SAT0457

SJÖGREN BIG DATA PROJECT, THE FIRST EXAMPLE OF DATA SHARING IN AUTOIMMUNE DISEASES: ANALYSIS OF 10475 WORLDWIDE PATIENTS

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Objectives: To take a "high-definition" picture of the main features of primary Sjögren syndrome (SjS) following a worldwide data-sharing cooperative merging of international clinical SjS databases.

Methods: The Big Data Sjögren Project Consortium is an international, multi-centre registry created in 2014 including leading clinical centres in SjS of the 5 continents that shared a harmonised data architecture and conducted cooperative online efforts to refine collected data of primary SjS patients fulfilling the 2002 classification criteria.

Results: By January 2018, the participant centres had included 10 475 patients from 22 countries, including 7637 (73%) patients from Europe, 1420 (14%) from America, 1186 (11%) from Asia, 167 (1.4%) from Australia and 65 (0.6%) from Africa. The cohort included 9781 (93%) women and 694 (7%) men, with a mean age at diagnosis of primary SjS of 53 years. The frequencies of fulfilment of the 2002 criteria were 92% for dry eye, 94% for dry mouth, 83% for abnormal ocular tests, 82% for positive minor salivary gland biopsy, 78% for abnormal oral diagnostic tests and 76% for positive anti-Ro/La antibodies. The frequency of positive immunological markers at diagnosis was 79% for ANA, 73% for anti-Ro, 49% for RF, 45% for anti-La, 13% for low C3 levels, 14% for low C4 levels and 7% for cryoglobulins.

Conclusions: International data sharing-based projects merging disperse clinical registries may be essential tools to increase current knowledge and to improve patient care in specific systemic autoimmune diseases.

Disclosure of Interest: None declared

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URINE SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR AS A POTENTIAL BIOMARKER OF LUPUS NEPHRITIS ACTIVITY

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Background: Over the recent years, soluble urokinase plasminogen activator receptor (suPAR) has been described as a valuable indicator of the activation state of the immune system. Our previous work supported that suPAR might be an objective marker for identifying systemic lupus erythematosus (SLE) patients with active disease. Urokinase plasminogen activator receptor (uPAR) expression is also induced in podocytes during renal diseases such as focal segmental

glomerulosclerosis (FSGS). In addition, levels of suPAR were found to be elevated in paediatric and adult patients with FSGS. Current noninvasive laboratory and clinical measures of lupus nephritis (LN) activity are not sensitive or specific enough to reliably measure the course of LN. Improved, noninvasive biomarkers are needed to accurately detect LN activity.

Objectives: To evaluate suPAR in urine as a potential biomarker of renal system-specific disease activity in SLE.

Methods: A prospective follow-up study was designed. 14 SLE patients with newly diagnosed LN and 31 healthy individuals were enrolled in this study. LN was the leading symptom of all SLE patients. Further organ involvements including arthritis, leucopenia, serositis, fever and rash also occurred at the time of LN diagnosis. 12 out of 14 LN were confirmed by renal biopsy. Urine samples were taken before the initiation of LN induction therapy, and monthly thereafter (6 to 11 times). Global and renal disease activity were defined using the SLE Disease Activity Index 2000 (SLEDAI-2K) and the SLEDAI-2K renal domain score. suPAR concentrations in the urine were measured with the suPARnostic Flex ELISA assay. Non-parametric testing was used for statistical analysis, including the Kruskal-Wallis test and the Mann-Whitney U test.

Results: All urine suPAR levels were elevated in SLE patients with active LN compared with patients with resolved LN and healthy controls (21.75 vs 4.93 and 5.09 ng/mL, respectively, $p < 0.0001$). suPAR levels were higher measured before than after the initiation of LN induction therapy in patients before resolution of active LN (29.46 vs 21.07 ng/mL, $p = 0.0122$). Prospective follow-up measurements also suggested that urine suPAR levels raised again in patients with a relapse of LN according to SLEDAI-2K renal domain score ($n = 3$; 5.45 vs 15.19 ng/mL, $p = 0.0127$).

