confirmed by x-rays. Analyses were performed with logistic regression (forward selection procedure). Outcome measures were incident fracture in general (yes/no), vertebral fracture (yes/no), and peripheral fracture (yes/no).

Results Of the 145 included patients, 131 (90%) were females and 100 (69%) Caucasian. The mean age was 41 years (SD 12) at baseline, and median follow-up was 7.2 years (IQR 612). A total of 42 incident fractures (vertebral and peripheral) occurred during 998 patient years. The incidence rate of vertebral and peripheral fractures was 2.0 per 100 patient years (95% CI 1.303.13), and 2.20 per 100 patient years (95% CI 1.453.35), respectively.

Any fracture (both vertebral and peripheral) was predicted by postmenopausal status and Caucasian ethnicity. Vertebral fractures were predicted by age, in which the older the SLE patient, the higher the odds of getting vertebral fractures. Peripheral fractures were predicted by history of stroke, postmenopausal status and moderate alcohol use (112 units per week). Use of higher dosages of alcohol (>13 units per week) did not reduce peripheral fracture occurrence. Table 1 shows the final prediction models.

Conclusions The results of our study suggest a twofold increased risk of both vertebral and peripheral fractures in SLE patients compared to the general population.^{1 2} Age, Caucasian ethnicity and postmenopausal status are important risk factors for incident fractures in SLE. In addition, special attention should be paid to SLE patients with a history of stroke since this subgroup of patients is at high risk of peripheral fractures.

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PERFORMANCE OF SLEDAI-2K RESPONDER INDEX-50 IN A RANDOMIZED PLACEBO-CONTROLLED TRIAL WITH 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 (50%) in each of the 9 organ-systems of SLEDAI-2K and generates a total score. We aimed to evaluate the performance of S2K RI-50 at 24 weeks in a randomized, placebo (PBO) controlled trial of UST in patients with moderate-to-severe SLE disease activity to ascertain a minimal threshold of partial improvement.

Methods The UST phase 2, PBO-controlled study enrolled adults with active disease (SLEDAI score 6 with 1 BILAG A and/or 2 BILAG B scores) despite standard-of-care therapy. Patients (n=102) were randomized (3:2) to receive UST IV~6 mg/kg or PBO at week (wk) 0, followed by SC injections of UST 90 mg q8w or PBO beginning at wk8, both added to standard of care. We calculated S2K RI-50 response in

Abstract 10 Table 1 S2K RI-50 response rates at Wk24 for various cut-offs to define response

Decrease from Baseline	UST (%) ^{a,b} (n=62)	PBO (%) ^{a,b} (n=40)	Difference between UST and PBO	p-value ^c
1 Point Decrease	95.3	88.6	6.7	0.13
2 Point Decrease	93.5	79.3	14.2	0.03
3 Point Decrease	84.1	70.9	13.2	0.08
4 Point Decrease	84.0	60.7	23.3	0.01
5 Point Decrease	73.5	50.7	22.8	0.02
6 Point Decrease	70.5	44.0	26.5	0.01

^a Values for subjects meeting treatment failure criteria are set to missing from point of treatment failure forward.

^b Response based upon multiple imputations for missing data from Wk16 to Wk24, where Markov chain Monte Carlo method is used to make missing pattern monotone and serial logistic regression is used to impute monotone missing. The imputation model includes treatment group and baseline SLEDAI-2K covariate.

^c Test for greater treatment effect in UST over PBO (alternative hypothesis) is based upon logistic regression with treatment group, baseline SLEDAI-2K, baseline medication use for SLE and race as covariates.

patients receiving UST (n=62) vs PBO (n=40) at wk24 using increasing S2K RI-50 reductions of 1, 2, 3, 4, 5, or 6 points from baseline to determine 50% improvement. In order to determine a minimal cut-off to discriminate a treatment effect reflecting partial improvement, nominal level was set at 0.05 for this post hoc analysis.

Results The performance of S2K RI-50 in detecting the treatment difference between UST and PBO with various cut-offs is presented in table 1. A 2-point reduction in S2K RI-50 was the lowest threshold to demonstrate a p-value<0.05. As an example, this could reflect partial improvement in one of the following: renal, arthritis, or myositis, or partial improvement in two of the following disease manifestations: rash, alopecia, mucosal ulcers, pleurisy, pericarditis, low complement or increased anti-dsDNA.

Conclusions S2K RI-50 captures partial improvement of 50% in SLE disease activity in the most common disease manifestations in SLE. S2K RI-50 could be used as an outcome in clinical trials as a clinically meaningful measure of partial improvement.

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INDUCTION OF VASCULITIC LESIONS IN LUPUS-PRONE MICE: A MODEL FOR LUPUS-ASSOCIATED PERIPHERAL VASCULAR DISEASE

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Background Systemic lupus erythematosus is an autoimmune disorder that affects many organs. Many patients develop vasculitis in skin and internal organs. There is no effective treatment for lupus-associated vasculitis. Research on the pathogenesis of lupus vasculitis has been hampered due to lack of appropriate model systems. Many patients with lupus develop chronic changes in skin, kidney and other organs, characterized by fibrosis. To understand the induction and mechanisms of fibrosis in lupus, we injected lupus-prone mice

with bleomycin that is known to induce fibrotic disease in otherwise normal C57/Bl6 mice, and monitored the animals for disease phenotype.

