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FRI0295 HIGH RISK OF IDIOPATHIC OSTEONECROSIS IN SLE PATIENTS WITH HIGH ANTIPHOSPHOLIPID SCORE AND HYPERTRIGLYCERIDEMIA

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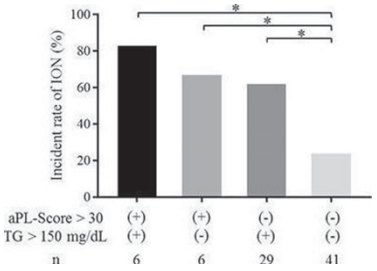
Background: Systemic lupus erythematosus (SLE) patients are prone to develop idiopathic osteonecrosis (ION) compared to other connective tissue disease patients or healthy subjects. ION has been shown to occur as a result of ischemia, however, the involvement of antiphospholipid antibodies (aPL) in its pathophysiology remains to be elucidated. In the last years, our group introduced a quantitative marker of aPL "antiphospholipid score (aPL-S)", which well reflected the risk of developing thrombosis [1].
Objectives: We aimed to identify the impact of aPL on the development of ION using aPL-S.
Methods: A single center retrospective study comprising 82 consecutive patients who were diagnosed SLE at the Rheumatology department of Hokkaido University Hospital and underwent magnetic resonance imaging (MRI) of hip joints from January 2000 to December 2016. Among all the enrolled patients, aPL-S, which is calculated from 0 to 86, as well as classical risk factors for ION were evaluated.
Results: All 82 patients (13 males and 69 females) were given glucocorticoids. ION of the femoral head was diagnosed by MRI scan in 37 patients. Male (ION(+): ION(-) 10/37 (27%) vs 3/45 (7%), p=0.016), malar rush (ION(+): ION(-) 22/37 (59%) vs 16/45 (36%), p=0.045), aPL positivity (ION(+): ION(-) 22/37 (59%) vs 15/45 (33%), p=0.026), high aPL-S (>30) (ION(+): ION(-) 9/37 (24%) vs 3/45 (7%), p=0.031), hypertriglyceridemia (fasting triglyceride levels >150 mg/dL) (ION(+): ION(-) 23/37 (62%) vs 12/45 (27%), p=0.002) and high dose of glucocorticoids (equivalent to 0.8mg/kg or more prednisolone) (ION(+): ION(-) 34/37 (92%) vs 21/45 (47%), p<0.001) were identified as risk factors for ION at univariate analysis. Multivariate analysis confirmed high aPL-S (OR 5.27; 95% CI 1.08 to 34.52, p=0.040), hypertriglyceridemia (OR 5.66; 95% CI 1.79 to 20.73, p=0.003) and high dose of glucocorticoids (OR 16.11; 95% CI 4.01 to 92.54, p<0.001) as independent variables. Of note, in 6 patients who had both high aPL-S and hypertriglyceridemia, 83% (5/6) developed ION (Figure 1). Conversely, systemic lupus erythematosus disease activity index and pulsed methylprednisolone therapy were not identified as risk factors for ION.



Conclusions: We newly identified high aPL-S as a risk factor for ION. Furthermore, SLE patients who have both high aPL-S and hypertriglyceridemia are at very high risk of ION. These findings suggest the involvement of microvascular occlusion in the pathophysiology of ION in SLE.
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Disclosure of Interest: None declared
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FRI0296 SINGLE CENTER EXPERIENCE WITH 300 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with diverse clinical manifestations.
Objectives: Here, we present 300 patients with SLE attending our clinic between 2001 and 2017.
Methods: Demographics, clinics, laboratory findings, Systemic Lupus International Clinics (SLICC)/American College of Rheumatology (ACR) damage index scores and treatments were analyzed. Diagnosis was confirmed with 1997 ACR (1) or 2012 SLICC (2) classifications. Descriptive statistical tests were used for analysis.
Results: Demographics and clinical characteristics are presented in Table 1. Anti-dsDNA was positive in 185 (61.6%), anti-Sm was positive in 35 (11.6%), anti-phospholipid antibodies was positive in 67 (22.3%), direct Coombs test was positive in 69 (23%) patients. Complement levels were low in 171 (57%) patients. In patients with renal disease, class IV lupus nephritis was the most common form (37 patients [12%]) followed by class II nephritis (34 patients [11%]). Forty-six patients had antiphospholipid syndrome. Treatments patients ever received are presented in Table 2. Cyclophosphamide treatment was given mostly for renal disease. Within 22 patients receiving rituximab, 2 had thrombocytopenia and 1 had hemolytic anemia unresponsive to other treatments, 1 had protein-losing enteropathy and 1 had lupus enteritis; the rest had lupus nephritis. One patient received intravenous immune globulin (IVIG) for severe neutropenia and 2 patients for severe thrombocytopenia. One patient received plasmapheresis for vasculitis. One patient received IVIG, plasmapheresis, rituximab for severe renal failure, alveolar hemorrhage requiring intensive care unit admission and 1 patient received same treatment for severe unresponsive hemolytic anemia.

