treatment withdrawal is contemplated. Until improved blood or urine biomarkers have been developed, repeat biopsy will remain a useful tool for the clinic.

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Oral presentations

01 HYDROXYCHLOROQUINE BLOOD LEVELS AND RISK OF THROMBOTIC EVENTS IN SYSTEMIC LUPUS ERYTHEMATOUS

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10.1136/lupus-2020-eurolupus.15

Background Hydroxychloroquine (HCQ) has a primary role in the treatment of systemic lupus erythematosus (SLE). Beyond its pleiotropic immunomodulatory effects on TLR and type I interferon signaling, HCQ use has been found to be protective for thrombosis in SLE. Optimal dosing of HCQ in SLE is unknown. The longitudinal measurement of HCQ blood levels may provide an opportunity to individualize weight-based dosing strategies and reduce risk of toxicity. We examined the association of HCQ blood levels with thrombotic events in a longitudinal SLE cohort.

Methods 812 SLE patients with HCQ level measured prior to the thrombosis were included: 93% female, 43% African-American, 46% Caucasian. HCQ blood levels were quantified by liquid chromatography-tandem mass spectrometry. Mean HCQ blood levels ($\pm$ SD) over all cohort visits prior to occurrence of thrombosis were calculated for each patient. Thromboses were defined as venous (DVT/PE or other venous) or arterial thrombosis (stroke, myocardial infarction, digital gangrene or other arterial).

Results Thrombosis had occurred during prospective follow up in 44 patients (5.4%), venous in 3.0% and arterial in 2.5%. Lupus anticoagulant was strongly associated with a history of any thrombosis (OR 3.25, $P<0.0001$), venous thrombosis (OR 3.53, $P<0.0001$), and arterial thrombosis (OR 3.08, $P<0.0001$). A prospective analysis shows that for any thrombosis and for venous thrombosis, the HCQ blood level was significantly lower. Higher prescribed doses of HCQ (as opposed to HCQ blood levels) were also associated with decreased odds of any thrombosis and venous thrombosis in a separate cross-sectional analysis (OR 0.88, $P=0.04$ and OR 0.83, $P=0.009$, respectively for each 1 mg/kg increase in prescribed HCQ).

Conclusions HCQ blood levels are inversely associated with risk of any thrombosis and of venous thrombosis in patients with SLE in a prospective analysis. Reduction of HCQ dosing, as suggested by the American Academy of Ophthalmologists, could reduce or eliminate the benefit of hydroxychloroquine to prevent thrombosis.

Acknowledgements The Hopkins Lupus Cohort is supported by NIH Grant RO1 AR 69572.

02 EFFECT OF TREATMENT ON ANTIPHOSPHOLIPID ANTIBODIES IN SLE

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10.1136/lupus-2020-eurolupus.16

Background Unlike primary antiphospholipid syndrome patients, most SLE patients with antiphospholipid antibodies are on one or more treatments for their SLE that might affect levels of their antiphospholipid antibodies. We examined the effect of prednisone and hydroxychloroquine on antiphospholipid antibodies in an SLE longitudinal cohort.

Methods 943 SLE patients, who were tested for each anticardiolipin isotype (aCL IgG, IgM and IgA; INOVA) and lupus anticoagulant (LAC; dRVVT with further confirmatory testing) for at least 10 quarterly clinic visits, were included. We compared visits positive for antiphospholipid antibodies (aCL>20 and aCL>40; dRVVT>45) to visits negative for antiphospholipid antibodies, with respect to treatment, using conditional logistic regression and conditioning on the patient.

Results Prednisone treatment significantly reduced the levels of aCL IgG isotypes (aCL IgG>40 and some prednisone but less than 10 mg/day, OR 0.61 95% CI 0.46–0.80 $p=0.0004$), but not aCL IgM, IgA, or LAC. Hydroxychloroquine treatment significantly reduced aCL IgG (aCL IgG>40, OR 0.35 95% CI 0.22–0.55 $p<0.0001$), aCL IgM (aCL IgM>40, OR 0.56 95% CI 0.36–0.87 $p=0.010$) and LAC (OR 0.71 95% CI 0.58–0.86 $p=0.007$) but not aCL IgA.

