
Median (IQR)	1.0 (0.9, 1.5)	1.3 (1.0, 1.7)	1.5 (1.0, 2.0)	1.5 (1.0, 2.0)	1.9 (1.3, 2.0)	1.5 (1.0, 2.0)	2.0 (1.5, 2.0)	1.8 (1.3, 2.0)	
SDI total score	n=39	n=81	n=308	n=64	n=74	n=52	n=97	n=96	0.021
Mean ± SD	1.1 ± 1.5	1.3 ± 1.7	1.4 ± 1.6	0.6 ± 1.1	1.1 ± 1.6	0.8 ± 1.2	1.1 ± 1.7	1.2 ± 1.7	
Median (IQR)	0.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)	0.0 (0.0, 1.8)	0.0 (0.0, 1.0)	0.0 (0.0, 2.0)	1.0 (0.0, 2.0)	
SDI group, n (%)	n=39	n=81	n=308	n=64	n=74	n=52	n=97	n=96	0.012
0	21 (53.8)	36 (44.4)	118 (38.3)	42 (65.6)	40 (54.1)	30 (57.7)	52 (53.6)	47 (49.0)	
1	7 (17.9)	18 (22.2)	85 (27.6)	13 (20.3)	15 (20.3)	13 (25.0)	19 (19.6)	20 (20.8)	
2+	11 (28.2)	27 (33.3)	105 (34.1)	9 (14.1)	19 (25.7)	9 (17.3)	26 (26.8)	29 (30.2)	

Any organ damage, n (%)	18 (46.2)	45 (55.6)	190 (61.7)	22 (34.4)	34 (45.9)	22 (42.3)	45 (46.4)	49 (51.0)	<0.001
Annualized flare rate^b	n=51	n=81	n=307	n=64	n=74	n=52	n=97	n=96	<0.001
Mean ± SD	0.7 ± 1.5	1.5 ± 1.2	1.4 ± 2.3	1.7 ± 1.2	0.8 ± 1.9	1.8 ± 1.0	2.3 ± 2.9	1.8 ± 3.0	
Median (IQR)	0.0 (0.0, 0.0)	2.0 (0.0, 2.0)	0.0 (0.0, 2.0)	2.0 (2.0, 2.0)	0.0 (0.0, 1.5)	2.0 (2.0, 2.0)	2.0 (0.0, 2.0)	2.0 (0.0, 2.0)	
≥1 flare^c, n (%)	12 (23.5)	54 (66.7)	149 (48.5)	50 (78.1)	19 (25.7)	44 (84.6)	59 (60.8)	58 (60.4)	<0.001
≥1 mild flare^c, n (%)	3 (5.9)	14 (17.3)	83 (27.0)	19 (29.7)	7 (9.5)	24 (46.2)	22 (22.7)	15 (15.6)	<0.001
≥1 moderate flare^c, n (%)	0 (0.0)	25 (30.9)	51 (16.6)	22 (34.4)	1 (1.4)	8 (15.4)	17 (17.5)	31 (32.3)	<0.001
≥1 severe flare^c, n (%)	1 (2.0)	11 (13.6)	17 (5.5)	8 (12.5%)	10 (13.5)	4 (7.7)	5 (5.2)	8 (8.3)	0.040
Conditions and comorbidities, n (%)	n=51	n=81	n=308	n=64	n=74	n=52	n=97	n=96	
Any comorbidity	30 (58.8)	74 (91.4)	266 (86.4)	52 (81.2)	64 (86.5)	46 (88.5)	75 (77.3)	80 (83.3)	<0.001
Joint disease (SLE/non-SLE)	3 (5.9)	64 (79.0)	212 (69.1)	43 (67.2)	42 (56.8)	39 (75.0)	44 (45.4)	67 (69.8)	<0.001
CVD/stroke risk factors	11 (21.6)	28 (34.6)	127 (41.4)	13 (20.3)	31 (41.9)	9 (17.3)	29 (29.9)	28 (29.2)	<0.001
Cancer	2 (3.9)	5 (6.2)	25 (8.1)	2 (3.1)	4 (5.4)	1 (1.9)	5 (5.2)	3 (3.1)	0.414
Renal disease (ESRD)	17 (33.3)	13 (16.0)	31 (10.1)	8 (12.5)	9 (12.2)	5 (9.6)	6 (6.2)	7 (7.3)	<0.001
CNS disorders	7 (13.7)	10 (12.3)	24 (7.8)	4 (6.2)	6 (8.1)	6 (11.5)	16 (16.5)	13 (13.5)	0.210
Diabetes mellitus (all)	1 (2.0)	4 (4.9)	35 (11.4)	7 (10.9)	6 (8.1)	3 (5.8)	2 (2.1)	5 (5.2)	0.029
Metabolic syndrome	0 (0.0)	3 (3.7)	7 (2.3)	1 (1.6)	3 (4.1)	3 (5.8)	0 (0.0)	3 (3.1)	0.339
Family history of autoimmune disease	10/34 (29.4)	31 (38.3)	97 (31.6)	15 (23.4)	16 (21.6)	15 (28.8)	12 (12.4)	28 (29.2)	0.005