Conclusions: Urine suPAR is a promising LN activity biomarker, given its isolated elevation in urine in active LN and pronounced decrease with LN improvement. It may potentially become a more convenient alternative to renal biopsy, the current gold standard of LN activity monitoring.

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SAT0459

OCCURRENCE OF LYMPHOMA IN SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-SERIES OF 38 PATIENTS

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Background: Patients with systemic lupus erythematosus (SLE) are at higher risk than the general population of developing lymphoma. Relatively little is known about the risk factors, the treatment and the outcome of lymphoma in SLE.

Objectives: We aimed to describe a cohort of patients suffering from lymphoma in the setting of SLE and to study the risk factors of developing this complication.

Methods: We collected clinical data of SLE patients with confirmed lymphoma in a multicentric and retrospective study. SLE patients were eligible for the study if they fulfilled at least 4 of the 1997 ACR criteria for SLE. Exclusion criteria were HIV or C hepatitis infection.

Results: We included 38 patients (34 women and 4 men) coming from 10 different French University Hospitals. The lymphoma occurred after the diagnosis of SLE for 35 patients, with a median (range) time of 8.8 years (0–39). In their past or present medical history, 11 (29%) had a haematological involvement (5 immune thrombocytopenias, 4 autoimmune hemolytic anemias and 2 patients with both). Nine patients (24%) had associated Sjögren syndrome. 22 patients (58%) had a polyclonal hypergammaglobulinemia. Before the occurrence of the lymphoma, 18 patients (47%) had received an immunosuppressant during a median (range) period of 67 months. 6–195 17 patients had an indolent B cell lymphoma (IBCL), 14 a high-grade B cell lymphoma (11 diffuse large B cell lymphoma [DLBCL]; 2 a primary DLBCL of the central nervous system; and 1 an iatrogenic immunodeficiency-associated lymphoproliferative disorder), 5 a Hodgkin's disease (HD), and 2 a T cell lymphoma. The EBER *in situ* hybridization stain was positive in 7 of the 13 patients assessed (3/3 HD, 3/7 DLBCL and 1/2 IL) and was not associated with the immunosuppressant prescription. The median (range) of the survey after the lymphoma was 28.5 month (0–235.1). The 14 DLBCL patients except 1 were treated with chemotherapy: 4 died, 9 were in complete remission and 1 was in progression. Regarding the 17 IBCL, 9 patients were treated with chemotherapy, 2

patients with surgery, 1 patient with radiotherapy and 5 patients were not treated: 3 patients had to short follow-up or were lost, 1 died, 2 developed a DLBCL, 4 were stable and 7 were in complete remission. The 5 HL were treated with chemotherapy and all were in complete remission.

Conclusions: IBCL and DLBCL were the most common type of lymphomas in SLE patients. Data suggest a role for EBV but not for exposition to immunosuppressant in the pathogenesis of SLE-associated lymphoma. The outcome of lymphoma in the setting of SLE seems not different from the outcome of lymphoma in the general population. A case-control study is ongoing to study the risk factors associated with the occurrence of lymphoma in SLE

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SAT0460

LONG-TERM IMMUNE PROTECTION FOLLOWING PNEUMOCOCCAL 13-VALENT/23-VALENT POLYSACCHARIDE VACCINE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Systemic lupus erythematosus (SLE) patients are at increased risk for *Streptococcus pneumoniae* infection. Although pneumococcal vaccination is an attractive method to prevent invasive pneumococcal infection, vaccination coverage remains dramatically low in SLE. Moreover, the efficacy of vaccination may be reduced in SLE patients and sequential pneumococcal vaccination using new conjugated pneumococcal vaccines in combination with 23-valent pneumococcal polysaccharide vaccine (PPV23) is now advocated.