Table 1. Demographics, clinical characteristics of patients

Age (years)	46±13 (min-max: 20–83; median: 45)
Duration of follow up (months)	58±52 (min-max: 1–180; median: 48)
Gender (Female/Male)	267 (89%)/33 (11%)
Muco-cutanous (n, %)	214 (71.3%)
Arthritis (n, %)	198 (66%)
Renal disease (n, %)	121 (40.3%)
Leukopenia/lymphopenia (n, %)	200 (66.6%)
Hemolytic anemia (n, %)	19 (6.3%)
Thrombocytopenia (n, %)	58 (19.3%)
Serositis (n, %)	55 (18.3%)
Nervous system disease (n, %)	24 (8%)
Anti-phospholipid Syndrome (n, %)	46 (15.3%)

Table 2. Treatment

Steroid/pulse treatment (n, %)	294 (98%)/65 (21.6%)
Hydroxycholoroquine (n, %)	300 (100%)
Azathioprine (n, %)	196 (65.3%)
Mycophenolate mofetil (n, %)	83 (27.6%)
Cyclophosphamide (iv) (n, %)	78 (26%); 10±4.5 cycles (min-max: 2–17)
Rituximab (n, %)	22 (7.3%)
Intravenous immunglobulin (IVIG) (n, %)	7 (2.3%)
Plasmapheresis (n, %)	4 (1.3%)

Conclusions: In long term, SLICC/ACR damage index was highest in patients received pulse steroid for renal disease (min:0, max:5). Four (1.3%) patients had pulmonary hypertension, 31 (10.3%) had avascular necrosis, 24 (8%) had viral infections requiring treatment or bacterial infections requiring admission due to immunosuppression, 12 (4%) had malignancy. SLE is an autoimmune disease requiring multi-faceted approach.
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[1]) Hochberg MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 40:1725 1997.
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FRI0297 ROLE OF SERUM INTERLEUKIN-6 IN BLOOD BRAIN BARRIER DAMAGES IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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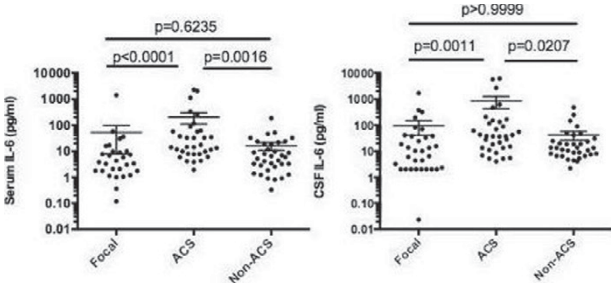
Background: Neuropsychiatric manifestation in systemic lupus erythematosus (NPSLE) is one of the most serious complications of the disease. We have recently demonstrated that the breakdown of blood brain barrier (BBB) plays a crucial role in the development of diffuse psychiatric/neuropsychological manifestations (diffuse NPSLE), allowing influx of neuron-reactive autoantibodies from systemic circulation into the brain. However, the mechanism of BBB damages remains unclear. On the other hand, although CSF interleukin-6 (IL-6) has been shown to be elevated in NPSLE, there has been no report on serum IL-6 in NPSLE.
Objectives: The present study was designed in order to elucidate the roles of serum IL-6 in the pathogenesis, especially in development of BBB damages, In NPSLE.
Methods: Paired serum and cerebrospinal fluid (CSF) samples were obtained from 101 SLE patients when they presented active neuropsychiatric manifestations (69 patients with diffuse psychiatric/neuropsychological syndromes [diffuse NPSLE] and 32 patients with neurologic syndromes or peripheral nervous system involvement [focal NPSLE]) and from 22 non-SLE control patients with non-

inflammatory neurological diseases. The levels of albumin and IL-6 in CSF and sera were measured by ELISA.
Results: Serum IL-6 as well as CSF IL-6 was significantly elevated in acute confusional state (ACS) compared with non-ACS diffuse NPSLE (anxiety disorder, cognitive dysfunction, mood disorder and psychosis) or focal NPSLE (figure). Q albumin (CSF/serum albumin quotient) was also significantly higher in ACS than in the other 2 groups of NPSLE. Of note, serum IL-6 (r=0.2801, p=0.0207), but not CSF IL-6 (r=0.1602, p=0.1918), was significantly correlated with Q albumin in patients with diffuse NPSLE, including ACS and non-ACS, although serum IL-6 was significantly correlated with CSF IL-6 in this population (r=0.3205, p=0.082).



