In addition, HCQ was associated with a 34% reduction in antidsDNA among AAs, but no significant reduction among CAs.

Table. Impact of treatment with HCQ on the odds of being positive for immunologic markers

Clinical marker	All Patients (n=951)		Caucasian Americans (n=462)		African Americans (n=409)	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Confirmed Lupus	0.65	0.0019	0.38 ¹	<0.0001	1.05 ¹	0.82
Anticoagulant	(0.50, 0.85)		(0.24, 0.58)		(0.69, 1.60)	
antidsDNA (% positive)	0.82	0.0005	0.90 ¹	0.19	0.66 ¹	<0.0001
	(0.73, 0.91)		(0.76, 1.06)		(0.56, 0.79)	
Low complement	0.71	<0.0001	0.71	<0.0001	0.73	<0.0001
	(0.64, 0.79)		(0.61, 0.83)		(0.62, 0.86)	
aCL IGG (% pos) ³	0.26	<0.0001	0.16 ¹	<0.0001	0.53 ¹	0.069
	(0.17, 0.39)		(0.09, 0.30)		(0.27, 1.05)	
aCL IGM (% pos) ³	0.45	0.0002	0.17 ¹	<0.0001	2.45 ¹	0.032
	(0.29, 0.68)		(0.09, 0.32)		(1.09, 5.55)	

¹ P-value for difference between Caucasian and African Americans < 0.0001.

Conclusion: HCQ use was associated with a substantial decline in the rates of positive immunologic biomarkers in SLE patients. The different impact of HCQ in different races suggests the existence of racial differences in SLE subtypes and may indicate the need for different treatment strategies.

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SAT0168

ONLY ONE THIRD OF REAL WORLD LUPUS PATIENTS MEET ELIGIBILITY CRITERIA FOR CLINICAL TRIALS: IMPLICATIONS FOR TRIAL VALIDITY AND GENERALISABILITY

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Background: Despite unprecedented drug development in SLE, the paucity of approved therapies remains a significant challenge. Recent trials have highlighted the need for minimising heterogeneity within SLE populations; however, there is concern this results in the recruitment of patients that are not representative of the SLE population.

Objectives: Our aim was to apply published trial eligibility criteria to patients with non-renal SLE in a large UK-wide register to quantify how accurately these clinical trials represent a real-world cohort.

Methods: A literature review of all major published double-blinded randomised phase III trials in non-renal SLE was performed (n=12). Inclusion and exclusion criteria common across the majority of clinical trials were applied to all patients recruited to the BILAG-BR (BILAG biologics register) starting either biological therapy or standard of care (SOC). We applied available data to common inclusion criteria including age ≥18 years, ACR 1997 SLE classification criteria, positive anti-dsDNA or ANA antibodies, active disease (defined as a BILAG A in 1 domain or a BILAG B in ≥2 domains, or a SLEDAI ≥6); and common exclusion criteria including restricted medication rules, active renal or neurological SLE (defined as a BILAG A in either domain), a history of hepatitis B or C, a history of malignancy (excluding basal cell carcinoma), CKD stage 4 or 5, a UPCR ≥100mg/mmol, and cytopenias (defined as neutrophils <1.0 x10⁹/L, platelets <10 x10⁹/L or Hb <70g/L). Baseline variables were compared using chi-squared test.

Results: As of July 2018, 837 patients were recruited to the BILAG-BR starting either SOC (n=125) or a biologic therapy (n=712). The commonest biologic and SOC therapy was rituximab (n=662, 93%) and mycophenolate (n=64, 51%) respectively. Patients taking SOC were more likely to have inactive disease, as well as having higher steroid doses and less exposure to previous cyclophosphamide or B cell therapy. In the biologic and SOC groups, 476 (67%) and 71 (57%) respectively met all inclusion criteria (table 1). One or more exclusion criteria were met by 324 (46%) of the biologics group and 46 (37%) of the SOC group. As such, 562 (67%) patients were not eligible to enrol in a clinical trial. The patients not eligible to participate were similar in age (P=1.0), gender (P=0.7) and ethnicity

(p=0.5) to those who were eligible. Median disease duration was longer in patients eligible to participate (2.9 vs. 5.1 years, p<0.01).