Objectives: We aimed to determine the efficacy of the prime-and-boost vaccination strategy using the 13-valent pneumococcal conjugate (PCV13) and 23-valent polysaccharide (PPV23) vaccines in SLE.

Methods: Consecutive SLE patients admitted from April to December 2015 in our daycare hospital unit (Paris, France) were enrolled to receive PCV13 vaccine followed by PPSV23 vaccine 8 weeks later. Immune protection, defined by an antigen-specific IgG concentration ≥ 1.3 $\mu\text{g/mL}$ for at least 70% of 7 pneumococcal serotypes (4, 6 B, 9 V, 14, 18 C, 19 F, 23 F), was assessed at baseline, 2 and 12 months. The primary endpoint was immune protection 12 months (long-term) after PCV13 shot.

Results: 37 consecutive adult SLE patients admitted in our daycare hospital unit (Department of Internal Medicine, Bichat Hospital, Paris, France) were screened for pneumococcal vaccination. Among them, 8 patients refused to be vaccinated, 7 patients accepted the vaccination but refused to complete the 12 months immune response follow up and 1 patient had already been vaccinated against pneumococcal infection. Eventually, 21 (40²⁵⁻⁷⁵ years; 85.7% female) SLE patients were included in the study and received the sequential PCV13/PPV23 pneumococcal vaccines. Only 12 patients (57.1%) reached the primary endpoint. Nine patients had no long-term protection with a seroconversion that never (n=4, not protected, NP) or only transiently (n=5, short-term protected, STP) occurred. B-cells defects and immunosuppressive treatment were associated with the NP status. A lower IgG2 serum level and a higher ratio of pre-germinal/post-germinal centre B cells were associated with the STP status. The serotype 19 F IgG titer measured 2 months after PCV13 had the best ability (sensitivity of 100% [95% CI: 47.8–100]; specificity of 91.7% [95% CI: 61.5–99.8]) to predict long-term protection.

Conclusions: The benefit of sequential PCV13/PPV23 vaccination in SLE is limited. Several factors are associated with long-term immune protection and may help to design selective schedule strategy and/or new vaccines.

Disclosure of Interest: None declared

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SAT0461

ULTRASONOGRAPHY OF SALIVARY GLANDS IN PRIMARY SJOGREN'S SYNDROME AND ASSOCIATION WITH DISEASE ACTIVITY, SEROLOGICAL MARKERS AND BIOPSY OF MINOR SALIVARY GLANDS

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Background: Parenchymal inhomogeneity of the salivary glands (SG) is the most relevant ultrasonographic (US) feature for diagnosis primary Sjogren's syndrome (pSS).

Objectives: To analysis parenchymal echostructure of SG in patients with established pSS and association USSG score with disease activity, serological markers and biopsy of minor salivary glands (MSG).

Methods: This study included 205 pSS patients (mean age 53.9 $\pm$ 11.5, disease duration 5.6 years) and 87 healthy controls (mean age 52.3 $\pm$ 14.7). All pSS patients fulfilled the AECG diagnostic criteria. The disease activity was evaluated by EULAR SS disease activity index (ESSDAI), Sjögren's Syndrome Disease Damage Index (SSDDI) and EULAR Sjogren's syndrome patient reported index (ESSPRI). The presence of ANAs assessed by indirect immunofluorescence assay on Hep-2 cells, anti SSA and anti SSB (commercial ELISA kit) and RF (nephelometry). The parotid and submandibular glands on both sides were examined by US using a GE LogiqE9 with a linear high-frequency transducer (6–15 MHz). Inhomogeneity of the SG were graded according to the De Vita scoring system. Grading 0 was for a homogeneous gland, 1 for mild inhomogeneity, 2 for evident inhomogeneity and 3 for a grossly inhomogeneous gland. The global SGUS score (0–6) was the sum of the scores of each pair of SG. Statistical analysis was performed by SPSS v19. Data were compared using *t*-test, χ^2 test and Mann-Whitney U test. The diagnostic accuracy of inhomogeneity was evaluated by area under the receiver operating characteristics curves (AUC-ROC). A multivariate linear regression analysis was performed to determine the factors associated with SGUS score.