All *p*-values are nominal; there have been no adjustments for multiplicity. Subgroups do not total overall population *n* due to missing data.

^aModified SLEDAI-2K score defined as the SLEDAI-2K assessment score without the inclusion of points attributable to lupus headache or laboratory results included in the renal, immunologic, or hematology domains.

^bThe annualized flare rate is calculated by dividing the number of flares by the follow-up time in days and multiplying by 365.25.

^cWithin 6 months of study entry.

ACR, American College of Rheumatology SLE classification criteria; CVD, cardiovascular disease; ESRD, end stage renal disease; IQR, interquartile range; SD, standard deviation; SDI, SLICC/ACR damage index; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC, Systemic Lupus International Collaborating Clinics; SPOCS, SLE Prospective Observational Cohort Study; UK, United Kingdom; USA, United States of America.

Table S3. SLE medications the SPOCS population at baseline, by country

	Australia (n=51)	Canada (n=81)	USA (n=308)	France (n=64)	Germany (n=74)	Italy (n=52)	Spain (n=97)	UK (n=96)	Nominal <i>p</i> -value
Number of medication classes (±AM)	n=51	n=81	n=308	n=64	n=74	n=52	n=97	n=96	<0.001
Mean ± SD	1.6 ± 0.8	1.3 ± 0.7	1.2 ± 0.8	1.4 ± 0.8	1.6 ± 0.8	1.8 ± 0.7	1.4 ± 0.9	1.2 ± 0.9	
Median (IQR)	2.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	1.0 (0.0, 2.0)	
Level of therapy, n (%)	n=51	n=81	n=308	n=64	n=74	n=52	n=97	n=96	<0.001
None (±AM)	6 (11.8)	12 (14.8)	62 (20.1)	10 (15.6)	3 (4.1)	1 (1.9)	18 (18.6)	27 (28.1)	
Monotherapy (±AM)	12 (23.5)	35 (43.2)	145 (47.1)	20 (31.2)	31 (41.9)	17 (32.7)	30 (30.9)	33 (34.4)	
Dual (±AM)	29 (56.9)	32 (39.5)	91 (29.6)	32 (50.0)	30 (40.5)	28 (53.8)	41 (42.3)	30 (31.2)	
Triple (±AM)	4 (7.8)	2 (2.5)	10 (3.3)	2 (3.1)	10 (13.5)	6 (11.5)	8 (8.2)	6 (6.2)	
Antimalarials, n (%)	43 (84.3)	66 (81.5)	249 (80.8)	54 (84.4)	55 (74.3)	39 (75.0)	82 (84.5)	74 (77.1)	0.580
Immunosuppressants^a, n (%)	39 (76.5)	53 (65.4)	142 (46.1)	27 (42.2)	49 (66.2)	31 (59.6)	49 (50.5)	53 (55.2)	<0.001
Biologics^b, n (%)	6 (11.8)	4 (4.9)	79 (25.7)	14 (21.9)	16 (21.6)	21 (40.4)	17 (17.5)	9 (9.4)	<0.001