Conclusions: These results indicate that serum IL-6 as well as IL-6 is involved in the pathogenesis of NPSLE. The data also confirm that the severity of BBB damages plays a crucial role in the development of ACS, the severest form of diffuse NPSLE. Finally, it is suggested that serum IL-6 might play a most important role in BBB breakdown in NPSLE, whereas CSF IL-6 might be involved in subsequent central nervous system inflammation.
Disclosure of Interest: None declared
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FRI0298 APPLICATION OF PROPENSITY SCORE-MATCHING METHODS TO COMPARE DATA FROM LONG-TERM EXTENSION TRIALS WITH DATA FROM AN EXISTING LUPUS REGISTRY

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Background: Phase III randomised controlled trials (BLISS 52 and 76) in patients with systemic lupus erythematosus (SLE) have established the efficacy and safety of belimumab plus standard SLE therapy (SoC) vs SoC alone. As with many continuation studies, the long-term extensions (LTE) of the BLISS trials (BEL112233/NCT00724867 and BEL112234/NCT00712933) were single-arm, open-label studies; therefore, comparative long-term efficacy of belimumab and SoC vs SoC was not assessed. Existing observational databases could provide a valuable source of comparison data.
Objectives: This study (BEL206347) explores the use of propensity score (PS) adjustment to enable a post-hoc comparison of LTE patients to patients from an existing SLE cohort, assessing long-term efficacy of belimumab plus SoC vs SoC using the SLICC/ACR Damage Index (SDI) as the outcome.
Methods: Potential PS model criteria were identified by a systematic literature review for factors predicting organ damage. PS model criteria were restricted to baseline (at index [first recorded disease activity of SLE Disease Activity Index {SLEDAI} $\geq$6] for SoC cohort) characteristics available for both cohorts, including age, gender, race, disease duration, clinical and laboratory characteristics, SLEDAI over time, baseline SLEDAI and SDI and SoC (e.g. corticosteroid use/dose). Patients with active severe lupus nephritis/central nervous system lupus, those who had received B-cell-targeted therapy or belimumab or those with an index date before 1990 were excluded from the SoC cohort. The primary PS procedure used 1:1 matching with a 20% calliper (PSM); alternatively, inverse PS weighting (IPSW) was used to preserve the LTE sample. The balance in baseline factors across cohorts pre-/post-PS-adjustment was assessed using standardised distance measures.
Results: The literature review identified the Toronto Lupus Cohort (TLC) as an external registry with a comparable patient cohort. Without PS-adjustment, the standardised distance across cohorts exceeded 25% for 13 of 17 baseline factors in the PSM model. After PSM, standardised distance was <10% for all factors, but less than half of the LTE patients were matched. Using IPSW, data from all patients could be used but with a weighted standardised distance of <10% for 8 and <25% for 15 of the 17 PSM model factors.
Conclusions: The TLC was identified as an existing lupus registry with the endpoints of interest and detailed clinical characteristics. PS matching further maximised the comparability of the LTE and TLC cohorts. The final predictors used in the matching will be validated by two SLE clinicians. The preliminary results indicate a statistically adequate balance in clinical characteristics is attainable. PS matching will allow comparison of long-term organ damage in patients with SLE receiving belimumab plus SoC vs SoC alone. This approach can be applied to other extension studies to assess long-term treatment effectiveness.
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Disclosure of Interest: M. Urowitz Grant/research support from: GSK, UCB and Eli Lilly, Consultant for: GSK, UCB and Eli Lilly, R. Wielage Consultant for: GSK, K. Kelton Consultant for: GSK, R. Ohsfeldt Consultant for: GSK, Amgen and AstraZeneca Hygieia, Y. Asukai Shareholder of: GSK, Employee of: GSK, S. Ramachandran Shareholder of: GSK, Employee of: GSK
