142.68), respectively. Increase in anti-dsDNA antibodies levels also predicted flares with an OR of 6.70 ($p=0.040$), while hypocomplementemia was not a significant risk factor.

Conclusion: Urine NGAL and L-PGDS perform better than conventional markers in predicting a lupus flare in its incipient phase, in particular preceding the corresponding change in serum complement. Urinary NGAL and L-PGDS levels seem to be potential tools for monitoring patients with SLE. Further studies are needed to determine their clinical utility in everyday practice.

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Table 1. Area under the curve (AUC), cut off values, sensitivity and specificity for L-PGDS, NGAL and standard biomarkers for disease flares.

Variables	AUC	95% CI	Cut off values	sensitivity	specificity
C3	0.683	0.555 - 0.793	107 mg/dl	94%	40%
Anti dsDNA antibodies	0.705	0.579 - 0.812	30 UI	55%	89%
PGDS	0.811	0.694 - 0.897	1500 ng/ml	78%	86%
NGAL	0.752	0.630 - 0.851	10.95 ng/ml	84%	63%

Abstract THU0249 – Figure 1

Abstract THU0249 – Figure 2

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THU0250

EARLY IMPROVEMENT IN SLEDAI-2K RESPONDER INDEX-50 PREDICTS SRI-4 RESPONSE IN A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF USTEKINUMAB (UST) IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: While traditional Systemic Lupus Erythematosus (SLE) Disease Activity Index 2000 (SLEDAI-2K) scoring assesses complete SLE response for individual disease manifestations, the SLEDAI-2K Responder Index-50 (S2K RI-50) evaluates responses using partial improvement ($\geq 50\%$) in each of the 9 organ systems of SLEDAI-2K. Ustekinumab (UST), a monoclonal antibody that targets the shared p40 subunit of the cytokines IL-12 & IL-23, is being investigated in patients with active SLE. We have previously shown in a Phase 2 placebo (PBO)-controlled trial of UST in SLE¹ that not only SLEDAI-2K and the SLE Responder Index 4 (SRI-4), but also S2K RI-50 can discriminate a treatment effect of UST vs PBO at week 24.^{2,3}

Objectives: Here, we aimed to ascertain whether a minimal threshold of partial improvement in S2K RI-50 could be used as an early predictor of SRI-4 response.

Methods: This phase 2, PBO-controlled study enrolled adults with sero-positive, active disease (SLEDAI score ≥ 6 with ≥ 1 BILAG A &/or ≥ 2 BILAG B scores) despite standard therapy. Patients ($n=102$) were randomized (3:2) to receive UST IV 6 mg/kg or PBO at week 0, followed by SC injections of UST 90mg or PBO q8w beginning at week 8, both added to standard of care. We calculated S2K RI-50 response through week 24 in all patients, including 60 patients receiving UST and 42 patients receiving PBO, using increasing cut-offs of S2K RI-50 reductions from baseline. To help determining a minimal cut-off that discriminated a treatment effect reflecting partial improvement, nominal p values are reported for this post hoc analysis. Logistic regression models were used to evaluate the relationship between reduction in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24, followed by correlation of binary response data between the two instruments.

Abstract THU0250 – Table 1.

Treatment Group	Visit	Correlation	Odds Ratio* [95% CI]	Predictive p-value*
Total Population	Week 12	0.62	7.6 [2.4-24.3]	0.0007
UST	Week 12	0.49	4.4 [1.1-16.9]	0.0311
PBO	Week 12	NE ^b	NE ^b	NE ^b
Total Population	Week 16	0.76	15.4 [4.2-55.8]	<0.0001
UST	Week 16	0.74	13.5 [2.6-69.8]	0.0020
PBO	Week 16	0.74	15.0 [1.7-130.7]	0.0142

* Predictive p-values and odds ratios are based upon logistic regression models. Predictive p-values are nominal and represent measures of the likelihood of association between a 2-point response in S2K RI-50 at week 12/16 and SRI-4 response at week 24 in the model.

^b Not estimable (NE) due to no values present in one cell in the 2x2 table.

UST = Ustekinumab, PBO = Placebo

Results: A 2-point reduction from baseline (improvement) in S2K RI-50 appeared to be the lowest threshold of response to demonstrate a treatment difference in the proportion of responders at week 24 with UST (93.5%) vs PBO (79.3%) ($\Delta 14.2\%$, $p=0.03$). The relationship between 2-point improvement in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24 is presented in the total study population and by treatment group (Table). In the total population, 78/102 (76.6%) patients at week 12 and 74/102 (72.5%) of patients at week 16 had at least a 2-point improvement in S2K RI-50. Of those, 47/78 (60.3%, $r=0.62$) at week 12 and 48/74 (64.9%, $r=0.76$) at week 16 achieved an SRI-4 response at week 24. Odds ratios for the association between SRI-4 response at week 24 and 2-point or greater improvement in S2K RI-50 were 7.6 (CI 2.4-24.3, $p=0.0007$) at week 12 and 15.4 (CI 4.2-55.8, $p<0.0001$) at week 16. Similar analyses performed by treatment group demonstrated that these relationships were consistent in the UST and PBO groups (Table).

