functioning (61.1 ± 24.9 versus 55.0 ± 26.5 ; $P < 0.001$), role physical (53.2 ± 26.9 versus 50.3 ± 27.7 ; $P = 0.036$), bodily pain (49.5 ± 23.8 versus 47.1 ± 25.3 ; $P = 0.016$), FACIT-Fatigue scores (30.5 ± 11.8 versus 29.3 ± 11.9 ; $P = 0.046$), EQ-5D scores (0.75 ± 0.18 versus 0.72 ± 0.19 ; $P = 0.004$) and EQ-5D visual analogue scale (VAS) scores (64.6 ± 19.4 versus 61.7 ± 18.6 ; $P = 0.001$). The difference in SF-36 physical functioning was the greatest one among the SF-36 parameters, exceeding the corresponding MCID (≥ 5.0 points). The association between AMA use and better physical functioning was still significant after adjustment for potential confounding factors (standardised coefficient, $\beta = 0.08$; $P = 0.001$). In this analysis, Asian patients performed better in physical functioning ($\beta = 0.07$; $P = 0.004$) while African/African American patients performed worse ($\beta = -0.07$; $P = 0.003$). High disease activity ($\beta = -0.09$; $P < 0.001$) and organ damage ($\beta = -0.12$; $P < 0.001$) were also independent factors of worse physical functioning, whereas corticosteroid use independently improved the outcome ($\beta = 0.06$; $P = 0.022$).

Conclusion: AMA use contributes to better physical functioning in patients with SLE, independently of other factors.

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FRI0206 HYDROXYCHLOROQUINE BLOOD LEVELS PREDICT RETINOPATHY IN SLE

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Background: Hydroxychloroquine (HCQ) retinopathy after 10 years or more of use is more frequent than previously appreciated. This led to new ophthalmology guidelines that changed the recommended dosing from 6.5 mg/kg to 5 mg/kg (1). However, it is not clear that the lower dose of hydroxychloroquine will have the same efficacy for SLE activity or the same protective role against cardiovascular risk factors and thrombosis.

Table 1. Risk of HCQ retinal toxicity (univariate)

Characteristic	No n (%)	Yes n (%)	p	P for Trend
Sex			0.1029	
Female	475 (96.2)	19 (3.8)		
Male	39 (90.7)	4 (9.3)		
Ethnicity			0.3804	
White	238 (94.4)	14 (5.6)		
Black	215 (96.4)	8 (3.6)		
Other	61 (98.4)	1 (1.6)		
Age			<0.0001	<0.0001
<45	215 (99.5)	1 (0.5)		
45-59	175 (95.6)	8 (4.4)		
60+	124 (89.9)	14 (10.1)		
HCQ max			0.0340	0.0143
1 (0 to 1182)	161 (98.8)	2 (1.2)		
2 (1183 to 1752)	157 (95.2)	8 (4.8)		
3 (1753 to 6281)	153 (93.3)	11 (6.7)		
HCQ duration			0.0006	0.0002
1 (0 to 8yrs)	158 (98.8)	2 (1.2)		
2 (9 to 15yrs)	139 (97.2)	4 (2.8)		
3 (16 to 48yrs)	154 (90.1)	17 (9.9)		
BMI			0.1701	0.0160
<20	50 (98.0)	1 (2.0)		
20-25	171 (97.7)	4 (2.3)		
25-30	159 (95.2)	8 (4.8)		
30-35	76 (95.0)	4 (5.0)		
35+	58 (90.6)	6 (9.4)		
HTN Ever			0.0020	
Yes	276 (93.2)	20 (6.8)		
No	238 (98.8)	3 (1.2)		

Objectives: We asked whether hydroxychloroquine blood levels could help identify those at greater future risk of retinopathy.

Methods: We analyzed data on 537 SLE patients from a clinical cohort who had repeated assessments of HCQ blood concentrations, and were evaluated one or more times for retinopathy (300 single retinopathy exam, 149 two and 88 three or more assessments). The patients were 92% female and 42% Caucasian. Hydroxychloroquine blood levels were performed as previously described. In our analysis, HCQ toxicity was defined dichotomously by a retina expert: all those with a value of "No" or "Possible" were categorized as not having HCQ toxicity, and those who had a "Yes" were categorized as having it. Mean and maximum HCQ blood concentration over all cohort visits prior to the final retinopathy assessment were calculated. Risk of HCQ toxicity was then assessed in tertiles defined by these variables.