Methods We injected MRL-MpJ-Fas lpr/lpr (MRL-lpr) mice with bleomycin (100 µg, subcutaneously on upper back) or PBS daily for 14 days. Following which, animals were monitored daily for 14 days. Photographs were taken for skin lesions. On day 28, skin, paws, lung, liver, and kidneys were harvested and tissues sectioned for H and E and Masson Trichrome staining. Immunohistochemistry was performed to detect blood vessels and endothelial cells, namely -smooth muscle actin (SMA) and CD31, respectively. Experiments were repeated in MRL-MpJ-Fas +/+ (MRL+/+) mice.

Results Around day 10 of injections, the tips of front and hind paw digits of 7 of 10 bleomycin-injected MRL-lpr and 3 of 3 bleomycin-injected MRL+/+ mice developed erythematous lesions that ulcerated. None of the controls (5 PBS-injected MRL-lpr, 3 PBS-injected MRL+/+, and 3 bleomycin-injected C57/Bl6 mice) developed such lesions. Such lesions have also not been observed in over 50 unmanipulated MRL-lpr and MRL+/+ mice or over 30 bleomycin-injected C57/Bl6 mice in our animal colony in previous studies. Histological and immunohistochemistry analyses showed increased infiltration, fibrosis, tissue destruction, and CD31 expression in bleomycin-injected MRL-lpr mice as compared to control animals. Masson's trichrome staining revealed significantly increased dermal fibrosis in bleomycin-injected MRL-lpr mice as compared to PBS-injected MRL-lpr mice. Preliminary analysis shows increased alveolar hemorrhage in bleomycin-injected MRL-lpr mice as compared to control mice.

Conclusions The vasculitic lesions that we observed in the digits of bleomycin-injected MRL-lpr and MRL+/+ mice mimics vasculitic lesions seen in patients with lupus. Thus, bleomycin injection in lupus-prone mice can serve as a model for chronic vascular changes seen in lupus and other systemic rheumatic diseases.

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EPIGENOME-WIDE ASSOCIATION STUDY REVEALS DIFFERENTIAL DNA METHYLATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH A HISTORY OF ISCHEMIC HEART DISEASE

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Background Patients with systemic lupus erythematosus (SLE) have an increased risk of cardiovascular disease (CVD), including ischemic heart disease (IHD). We performed a case-case epigenome-wide association study (EWAS) for IHD in patients with SLE to identify phenotype-specific differences in DNA methylation.

Methods DNA methylation in peripheral blood samples from two independent cohorts of Swedish SLE patients (n=347 and n=201, respectively) was assayed on the HumanMethylation450k BeadChip array, targeting 485,000 CpG sites across the genome. Clinical data were retrieved from medical charts and individuals with a history of CVD were identified in both cohorts. Differential DNA methylation between SLE patients with a history of IHD (n=20 and n=17, respectively) and SLE patients without any CVD events prior to DNA sampling

was tested using a logistic regression model including age, sex and cell type distribution as covariates. Differentially methylated CpG sites in the discovery cohort were defined as $p < 1.3E-7$ for association based on Bonferroni correction and an absolute average difference in methylation beta of $|| > 0.05$. Significance in the replication cohort was determined as $p < 0.05$ and same direction of effect.

Results The top associated differentially methylated CpG sites that were replicated were identified at programmed cell death 1 (PDCD1, $p(\text{disc})=3.2E-13$; $p(\text{repl})=0.03$), perforin 1 (PRF1, $p(\text{disc})=1E-12$; $p(\text{repl})=0.03$) and ZFP36 ring finger protein like 1 (ZFP36L1, $p(\text{disc})=1.3E-11$; $p(\text{repl})=0.002$), all of which are implicated in apoptotic processes. Functional pathway analysis of genes containing sites with altered methylation in SLE IHD pointed to muscle contraction ($p=4.3E-10$), cardiac conduction ($p=2.2E-7$) and role of agrin in postsynaptic differentiation ($p=2.9E-7$) as the most significantly enriched pathways.

Conclusions The results of this study highlight genes and pathways that may be implicated in the pathogenesis of and/or recovery from IHD in patients with SLE. The differentially methylated CpG sites identified in this study can serve as candidates for further evaluation by functional studies and as potential biomarkers for IHD in patients with SLE.

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THE ASSOCIATION BETWEEN THE DOSE OF GLUCOCORTICOIDS AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CROSS-SECTIONAL STUDY

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Background Glucocorticoids (GC) is a mainstay of treatment for systemic lupus erythematosus (SLE) but generally known to affect the health-related quality of life (HRQOL). The aim in this study is to investigate the association between the current dose of GC and HRQOL in SLE patients.

Methods This was a cross-sectional study using baseline data of nationwide SLE patients registry (LUNA) from April 2018 through September 2018. Participants were outpatients with SLE aged 20 years or older. The exposure was the current dose of GC (an equivalent of daily prednisolone). The primary outcome was the HRQOL score of Lupus Patient Reported Outcome (LupusPRO). We included age, sex, and damage in covariates to be particularly considered for the effect of GC-related damage. Damage was divided into GC-related damage and other damage using the SLICC damage index (SDI). GC-related damage was defined as the presence of diabetes mellitus, osteonecrosis, osteoporotic fractures and cataracts. We used a linear regression model to assess the association between the current dose of GC and the HRQOL and further evaluated which of the current daily dose of GC