Conclusion: 2K RI-50 captures partial improvement of $\geq 50\%$ in SLE disease activity and could be a useful outcome in clinical trials to predict early clinical response. These findings will be confirmed in an ongoing Phase 3 study.

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THU0251

ASSOCIATION OF SMOKING STATUS AND TOTAL AND INDIVIDUAL DAMAGE INDEX IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Smoking is a risk factor for systemic lupus erythematosus (SLE). It has been associated with increased disease activity and decreased effectiveness of hydroxychloroquine in cutaneous lupus.

Objectives: The objective of the study was to determine the association between smoking status and total and individual damage items in SLE.

Methods: We analyzed data from the Hopkins Lupus Cohort. Damage was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index. Fisher's exact test and Wilcoxon test were used in exploratory analysis. Logistic regression was used to estimate the association between damage and smoking status (ever/never). Odds ratios and 95% confidence intervals were reported. Stratification by ethnicity was done for individual damage items that were found to be significantly associated with smoking.

Results: The prevalence of ever smokers in our cohort was 36%. SLE patients who ever smoked had higher odds of total damage with higher mean total damage index scores ($p < 0.0001$). Data for individual damage items significantly associated with smoking are presented in Table 1.

The association between cataract and smoking was still present after adjusting for ethnicity, diabetes, and prednisone use in a multivariate regression model ($OR = 1.4$, $p = 0.0083$).

Stratification by ethnicity showed that African- American SLE patients who ever smoked were more likely to have cataract, scarring chronic alopecia, extensive scarring, skin ulceration, pulmonary hypertension, cerebrovascular events, cardiomyopathy, and diabetes compared to non-smokers. Caucasian SLE patients who ever smoked were more likely to have extensive scarring, gastrointestinal infarction and resection, and muscle atrophy (Table 1).

Abstract THU0251 – Table 1. Relationship between SLICC/ACR Damage Index Items and Smoking (ever/never)

ALL		Caucasian		African American	
Damage Item	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)
p-value					
Total damage	1.73 (1.44, 2.07)	< 0.0001	1.55 (1.22, 1.97)	0.0003	1.96 (1.44, 2.66)
<0.0001 Cataract	1.50 (1.17, 1.92)	0.00122	0.96 (0.68, 1.36)	0.8176	2.26 (1.56, 3.28)
<0.0001 Scarring alopecia	2.08 (1.42, 3.06)	0.00019	1.63 (0.60, 4.45)	0.3320	2.24 (1.46, 3.47)
0.0003 Extensive scarring or panniculum other than scalp	3.37 (1.95, 5.85)	0.0001	2.57 (1.01, 7.03)	0.0522	3.68 (1.90, 7.47)

0.00017					
Skin ulceration	2.76 (1.37, 5.57)	0.00465	2.03 (0.8, 5.36)	0.1370	4.45 (1.48, 16.32)
0.0121					
Pulmonary	0.00367	1.11 (0.70, 1.75)	0.6430	hypertension 1.79 (1.21, 2.63)	1.53 (1.15, 2.03)
0.00334					
Infarction or resection of bowels	1.42 (1.12, 1.79)	0.0032	1.37 (1.03, 1.84)	0.0338	1.36 (0.90, 2.04)
0.1461					
Pancreatitis	3.57 (1.07, 11.88)	0.0382	2.44 (0.68, 8.67)	0.1694	N/C
N/C					
Muscle atrophy	1.80 (1.11, 2.94)	0.0183	2.62 (1.26, 5.44)	0.0099	1.09 (0.54, 2.19)
0.8210					
Coronary artery disease	2.26 (1.50, 3.41)	0.0001	2.33 (1.39, 3.91)	0.0013	2.35 (1.13, 4.89)
0.0226					
Myocardial Infarction	2.30 (1.29, 3.32)	<0.0001	2.17 (1.30, 3.62)	0.0032	2.22 (1.27, 3.87)
0.0051					
				Cardiomyopathy	1.94 (1.29, 2.93)
0.0016	1.64 (0.81, 3.30)	0.1687	2.18 (1.27, 3.74)	0.0045	
				Claudication	4.53 (2.17, 9.48)
<0.0001	3.86 (1.47, 1.10)	0.0060	4.91 (1.55, 15.52)	0.0068	
				Cerebrovascular accident	1.41 (1.08, 1.84)
0.0127	1.16 (0.80, 1.69)	0.4279	1.69 (1.13, 2.54)	0.0115	
Diabetes	1.72 (1.29, 2.28)	0.0002	1.33 (0.88, 2.03)	0.1764	2.08 (1.39, 3.12)
0.0004					

N/C: data are not sufficient for calculating odds ratio

Conclusion: Smoking is a modifiable factor for organ damage in SLE. It is already known that it interferes with the efficacy of hydroxychloroquine. Now we are able to prove that smokers have more cutaneous damage (scarring) even after stratification for ethnicity. As expected, smokers had more cardiovascular damage. New findings include associations with gastrointestinal damage, cataracts, pulmonary hypertension, pancreatitis and diabetes.

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