Table 1. Patients from the BILAG-BR who meet eligibility criteria for major SLE clinical trials

Inclusion criteria	Biologic (n=712)	SOC (n=125)	P value
Age ≥18 years	706	122	0.1
Meet ACR criteria for SLE	675	116	0.4
Antibody positive	567	99	0.9
Active disease	626	97	<0.01
Total meeting all inclusion criteria	476	71	0.03
Exclusion criteria	Biologic (n=712)	SOC (n=125)	P value
Steroids >40mg prednisolone	9	8	<0.001
Active CNS SLE	39	7	1.0
Active renal SLE	138	28	0.4
Hepatitis B or C	20	1	0.2
Malignancy	52	5	0.2
Cyclophosphamide <90 days before entry	37	0	<0.01
B cell therapy <1 year before entry	50	0	<0.01
CKD 4/ 5	22	3	0.7
UPCR ≥100mg/mmol	92	20	1.0
Low blood counts	25	1	0.1
Pregnancy	3	1	0.6
Total number of patients excluded	324	46	0.1
Total NOT* eligible for clinical trial (n)	562/837 (67%)		1.0

Conclusion: In a large national register of SLE patients, we found that two thirds of patients would not be eligible for recruitment to clinical trials using published inclusion and exclusion criteria. These results suggest that clinical trial recruits are not fully representative of the target disease population. This limits the generalisability of clinical trial results and supports the need for evidence from real world studies to fully understand the effectiveness of new therapies.

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SAT0169

HYDROXYCHLOROQUINE PRESCRIPTION PATTERNS IN EUROPE - THE EUROPEAN SURVEY FOR LUPUS PATIENTS (ESLP)

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Background: Long-term use of hydroxychloroquine (HCQ) is very common in patients with lupus erythematosus. It has been associated with wide-ranging benefits and it is generally well tolerated¹. However, long-term use (i.e. > 5 years) and high-dose HCQ (i.e. > 5 mg/kg/day) are both considered to be risk factors for developing HCQ retinopathy².

Advances in our understanding of HCQ retinopathy has led to changes in the recommendations for HCQ dosing and retinopathy screening¹⁻³. The latest EULAR guidelines for the management of systemic lupus erythematosus (SLE)⁴ recommend a maximum HCQ dose of 5 mg/kg/day and ophthalmological screening at baseline and annually after 5 years of HCQ treatment.

Objectives: To assess whether recent EULAR guidelines regarding HCQ dosing and retinopathy screening are affecting prescription patterns and screening frequencies in Europe.

Methods: Patients in Europe were given the opportunity to complete the online European Survey for Lupus Patients (ESLP) initiated by LUPUS EUROPE. The survey was promoted on social media from the 26th of June – 11th of July 2019. The survey consisted of 29 questions. Each participant was asked, among other things, to report their body weight (kg), daily HCQ dose and if they have received baseline screening and/or regular eye examinations.

Results: The online survey was completed by 2938 lupus patients from 36 countries. The majority were female (86.5%) and diagnosed with SLE (85.7%). The daily HCQ dose (mg/kg) was available from 1678 patients (57.1%). The median ± IQR HCQ dose was 4.3 ± 2.5 mg/kg/day with a median treatment duration of 7 years (IQR: 3 – 14). The recommended daily HCQ dose of 5 mg/kg was exceeded by 618 patients (36.8%). Low HCQ dose (≤ 4 mg/kg) was reported by 769 patients (45.8%). In addition, 284 out of 1786 patients (15.9%) reported they skipped HCQ once a week or more often. Nevertheless, only 8.7% of patients reported that they were more likely to skip HCQ than other medication. Patients from Belgium, Israel, France and Portugal reported the highest HCQ dosages. In contrast, patients from Spain reported the lowest HCQ dosages (Figure 1).

Moreover, 935 out of 1137 patients diagnosed in the past 10 years (82.2%) reported that they have received an ophthalmological screening at baseline. Lastly, 1167 patients reported long-term use of HCQ (i.e. ≥ 5 years). Only about 64% of them (n=748) reported that they receive regular eye examinations (i.e. at least once every year).

Conclusion: Studies have suggested that prescription patterns in the USA and UK were already affected by guidelines regarding HCQ dosing¹. We show large inter- and intra-country variations of HCQ dosing in Europe. Additionally, most centers fail to follow recent recommendations⁴ regarding annual screening of retinopathy in case of long-term HCQ use.

More research is needed to assess the clinical efficacy of low-dose HCQ and to confirm whether proper screening modalities are being employed as recommended by recent guidelines²⁻⁴.

