TABLE 1	OR	p
SELENA-SLEDAI	1.10 (1.06-1.14)	<0.001
SLICC/ACR DI	1.27 (1.16-1.38)	<0.001
Elevated creatinine	2.08 (1.66-2.61)	<0.001
Active nephritis	3.52 (1.94-6.37)	<0.001
Hepatitis C	4.82 (1.89-12.27)	=0.002
Diabetes	3.87 (2.06-7.26)	=0.0001
Cancer	3.60 (2.01-6.42)	=0.000
Corticosteroids (Prednisone > 10mg/day)	1.81 (1.07-3.09)	=0.023
Immunosuppressors	11.44 (7.31-17.92)	=0.000
Antimalarials	0.39 (0.25-0.61)	=0.000
Renal Transplant	5.64 (2.63-12.1)	=0.000
Dialysis	0.39 (0.25-0.61)	=0.000

recurrence and mortality were high. Immunosuppressors use, comorbidity and damage were all associated to bacteraemia.

Disclosure of Interest: None declared

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OP0043 THE NUMBER OF CIRCULATING REGULATORY T CELLS IS REDUCED AND LOW-DOSE IL-2 SELECTIVELY STIMULATES ITS PROLIFERATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The imbalance of T help 17 cells (Th17)/regulatory T cells (Tregs) is considered to be a pivotal cause of autoimmune diseases¹, including systemic lupus erythematosus (SLE). However, previous reports^{1,2} describing the respective changes of Tregs and Th17 cells in SLE patients were controversial because a few samples or diverse markers were used to identify Tregs with little consensus.

Objectives: To clarify the status of Tregs and Th17 in SLE, we investigated the frequencies of Tregs and Th17 cells on a large scale and whether those defects can be corrected by the supplementation of low-dose human recombinant interleukin-2 (IL-2).

Methods: Two hundred and thirty-five SLE patients (219 women and 16 men), with mean age of 37.80±14.00 years, were enrolled. The disease activity using European League Against Rheumatism (EULAR) criteria was judged for SLE patients with erythrocyte sedimentation rate (ESR) and SLEDAI scores. The frequencies of CD3+CD4+FOXP3+Treg cells and Th17 cells in peripheral blood from these patients were measured by flow cytometry. And low-dose IL-2 was used among 127 patients at a dosage of fifty WIU every day for five days. Immunological and clinical assessments were performed again at the end of IL-2 treatment. Ninety healthy volunteers, matched for patients' age and gender, were also included for the estimation of CD4+ T cell subsets.

Results: As compared to healthy controls (median of Treg cells: 33.09 cells/ul), the frequencies of circulating CD4+CD25+FOXP3+Treg cells were significantly decreased in SLE patients (median: 15.49 cells/ul, $P<0.001$). The median ratios of Th17/Tregs cells in patients were greatly higher than those of healthy volunteers [0.42 (0.19, 0.88) vs. 0.21 (0.15, 0.34), $P<0.001$]. There was not significantly different in circulating Th17 cell between two groups. Moreover, CD4+CD25+FOXP3+Treg cells were negatively correlated with ESR and SLEDAI score ($r=-0.198$, $P=0.01$; $r=-0.25$, $P=0.002$). While no obvious correlation was seen between Th17 cells and SLEDAI score. After IL-2 therapy in SLE, there was a four-fold increase in circulating CD4+CD25+FOXP3+Treg cells [43.73 (24.08,74.22) vs. 11.95 (7.51,20.34), $P<0.001$], whereas Th17 cells were increased slightly. The ratio of Th17/Tregs was decreased significantly in patients with IL-2 treatment [0.19 (0.09,0.41) vs. 0.52 (0.23,0.95), $P<0.001$], tended to balance and had no difference with healthy individual ($P=0.275$).

Conclusions: With the increase of disease activity, CD4+CD25+FOXP3+Treg cells were gradually reducing, while Th17 cells did not show a significant change, indicating that the reduction of Tregs but not the elevation of Th17 cells may be the major reason for imbalance of Th17/Tregs. It is speculated that SLE is an autoimmune disease triggered by the defect of immunotolerance. More importantly, low-dose IL-2 selectively modulated the abundance of Tregs, which effectively induced autoimmune tolerance and further improved clinical symptoms.

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OP0044 ANTIBODIES ANTI-SACCHAROMYCES CEREVISIAE IN PRIMARY SJÖGREN'S SYNDROME: PREVALENCE, CLINICAL ASSOCIATIONS AND POSSIBLE CROSS-REACTIVITY WITH DISEASE SPECIFIC AUTOANTIGENS

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Background: *Saccharomyces cerevisiae* is a common yeast used in the food industry. Antibodies against the phosphopeptidomannan part of the cell wall of *S. cerevisiae* (ASCA) are a well established biomarker of Crohn's disease and have been assessed in several organ-specific and systemic autoimmune diseases (ADs) (1–2). Although the pathogenic significance of ASCA is not yet fully understood, the molecular mimicry of self-antigens in several associated ADs has been suggested as putative mechanism.