Results:

Conclusion: Our data show that the risk of HCQ retinopathy is higher in men and Caucasians. As expected, it is higher in older patients and with greater duration. We also found that BMI and hypertension were predictive of HCQ retinopathy. For the first time, our data show the utility of HCQ blood levels in predicting retinopathy. This would allow clinicians to either decrease dose or increase monitoring in those with high blood levels.

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FRI0207 BASELINE LEVELS OF BAFF, APRIL AND CD8+ EFFECTOR MEMORY CELLS AS PREDICTORS OF SLEDAI RESPONSE TO BELIMUMAB THERAPY

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Background: Systemic lupus erythematosus (SLE) patients show high circulating levels of BlyS (B lymphocyte stimulator, also known as BAFF) and of other cytokines belonging to the tumor necrosis factor (TNF) superfamily [1]. Belimumab is a monoclonal antibody against soluble BlyS used for treatment of refractory SLE. Although B cells are the main target of this therapy, a BlyS-dependent T cell activation pathway has also been demonstrated [2]. Clinical studies showed that high levels of anti-DNA antibodies and low complement at baseline are predictors of response to Belimumab treatment.

Objectives: Our study aims at exploring the role of biomarkers belonging to the TNF superfamily and of effector T-lymphocytes as predictors of response.

Methods: Twenty-one patients with SLE received Belimumab. Clinical evaluation and laboratory test were performed at baseline and after six and twenty months of therapy. Biomarkers belonging to the TNF superfamily (BAFF, APRIL, sBCMA, sCD40L, sTACI, TWEAK) were tested by high-sensitivity ELISA in all patients and lymphocyte immunophenotyping was performed by flow cytometry in ten subjects. SLE-disease activity was assessed by SLEDAI-2K score.

Results: BAFF and APRIL baseline serum levels and the number of CD3+CD8+ effector memory T cells were correlated positively with SLEDAI-2K improvement after 12 months of treatment (Pearson correlation=0.535 ($p=0.015$), 0.504 ($p=0.023$) and 0.654 ($p=0.040$)). After backwards exclusion from linear regression analysis including SLEDAI-2K, effector T cell relative number and BAFF or APRIL at baseline, only APRIL remained as significant independent predictor of SLEDAI-2K improvement after 12 months of therapy (adjusted R square=0.649; $p=0.025$). Moreover, after comparing TNF-family members serum levels and SLEDAI-2K at baseline, only BAFF showed the best predictive value (adjusted R 0.564, $p < 0.001$).

Conclusion: In our cohort of SLE patients, baseline serum level of APRIL together with percentage of CD3+CD8+ effector memory cells, or BAFF serum level alone resulted as best predictors of response to Belimumab. Considering that immunophenotyping is often not done in clinical practice, BAFF baseline serum levels alone could be used routinely as a good predictor of response to therapy, as suggested by post-hoc analyses of the BLISS study and showed by a recent "real-life" observational study [3].

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FRI0208

IDENTIFYING LUPUS PATIENT SUBSETS AND SPECIFIC PHARMACODYNAMIC CHANGES THROUGH IMMUNE CELL DECONVOLUTION OF GENE EXPRESSION DATA IN ATACICEPT-TREATED PATIENTS IN THE APRIL-SLE STUDY

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Background: The Phase 2/3 APRIL-SLE study evaluated the safety and efficacy of atacicept, a dual inhibitor of the B lymphocyte stimulator (BLyS) and a proliferation-inducing ligand (APRIL), in systemic lupus erythematosus (SLE).

Objectives: The goal of this post-hoc analysis was to use cell-based gene signatures on gene expression data from the APRIL-SLE study to identify clusters of patients with potential to flare and to assess clusters for differences in treatment effects of atacicept vs placebo.