OCS^c, n (%)	37 (72.6)	55 (67.9)	145 (47.1)	50 (78.1)	57 (77.0)	41 (78.8)	70 (72.2)	51 (53.1)	<0.001
Cumulative glucocorticoids^d, g	n=32	n=51	n=142	n=48	n=56	n=41	n=70	n=51	<0.001
Mean ± SD	5.7 ± 6.3	2.4 ± 3.1	2.2 ± 2.9	2.0 ± 1.7	2.0 ± 2.5	3.0 ± 3.2	2.1 ± 1.7	2.5 ± 2.4	
Total glucocorticoids^e, mg/day									<0.001
Mean ± SD	15.5 ± 17.3	6.6 ± 8.5	6.2 ± 8.0	5.4 ± 4.5	5.4 ± 6.9	8.2 ± 8.7	5.7 ± 4.7	6.7 ± 6.6	
Cumulative glucocorticoids^d, g [including 0 mg]	n=46	n=77	n=305	n=62	n=73	n=52	n=97	n=96	<0.001
Mean ± SD	3.9 ± 5.9	1.6 ± 2.8	1.0 ± 2.3	1.5 ± 1.7	1.5 ± 2.4	2.3 ± 3.1	1.5 ± 1.7	1.3 ± 2.1	
Total glucocorticoids^e, mg/day [including 0 mg]	n=46	n=77	n=305	n=62	n=73	n=52	n=97	n=96	
Mean ± SD	10.8 ± 16.1	4.4 ± 7.6	2.8 ± 6.3	4.2 ± 4.6	4.2 ± 6.4	6.4 ± 8.4	4.1 ± 4.7	3.6 ± 5.9	
Total glucocorticoid daily dose^e, n (%)	n=46	n=77	n=305	n=62	n=73	n=52	n=97	n=96	<0.001
No glucocorticoids	14 (30.4)	26 (33.8)	163 (53.4)	14 (22.6)	17 (23.3)	11 (21.2)	27 (27.8)	45 (46.9)	
Dose ≤7.5 mg	16 (34.8)	37 (48.1)	102 (33.4)	33 (53.2)	48 (65.8)	28 (53.8)	54 (55.7)	35 (36.5)	
Dose >7.5 mg	16 (34.8)	14 (18.2)	40 (13.1)	15 (24.2)	8 (11.0)	13 (25.0)	16 (16.5)	16 (16.7)	

All *p*-values are nominal; there have been no adjustments for multiplicity. Subgroups do not total overall population n due to missing data.

^aCytotoxic or immunosuppressive agents included cyclophosphamide, methotrexate, mycophenolate mofetil/mycophenolic acid (MMF/MPA), azathioprine, tacrolimus, mizoribine, leflunomide, or cyclosporine; ^bBelimumab or rituximab; ^cNumber of patients with at least one ongoing glucocorticoid prescription or at least one prescription recorded in the previous year; ^dThe sum of all glucocorticoids received in the past 365 days, standardized to g/year; ^eCumulative glucocorticoids divided by 365 to convert to daily dose and group patients into daily dose groups.

AM, antimalarial; Biologics, belimumab or rituximab; IFNGS, type I interferon gene signature; IQR, inter-quartile range; SD, standard deviation; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000; SLICC, Systemic Lupus International Collaborating Clinics; SPOCS, SLE Prospective Observational Cohort Study.