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FRI0299 N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-PROBNP) LEVEL IN PATIENTS WITH UNTREATED SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives: The aim of this study was to determine NT-proBNP serum levels in patients with untreated SLE, thus ruling out any potential effect of SLE therapy: to analyze any possible correlation between NT-proBNP values and traditional risk factors (TRF), inflammatory markers and myocardial function parameters.
Methods: The study included 28 pts (82% females, aged 28,5 [25,0–32,0] years (median [interquartile range 25%>75%]) with untreated SLE (ACR criteria, 1997) and 27 healthy controls (89% females, age 30,0 [23,0–49,0] years). None of SLE pts was treated either with prednisone or cytotoxic drugs at the moment of inclusion, 5 (18%) pts received hydroxychloroquine 200 mg/day. SLE-related factors, including disease duration, clinical features, SLE Disease Activity Index (SLEDAI 2K) and Systemic Lupus International Collaborating Clinics damage index (SLICC/DI) were evaluated in parallel with relevant laboratory findings (blood and urine tests, CRP, IL-6, INF-α, immunoglobulins G, A and M, C3 and C4 complement fragments and others), autoantibodies (ANA, antiDNA, ENA-SSA, -SSB, -Sm, -RNP-70, aPL), echocardiography was performed using standard techniques. Serum levels of NT-proBNP (pg/ml) were measured using electrochemiluminescence method Elecsys proBNP II (Roche Diagnostics, Switzerland). Normal NT-proBNP levels should vary within $\leq$125,0 pg/mL.
Results: Mean SLE duration was 21,0 [5,0–60,0] months, SLEDAI 2K score - 11 [8–9], SLICC/DI score - 0 [0–0]. SLE pts had higher levels of NT-proBNP vs control (160,7 [88,6–335,4] vs 55,2 [36,6–70,3] pg/ml, p<0,001). Elevated levels of NT-proBNP (>125,0 pg/ml) was detected in 18 (64%) SLE pts. In SLE pts NT-proBNP serum levels showed positive correlation with creatinine (r=0,480, p<0,01), uric acid (r=0,427, p<0,05), ACL IgG (r=0,710, p<0,001), antiDNA (r=0,395, p<0,05), ANA levels (r=0,256, p<0,05), left ventricle (LV) end-systolic dimension (r=0,442, p<0,05), mean pulmonary artery pressure (r=0,486, p<0,05); and negative correlation with hemoglobin level (r=-0,493, p<0,01), C4 complement component (r=-0,475, p<0,05), glomerular filtration rate (r=-0,558, p<0,01) and LV ejection fraction (r=-0,505, p<0,01); left ventricular diastolic dysfunction (DDLV) was only in pts with NT-proBNP levels >125,0 pg/ml. Mean NT-proBNP concentration in verified DDLV cases (n=5 (18%)) considerably exceeded normal values, reaching up to 799,2 [276,6–1777,0] pg/ml.
Conclusions: Untreated SLE patients without a history of myocardial infarction, coronary procedure or any evidence of heart failure demonstrated higher NT-proBNP concentration as compared to healthy controls (p<0,001). NT-proBNP levels showed correlation with numerous SLE markers (ACL IgG, ANA, antiDNA, C4 fragment of complement), kidney function (creatinine, uric acid, glomerular filtration rate) and myocardial function (end-systolic dimension of the LV, mean pulmonary artery pressure, LV ejection fraction). No correlation was documented between NT-proBNP concentration and TRF or inflammatory markers (CRP, IL-6, INF-α). All abovementioned data suggest presumable SLE-associated autoimmune damage of cardiomyocytes and/or mediated decrease of myocardial function caused by kidney disease.
Disclosure of Interest: None declared
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FRI0300 NEUROLOGICAL INVOLVEMENT IN PRIMARY SJÖGREN SYNDROME

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Background: Prevalence of neurological involvements (NI) in primary Sjögren Syndrome (pSS) varies from 10 to 60% and depends on whether they are screened systematically or only when they are symptomatic.
Objectives: The aim of the study was to describe the prevalence, clinical patterns and treatment of NI in pSS.
Methods: We performed a retrospective study of patients with pSS (American-European Consensus Group criteria) and followed in an internal medical department over a period of 15 years. Patients with NI were enrolled after excluding other potential causes. We did investigate neurologic systems only when patients present with symptoms.
Results: Primary Sjögren Syndrome was diagnosed in 155 patients, 41 had neurological manifestations (26.4%). They were 5 male and 36 female. The mean age at disease onset was 49 +/-13 years. The average delay from NI onset to pSS diagnosis was four months for peripheral nervous system (PNS) and 12