Conclusions Prednisone does not reduce IgM or IgA isotypes of anticardiolipin, or LAC. These results explain why prednisone does not reduce thrombosis in SLE. Hydroxychloroquine, on the other hand, significantly reduces all antiphospholipid types except for the IgA isotype of anticardiolipin. This may explain why IgA isotypes are more common in SLE. It may also explain why hydroxychloroquine leads to only a 50% reduction in thrombosis, as IgA isotypes do confer some risk of thrombosis.

Acknowledgements The Hopkins Lupus Cohort is supported by NIH Grant RO1 AR 69572.

03 CHANGES IN GUT MICROBIOTA AFTER SYMBIOTIC SUPPLEMENTATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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10.1136/lupus-2020-eurolupus.17

Background Systemic lupus erythematosus (SLE) is a chronic multiorgan autoimmune disease with high morbidity. The pathogenesis is multifactorial. Gut dysbiosis plays a role in the pathogenesis of systemic lupus erythematosus (SLE). It can cause systemic inflammation.

Methods We conducted a randomized, double-blind, placebo-controlled trial to investigate whether synbiotic supplementation could improve gut microbiota composition and function in patients with SLE.

Results Forty six SLE patients were randomised to two groups: the synbiotic group received synbiotic capsule (*Lactobacillus helveticus* R0052 60%, *Bifidobacterium infantis* R0033 20%, *Bifidobacterium bifidum* R0071 20% and 80 mg fructo-oligosaccharides) for 60 days and placebo group. In the synbiotic-supplemented group, 21 patients completed the intervention. In the placebo group, one was excluded from the final analysis because she needed antibiotic treatment for 33 days. We analysed 16s rRNA microbiome data from 89 faecal samples of the 46 patients. We found increases in the *Firmicutes* to *Bacteroidetes* ratio, butyrate metabolism and nitroto- luene degradation after synbiotic supplementation. We also found a decrease in potentially pathogenic species and an increase in beneficial species.

Conclusion Synbiotic supplementation affect the composition and functions of gut microbiota in patients with systemic lupus erythematosus.

04

BARICITINIB-INDUCED CHANGES IN STAT-ASSOCIATED GENE EXPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2020-eurolupus.18

Background Baricitinib, an oral selective Janus kinase (JAK)1 and 2 inhibitor, resulted in significant clinical improvements in patients with active systemic lupus erythematosus (SLE) receiving standard background therapy in the phase 2 study JAHH (NCT02708095). Baricitinib may impact key cytokines implicated in the pathogenesis of SLE through effects on the JAK/signal transducer and activator of transcription (STAT) signaling pathway. The impact of baricitinib on STAT-related gene expression and associations with clinical response in SLE were evaluated.

Methods 314 patients were randomized 1:1:1 to receive once-daily placebo, baricitinib 2-mg, or baricitinib 4-mg for 24 weeks in JAHH. Patients were ≥ 18 years of age, had a

Abstract 04 Table 1 Number of STAT –related genes whose variation has statistically significant association to SLEDAI-2K variation

STAT	Week	Number of downstream genes	Number of downstream genes with FDR < 0.1	Number of downstream genes with P < 0.05
STAT1	2	135	30	45
STAT1	4	135	0	5
STAT1	12	135	0	2
STAT1	24	135	0	1
STAT2	2	38	11	13
STAT2	4	38	0	2
STAT2	12	38	0	0
STAT2	24	38	0	0
STAT4	2	6	0	1
STAT4	4	6	0	0
STAT4	12	6	0	0
STAT4	24	6	0	0

Spearman rank coefficient correlations between variation in SLEDAI-2K (from baseline) and variation in log2 expression (from baseline) of genes were computed at weeks 2, 4, 12, and 24 with baricitinib 4-mg treatment and tested for statistically significant differences from zero. Genes analyzed were downstream of STAT1, STAT2, or STAT4 as selected from the MetaCore Database. The number of selected downstream genes for each STAT is shown, along with the number of statistically significant genes.

FDR=false discovery rate; SLEDAI-2K=Systemic Lupus Erythematosus Disease Activity Index-2000; STAT=signal transducer and activator of transcription