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Figure 1. HCQ dose (mg/kg/day) reported by patients (• median HCQ dose). PRT: Portugal, POL: Poland, NLD: Netherlands, ITA: Italy, ISR: Israel, GRC: Greece, FRA: France, FIN: Finland, ESP: Spain, DEU: Germany, CHE: Switzerland, BEL: Belgium.

SAT0170

COMPOSITE OF RELEVANT ENDPOINTS FOR SJÖGREN'S SYNDROME (CRESS)

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Background: Defining a primary study endpoint that is able to discriminate between active treatment and placebo is crucial for clinical trials in primary Sjögren syndrome (pSS). Recent trials used the validated ESSDAI as primary endpoint, but found large 'response rates' in the placebo group too. Since pSS is a very heterogeneous disease, a composite endpoint including multiple aspects (i.e., systemic, patient-reported, functional and biological) may be more appropriate to demonstrate clinical efficacy.

Objectives: To develop a composite endpoint for pSS based on expert opinion and analysis of trial data.

Methods: Based on expert opinion, 5 items were found to be most relevant to assess the effect of treatment in pSS patients: ESSDAI, ESSPRI, OSS, SWS and RF/IgG (Figure 1). These items were tested using data at week 24 of the randomized, double blind, placebo-controlled ASAP-III trial.¹ ROC analysis was used to assess the discrimination of effect between the abatacept (n=40) and placebo (n=39) treatment groups. The optimal cut-off point per item was defined by the highest sum of sensitivity and specificity. The percentage of patients responding to the individual items (Figure 1) and the composite endpoint (named CRESS) was calculated.

Results: For ESSDAI, ROC analysis showed that both absolute and relative change in ESSDAI were not able to discriminate between treatment groups (AUC 0.536 and 0.559) and no optimal cut-off point could be identified. According to an in SLE developed endpoint and based on expert opinion, it was decided to aim for the validated definition of low disease activity (ESSDAI<5)².

For ESSPRI, ROC analysis (AUC 0.629) showed an optimal cut-off point of -13.8%. Therefore, the validated definition of ESSPRI response ($\geq -15\%$ or 1 point)² was used. For OSS and SWS, ROC analysis (AUC 0.555 for OSS>3 at baseline and AUC 0.556 for SWS>0 at baseline) could not identify an optimal cut-off point, so the definitions based on expert opinion were kept (Figure 1).

For serological items, ROC analysis (AUC 0.861 for RF>0 at baseline and 0.615 for IgG) showed optimal cut-off points of $\geq 25\%$ decrease in RF or $\geq 5\%$ decrease in IgG. Responding to ≥ 3 of the 5 items discriminated best between the abatacept and placebo groups. The final response rate to our composite endpoint (CRESS responders) was 55% vs. 13% in the abatacept and placebo groups, respectively (P<0.001). Further analysis of how many patients who met the composite endpoint also met the single endpoints and vice versa demonstrated that all individual items contributed to the overall response rate.

Conclusion: This concept of the new 'Composite of Relevant Endpoints for Sjögren's Syndrome' (CRESS) is developed. With this composite endpoint, it is possible to discriminate between abatacept and placebo response in pSS patients. Additional validation analyses in independent, global, multi-center, placebo-controlled trials of biological DMARDs in pSS and NECESSITY will be performed.

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Figure 1. Overview of the Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS): domains, measurements, definition of response and percentage of responders at week 24 of abatacept and placebo groups.

Domain	Measurement	Definition of response	Responders abatacept group	Responders placebo group
Systemic disease activity	ESSDAI	Score<5 (low disease activity)	35%	22%
Patient-reported symptoms	ESSPRI	Decrease of ≥ 1 point or 15% from baseline	58%	22%
Tear gland function	OSS	Decrease of $\geq 25\%$ from baseline, or if normal score at baseline (<3) no increase to abnormal as response	60%	51%
Salivary gland function	SWS	Increase of $\geq 25\%$ from baseline, or if score is 0 at baseline any increase	51%	43%
Serological	RF/IgG	Decrease of $\geq 25\%$ from baseline in RF or decrease of $\geq 5\%$ from baseline in IgG	73%	30%
Composite endpoint CRESS responder	All above	Response to ≥ 3 of the 5 items	55%	13%

ESSDAI: EULAR Sjögren's syndrome disease activity index; ESSPRI: EULAR Sjögren's syndrome patient reported index; OSS: ocular staining score; SWS: stimulated whole saliva; RF: rheumatoid factor; IgG: immunoglobulin G.

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