weeks), with 4 having CR and 6 PR. The median response duration (MRD) was 12 weeks.

Conclusion: Our study provided preliminary but promising clinical evidence for iguratimod in treating refractory LN patients. A large randomized clinical trial is needed to establish its safety and efficacy for refractory LN.

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FRI0216B

SELECTIVE IRAK4 INHIBITOR DAMPENS MYD88 SIGNALING AND AMELIORATES INFLAMMATION AND FIBROSIS IN A MOUSE MODEL OF LUPUS NEPHRITIS

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Background: IRAK4 is an important signaling mediator of the innate immune system. IRAK4 initiates MyD88-dependent signaling from most TLRs and from IL-1Rs, resulting in downstream production of pro-inflammatory cytokines¹.

Objectives: Inhibition of IRAK4 kinase activity is a promising therapeutic approach for the treatment of autoimmune diseases, such as lupus. To this end, we identified a potent and highly selective inhibitor of IRAK4 kinase activity, BIIB-IRAK4i.

Methods: Recombinant kinase assays and DiscoverX kinome scan were used to measure BIIB-IRAK4i kinase inhibition and selectivity, respectively. BIIB-IRAK4i-mediated proximal and distal pharmacodynamics effects (PD) were measured in both cell lines and whole blood assays. The ability of BIIB-IRAK4i to inhibit cytokine production induced by TLR ligands was measured *in vitro* and *in vivo*. Acute antibody-mediated lupus nephritis mouse model, which is a TLR-7 dependent and characterized by severe glomerular proliferative lesions with crescent formation, was used to determine the efficacy of BIIB-IRAK4i.

Results: BIIB-IRAK4i displayed equipotent proximal inhibition of MYD88 signaling and distal inhibition of cytokine production *in vitro*. BIIB-IRAK4i led to potent inhibition of cytokine production in whole blood assays stimulated with various synthetic TLR ligands as well as more physiological stimuli such as immune complexes, a hallmark of lupus pathogenesis. BIIB-IRAK4i inhibited TLR9-mediated cytokine production with same potency *in vitro* and *in vivo*. In addition, BIIB-IRAK4i decreased both inflammation and fibrosis in an acute antibody-mediated lupus nephritis mouse model. BIIB-IRAK4i inhibited crescent formation as well as markers of tubulointerstitial fibrosis, which are both associated with decreased survival and adverse outcomes in human lupus nephritis.

Conclusion: Our study highlights that pharmacological inhibition of IRAK4 can reverse two key components of lupus nephritis; the inflammatory and the fibrotic response.

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SLE, Sjögren's and APS – clinical aspects (other than treatment)

FRI0217

PREGNANCY OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN TERTIARY UNIVERSITY HOSPITAL IN EGYPT

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Background: Pregnant systemic lupus erythematosus (SLE) patients have various risks to their fetus and themselves because a severe disease flare may be life-threatening, and some of the medications that are used to treat SLE adversely affect fetus.⁽¹⁾

Objectives: To evaluate the pregnancy outcome in SLE patients and to determine the predictive factors for adverse fetal and maternal outcomes.

Methods: The study was conducted on the pregnant SLE patients attending Rheumatology department, Zagazig University hospitals in the period from January 2013 to January 2018. The data was collected retrospectively; demographic, laboratory and serological data on all patients, age at the onset of SLE, disease duration, systems affected, their disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), treatment received immunosuppressive regimen (dose and duration) before and during pregnancy, SLE flare during pregnancy, the fetal and the maternal outcomes.

Results: Fifty-two pregnancies were observed in 49 SLE patients with mean age of (27.5±5.6), mean SLE disease duration (3.7±2.2) and mean SLEDAI (5.4±6.1). 39 (75%) pregnancies with successful live births and 13(25%) fetal losses were observed. 36 of the live births (92.3%) were full-term and 3 (7.7%) were preterm births. Fetal losses included six spontaneous abortions, 3 stillbirths and 4 therapeutic abortions; 2 of them due to observed fetal anomalies and one due to life threatening lupus flare. We found SLEDAI significantly higher in patients with lost pregnancies ($p<0.0001$) than successful pregnancies. Proteinuria during pregnancy was a predictive factor for adverse fetal outcomes (odds ratio [OR] 19.7; $P<0.0001$), also the presence of antiphospholipid antibodies (OR 15.3; $P<0.0001$), low C3 and C4 (OR 15.3; $P<0.0001$), anti-RO antibodies (OR 11.1; $P=0.02$), anti-LA (OR 4.7; $P=0.03$), chronic hypertension (OR 54.8; $p<0.0001$) and SLE flares (OR 32; $p=0.003$). SLE flares occurred in 10 pregnancies (19.2%), mostly during the second trimester (60%). Renal involvement (70%) was the most common SLE flare during pregnancy. SLE flares during pregnancy were highly associated by nephritis prior to pregnancy (adjusted OR 9; $P=0.04$) and the presence of antiphospholipid antibodies (adjusted OR 12; $p=0.01$).