Methods: A published immune cell deconvolution algorithm (Abbas *et al*, 2009) was applied to whole-blood gene expression data from APRIL-SLE patients to identify relative proportions of 17 immune cell types. Patients were then grouped into clusters based on these immune cell profiles using a k-medoid clustering algorithm and were compared to each other based on patient characteristics, biomarkers and clinical efficacy. In addition, baseline expression and change in expression of putative APRIL-responder genes were compared among clusters. APRIL-responder genes were identified by combining differential expression results from the APRIL-SLE study (Week 52 vs Day 1 randomization) and tabalumab (targets BLyS only) Phase 3 studies (Week 52 vs baseline; GSE88887).

Results: Patient gene expression data (N=105; placebo, n=30; atacicept 75 mg, n=40; atacicept 150 mg, n=35) were used to group patients into five main clusters (P1-P5) by predominant characteristic cells: P1, T helper cells; P2, plasma cells; P3, neutrophils and B cells; P4, B cells; P5, activated dendritic cells. Patients in P2 and P5 were more likely to have positive anti-dsDNA antibodies (≥ 30 IU/ml), elevated BLyS; ≥ 1.6 ng/ml, and high interferon gene signature in the blood than other those in other clusters. Patients in P2 were most likely to have low complement C3 and C4 levels. Placebo-group flare rates in P2 (100%), P4 (100%) and P5 (83%) were markedly higher than in P1 (33%) and P3 (29%). In P2, P4, and P5 the median time-to-flare was much lower with placebo (85, 98.5, and 115.5 days, respectively) than with atacicept 150 mg (over 364 days for all three clusters). A comparison of differentially-expressed genes from clinical studies of SLE patients treated with

atacicept and tabalumab revealed possible APRIL-responder genes: SDC1, PARM1 and MZB1. These genes had a higher baseline expression in P2 and P4 compared with other clusters. SDC1 was reduced from baseline more in P2, P4, and P5 after atacicept treatment, while PARM1 and MZB1 decreased after atacicept treatment in P2 and P4.

Conclusion: These post-hoc analyses revealed different subsets of SLE patients based on their molecular profiles. Atacicept may have different treatment effects in the identified patient subsets vs placebo, providing insights into potential mechanisms of flare in SLE.

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FRI0209

LOW-DOSE GLUCOCORTICOID COULD AFFECT ADVERSE PREGNANCY OUTCOMES, ESPECIALLY IN PRETERM BIRTH, LIGHT-FOR-DATE NEWBORNS, PRETERM PREMATURE RUPTURE OF MEMBRANE IN CONNECTIVE TISSUE DISEASE PATIENTS

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Background: Connective tissue disease (CTD) often occurs in women of child-bearing age, and flare-ups during pregnancy. Therefore, it is important to manage their disease activities with the treatment which have no influence on fetal growth and development. Among the treatment during pregnancy glucocorticoid is most often used for maintain or control to flare-ups of CTD disease activities. However, prolonged use of glucocorticoid during pregnancy is considered to increase the risk of adverse pregnancy outcomes (APOs) including preterm birth, intrauterine growth restriction, and premature rupture of membrane (PROM) (1, 2).

Objectives: The aim of this study is to reveal the dose of glucocorticoid which influences on APOs.

Methods: We investigated 164 pregnant patients complicated with CTD from March 2006 to January 2019. All these patients were managed their disease activities throughout pregnancy in our institute. APOs including preterm births, light-for-date (LFD) newborns, PROMs in these pregnant patients were examined retrospectively. We analyzed the association between APOs and the incidence or mean dose of glucocorticoid use during pregnancy.

Results: Underlying CTD is Systemic lupus erythematosus (25.3%), Sjogren's syndrome (24.9%), rheumatoid arthritis (18.1%), Antiphospholipid syndrome (8.8%), mixed connective tissue disease (6.7%), and others. Glucocorticoid was administered in 96 cases, which tended to be earlier gestational week at delivery (37.5 $\pm$ 3.0 vs. 38.9 $\pm$ 1.5, P<0.01) and lower birth weight of newborns (2601.9 $\pm$ 603.0 vs. 3019.0 $\pm$ 480.8, P<0.01) significantly. Compared with full-term birth, the cases of preterm birth had higher dose of glucocorticoid during pregnancy significantly (P<0.01). Logistic regression analysis for preterm birth revealed the cut-off value of mean prednisolone dose as 7.5 mg per day (Figure 1). Similarly, the