Table S4. Baseline immunosuppressant and antimalarial use, by IFNGS status

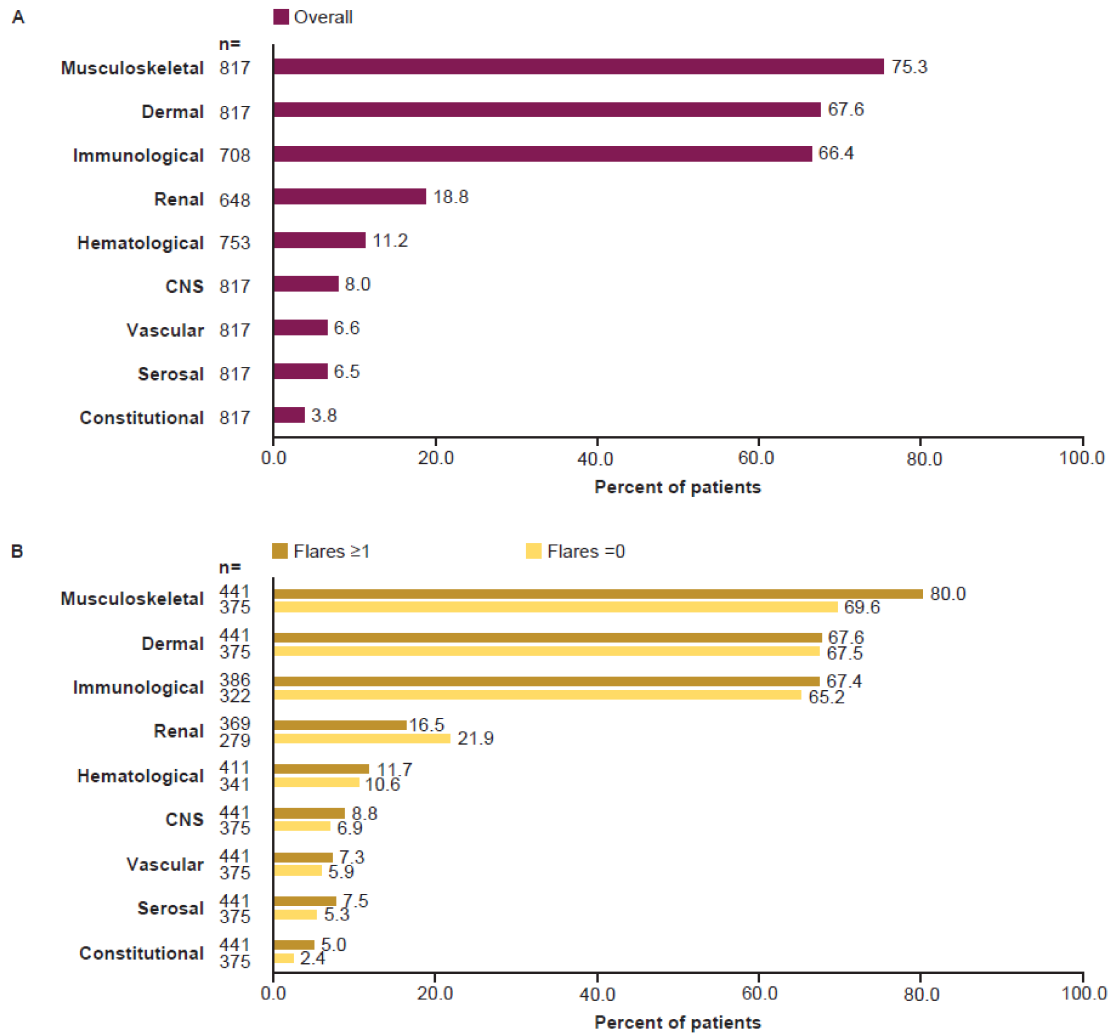
n (%)	Overall (N=823)	IFNGS		
		High (n=522)	Low (n=217)	Nominal <i>p</i> -value
Antimalarials	662 (80.4)	407 (78.0)	189 (87.1)	0.004
Antimalarials without immunosuppressants^a	313 (38.0)	172 (33.0)	109 (50.2)	<0.001
Antimalarials with immunosuppressants	349 (42.4)	235 (45.0)	80 (36.9)	0.041
Immunosuppressants	443 (53.8)	303 (58.0)	95 (43.8)	<0.001
Immunosuppressants without antimalarials	94 (11.2)	68 (13.0)	15 (6.9)	0.0165
Immunosuppressants with antimalarials	349 (42.4)	235 (45.0)	80 (36.9)	0.041

^aCytotoxic or immunosuppressive agents included cyclophosphamide, methotrexate,

mycophenolate mofetil/mycophenolic acid, azathioprine, tacrolimus, mizoribine, leflunomide, or cyclosporine.

IFNGS, type I interferon gene signature.

Figure S1. Baseline clinical manifestations by organ system involvement in the SPOCS population, A) overall and B) by baseline flares



CNS, central nervous system; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000; SPOCS, SLE Prospective Observational Cohort Study.