Conclusion: Favorable pregnancy outcome was observed in Egyptian SLE patients; particularly in those with longer period of remission. Planned pregnancy is very important to reduce undesirable fetal and maternal outcomes in SLE patients. The presence of lupus nephritis, chronic hypertension, antiphospholipid syndrome, active disease at the onset of pregnancy, and proteinuria were highly associated with bad outcome.

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FRI0218

IMMUNOPHENOTYPIC SUBGROUPS OF SLE DEFINED BY AUTOANTIBODIES, GENE EXPRESSION AND FLOW CYTOMETRIC ANALYSIS

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Background: SLE may be stratified according to a range of different immune assessments but the relationships between these are less well defined. MASTERPLANS is an MRC-funded consortium that seeks to identify immunophenotypic subgroups of patients that predict response to therapy.

Objectives: Our objective here was to analyse a clinically well-phenotyped patients using a suite of immune assessments and identify inter-relationships between these features as well as subgroups of patients who may differ in response to therapy.

Methods: 143 SLE patients were evaluated for clinical phenotype using BILAG-2004, autoantibodies using radioimmunoprecipitation (IP, University of Bath), two interferon scores (IFN-Score-A and IFN-Score-B), flow cytometry for major circulating immune cell subsets, as well as the surface protein expression of tetherin on each subset, a cell-specific assay for IFN response.

Unsupervised hierarchical clustering was used to define autoantibody subgroups. IFN scores (reflected dCT) were compared between the groups using multivariate models. Other variables were compared using Kruskal-Wallis test with pairwise comparisons.

Results: Using IP, 141 patients could be divided into five subgroups: U1RNP/Sm+ only (n=23), Ro60+ only (n=8), U1RNP/Sm+Ro60+ (n=6), Ro60+Ro52+La+ (n=11), Ro52+ (n=16) and other ANA (n=77).

Antibody subgroups was strongly associated with IFN-Score-A ($F=4.39$, $p=0.001$). Expression was lowest for "other ANA", intermediate for single antibody groups, and highest with multiple positive antibodies. Multivariate linear regression, including interaction terms between antibody types, revealed that Ro60 and U1RNP/Sm were the independent predictors of IFN-Score-A level ($p=0.051$ and 0.009 respectively). There was no association between autoantibody status and IFN-Score-B ($F=0.973$, $p=0.438$).

In flow cytometry, the U1RNP/Sm group was notable for significantly lower numbers of CD4-T-cells and memory-B-cells. Memory -B-cells were also lower in antibody-positive groups compared to "other ANA". Tetherin expression was increased in antibody positive groups, but to a similar extent on most cell subsets. Memory B cell tetherin was significantly higher in the groups with multiple positive antibodies.

U1RNP/Sm+ was associated with renal involvement ($p=0.004$). Mucocutaneous involvement was greater in the Ro60+Ro52+La+ group ($p=0.037$).

Conclusion: This cohort revealed relationships between immune features. U1RNP/Sm antibody was notable for defining a group of patients with a cluster of immune abnormalities, including the greatest elevation of IFN activity, greater abnormalities on flow cytometry and clinical renal involvement. This was independent to the IFN-Score-B high status that predicts better clinical response to rituximab (presented elsewhere at this conference). Future work in MASTERPLANS will investigate the significance of these subgroups for response to therapy.

Table 1: Multivariate analysis of antibody status and IFN Score A

Predictor	Ab-Negative Score-A Mean(SD)	Ab-Positive Score-A Mean(SD)	Univariate OR (95% CI)	P	Multivariable OR (95% CI)	P
U1RNP/Sm	3.59 (2.89)	1.46 (1.53)	-2.4 (-2.7, -0.34)	0.012	-2.7 (-2.7, -0.4)	0.009
Ro60	3.75 (2.82)	1.83 (1.72)	-3.1 (-3.0, -0.83)	0.001	-2.0 (-2.7, 0.0)	0.051
La	3.39 (2.72)	1.51 (1.39)	-2.0 (-2.7, -0.4)	0.046	-0.35 (-2.7, 1.9)	0.73
Ro52	3.52 (2.80)	1.95 (1.53)	-2.1 (-2.9, -0.22)	0.023	-0.86 (-2.4, 0.9)	0.39
U1RNP+Ro60	N/A	N/A	N/A	N/A	0.05 (-2.1, 2.1)	0.67
Ro60+Ro52	N/A	N/A	N/A	N/A	0.27 (-1.3, 1.8)	0.21
Ro52+La	N/A	N/A	N/A	N/A	-0.41 (-10.5, 1.26)	0.12