Results: Xerophthalmia and xerostomia were presented in 185/205 (90.2%) and 186/205 (91.2%), respectively. According to ESSDAI, the majority of pSS patients 88/205 (43%) had moderate disease activity. Seventy-eight per cent of pSS patients were anti-SSA positive, 44% anti-SSB positive. Biopsy of MSG was positive in 140/172 (81.4%) pSS patients. US abnormalities were established in 197/205 (96%) pSS patients and in 16/85 (18%) controls ($p<0.0001$). The median SGUS was significantly higher in pSS patients in comparison with control group [median (range) 4 (0–6) vs. 0 (0–2), $p<0.0001$]. The diagnostic accuracy of parenchymal inhomogeneity was high, AUC-ROC 0.89 (0.02) with cut-off ≥ 2 (Sp 89.5%, Sn 89.3%). Out of 197 pSS patients with abnormal findings, the most patients had US score 4 (47%), while 81% in control group had score 0. After adjustment for potential confounders variables, dry mouth ($B=1.192$, $\beta=1.542$; $p=0.04$), ESSDAI ($B=0.184$, $\beta=1.203$; $p=0.008$) and biopsy of MSG ($B=1.006$, $\beta=2.735$; $p=0.05$) were significantly associated with advanced US changes of SG. Dry eyes, SSDAI, ESSPRI and serological markers were not associated with USSG score ($p>0.05$).

Conclusions: Our findings confirmed that parenchymal inhomogeneity of the salivary glands is the reliable feature for primary Sjogren's syndrome. Presence of xerostomia, objective disease activity as by ESSDAI and pathological findings of biopsy of minor salivary glands had predictive value for advanced US change of salivary glands.

Disclosure of Interest: None declared

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SAT0462

PD-1+CXCR5-CD4+T CELLS MAY PLAY AN IMPORTANT ROLE IN THE SEVERITY OF SYSTEMIC ERYTHEMATOSUS LUPUS

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Background: CD4⁺ T cells are central mediators in specific autoimmune diseases; however, it remains challenging to define their key effector functions in systemic erythematosus lupus (SLE), a chronic immune-mediated damage to the whole system. Programmed death 1 (PD-1), a negative T cell regulator to maintain peripheral tolerance, induces negative signals to T cells during interaction with its ligands. PD-1⁺CD4⁺T cells could be divided into PD-1⁺CXCR5⁺CD4⁺T peripheral helper cells and PD-1⁺CXCR5⁺CD4⁺ T (Tfh) cells according to CXCR5 expression. PD-1⁺CXCR5⁺CD4⁺T peripheral helper (Tph) cells were proven to promote B cell responses and antibody production in rheumatoid arthritis Rao DA, Nature, 2017.¹ Tfh cells were required for the generation of most memory B cells and long-lived plasma cells in SLE. However, what the role of Tph cells in the pathogenesis of SLE was unknown.

Objectives: We assessed that whether Tph cells were associated with clinical profiles of patients with SLE.

Methods: This cohort study included 36 patients with SLE from the Division of Rheumatology, the first Affiliated Hospital, college of medicine, Zhejiang University. All SLE patients fulfilled the American College of Rheumatology revised classification criteria. 26 Age- and sex-matched healthy individuals had no connective tissue disorders, neoplasms or current infections. Here we used flow cytometry to analyse PD-1⁺CXCR5⁺CD4⁺T cells in peripheral blood from patients with SLE. Correlation between Tph cells and other parameters was investigated by Spearman's correlation coefficient test, and comparisons between groups were performed using nonparametric Mann-Whitney test.

Results: Firstly, we revealed a markedly expanded population of Tph cells (8.95 $\pm$ 6.35 vs. 2.67 $\pm$ 1.22, $p<0.0001$) in the circulation of patients with SLE (n=36),