*Note these are untransformed dCT values, so numerically higher values represent lower gene expression

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FR10219

CD4+CD25+FOXP3+ REGULATORY T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: THE NEGATIVE ASSOCIATION WITH DISEASE ACTIVITY, ACUTE COURSE, TRANSITIONAL B CELLS AND IGG LEVELS

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Background: CD4+ CD25+ Foxp3+ regulatory T (Treg) cells play a key role in maintaining peripheral tolerance and preventing autoimmune disease. Quantitative and/or qualitative deficiencies of Treg have been associated with immune disturbances in systemic lupus erythematosus (SLE).

Objectives: The main goal of the study was to determine the relationship of CD4+CD25+FoxP3+Treg cells with clinical and immunological manifestations in SLE patients (pts).

Methods: Frequencies and absolute numbers of peripheral blood CD4+CD25+FoxP3+Treg cells were assessed in 21 healthy donors and 20 SLE pts (2012 SLICC classification criteria); (1M/19F); age 32±13 years; disease duration median (25–75 percentile) 5(1–10) years; SLEDAI2K≥10 - 15(10–22) (14 pts), <10 - 7(6–8) (6 pts). All pts were treated with prednisone, hydroxychloroquine, azathioprine, mycophenolate mofetil, cyclophosphamide. CD4+CD25+FoxP3+ Treg cells and B-cell subsets were analyzed using multicolor flow cytometry.

Results: Compared with healthy donors, SLE pts demonstrated significantly lower the absolute number of Tregs (0.05; 0.04–0.06 vs 0.03; 0.02–0.05×10⁹/L, $p<0.036$), with a high percentage of Treg (8.8; 7.5–10.5 vs 12.0; 8.8–17.0%, $p<0.02$). The median percentage of Tregs was lower in pts with acute SLE compared to chronic SLE pts (9.0; 8.3–9.9 vs 13.5; 12.7–18.7%, $p<0.02$). SLE pts with high activity had a lower frequencies of Tregs (10.2; 8.5–15.0 vs 15.8; 12.7–20.4%, $r=-0.51$, $p<0.05$). Low count of Tregs correlated with elevated level of IgG ($r=-0.52$, $p<0.05$). Absolute number of Tregscorrelated negatively with percentage and absolute count of transitional (CD19+IgD+CD10+CD38++CD27-) B cells ($r=-0.66$ and $r=-0.63$, $p<0.05$).

Conclusion: Decreased amount of T regs in SLE is associated with high disease activity, acute course and expansion of autoreactive B cells.

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FR10220

OCULAR SURFACE INFLAMMATORY MARKERS CORRELATED WITH IMMUNOLOGICAL PARAMETERS IN PRIMARY SJÖGREN'S SYNDROME

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Background: In Sjögren's Syndrome (SS), ocular damage is mediated by inflammation induced by antibodies, enzymes, and other effectors that could be used as clinical indicators of the ocular surface damage. There is evidence suggesting that increased activity of matrix metalloproteinases (MMPs) is correlated with an increased ocular damage because of its potential inflammatory activity and could be used as a potential therapeutic target for dry eye^{1,2}. Very few studies have addressed the role between the ocular MMPs and the clinical parameters of SS.

Objectives: To determine the level of correlation between the serological profile of autoantibodies with ophthalmological parameters at the cornea level.

Methods: Cross-sectional, observational, and descriptive study. Sixty patients with a diagnosis of primary Sjögren's syndrome (pSS) classified according to the ACR/EULAR 2016 criteria were included. The following measurements were made: Schirmer test, lacrimal osmolarity, ocular staining score (OSS), and ocular surface disease index (OSDI) and metalloproteinase-9 (MMP-9) in tear and antibodies were measured in peripheral blood serum: RF isotypes (IgA, IgG, IgM), anti-SSA/Ro and anti-SSB/La in.

Results: Fifty-eight women participated (96.7%) with an average age of 53 years (± 13.01) (Table 1). We found a positive correlation between OSS and RF-IgM ($\rho=0.385$ $P=0.002$), RF-IgA ($\rho=0.256$ $P=0.049$), and anti-Ro/SSA ($\rho=0.302$ $P<0.019$). We found a statistically significant association between the seropositivity of the Anti-SSA/Ro antibody and the presence of MMP-9 in tears (OR 4.38, CI 95% 0.877–21.92, $P=0.057$). A