Objectives: Since to date ASCA have not been tested in primary Sjogren's syndrome (pSS), the purpose of this study was to assess these antibodies in a large cohort of pSS patients and investigate their significance as potentially helpful biomarker in a clinical setting.

Methods: One hundred and four patients with pSS according to the 2002 American European Consensus criteria and 30 healthy donors (HD) were enrolled. ASCA IgG+IgA were assessed in serum samples with ASCA screen dot (Alphadia sa/nv). T cell phenotyping was performed in paired peripheral blood samples by flow cytometry. To compare the amino acid sequence of mannan of *Saccharomyces cerevisiae* and well characterized auto-antigens peculiar of pSS (52kD and 60kD Ro/SSA, La/SSB) we browsed the protein database of the National Center for Biotechnology Information (NCBI) and run the Basic Local Alignment Search Tool (BLAST).

Results: ASCA were detected in 5 out of 104 pSS patients, therefore the prevalence in our cohort is 4.8%. None of the ASCA+ pSS patients displayed IBD or other autoimmune conditions that could account for ASCA positivity. ASCA+ pSS patients displayed more frequently a reduction of C3 and C4 complement fractions as well as pulmonary, articular and cutaneous involvement (all $p<0.05$). Binary logistic regression revealed that ASCA+ pSS patients display an odds ratio of 14 ($p=0.006$) to have cutaneous manifestations of pSS. All ASCA+ patients but only 39% of ASCA- patients displayed anti-Ro52, anti-Ro60 and anti-La autoantibodies together ($p=0.01$). No differences concerning T regulatory and Th17 cell proportion could be observed in ASCA+ compared to ASCA- pSS patients. *S. cerevisiae* mannan displays a consistent similarity with 52kD and 60kD Ro/SSA, La/SSB autoantigens. The highest similarity was observed when aligning the mannan with 60kD Ro/SSA (identities 7/11, 64%; positives 8/11, 72%, E value 2.2.).

Conclusions: Our study assessed for the first time ASCA IgG+IgA with a highly specific immunoblot assay in a large cohort of pSS patients, showing that ASCA positivity identifies a peculiar clinical and serological pSS phenotype. In particular, ASCA+ pSS patients display anti-Ro52, anti-Ro60 and anti-La antibodies, low complement and cutaneous involvement. The high similarity between *S. cerevisiae* mannan and Ro60/SSA autoantigen may suggest that: i. ASCA may bind pSS autoantigens, such as anti-Ro, as already postulated for other autoantigens (2); ii. ASCA may bind more likely Ro60 autoantigen rather than the Ro52 or La autoantigens in pSS. A possible pathogenic/prognostic significance of ASCA in pSS may therefore be speculated.

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Disclosure of Interest: None declared

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OP0045 PREDICTORS OF PERSISTENT DISEASE ACTIVITY AND PERSISTENT LONG QUIESCENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS – RESULTS FROM THE HOPKINS LUPUS COHORT

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Background: Systemic lupus erythematosus (SLE) is characterized by a diversity of disease activity.

Objectives: The aim of this study was to identify prognostic factors of persistent disease activity and persistent long quiescence using baseline demographics and clinical characteristics.

Methods: Patients enrolled in the Hopkins Lupus Cohort from 1987 to 2014, who had at least 3 visits per year during 3 years following cohort inclusion and available information on disease activity were included. Three major patterns of SLE disease activity over time (1 year intervals) based on the modified SLE Disease Activity Index have been previously described: long quiescent (LQ), chronic active (CA) and relapsing-remitting (RR) (1). Based on maintenance of the aforementioned

patterns over 3 consecutive years, patterns have been defined as: Persistent Long Quiescent (pLQ), Persistent Relapsing-Remitting (pRR), Persistent Chronic Active (pCA) and Mixed, at least 2 different pattern types. Predictors of pCA (vs. pLQ, pRR and mixed) and pLQ (vs. pCA, pRR and mixed) were identified by univariate and multivariate logistic regression analyses. Several baseline demographics (age, sex, ethnicity, disease duration, tobacco use, years of education and combined annual family income), disease characteristics at baseline (SLEDAI, PGA) and treatment categories (hydroxychloroquine, prednisolone and cytotoxic treatment followed at $\geq 75\%$ of visits vs $<75\%$ of visits) were used as independent variables. **Results:** 916 patients were identified. The results of the univariate analyses for pCA are shown in table 1. In the multivariate model, African American ethnicity (OR: 2.43, 95% CI: 1.19–4.94, p: 0.01) and high baseline SLEDAI (OR: 1.09, 95% CI: 1.03–1.16, p: 0.004) remained significant predictors of pCA. Higher education (>12 years; OR: 2.16, 95% CI: 1.11–4.20, p: 0.02) and low baseline SLEDAI (OR: 0.62, 95% CI: 0.52–0.75, p: <0.001) were significant predictors of pLQ in the multivariate analysis while African American ethnicity (OR: 0.36, 95% CI: 0.16–0.78, p:0.01) and female patients (OR: 0.26, 95% CI: 0.12–0.56, p:0.001) were less likely to achieve persistent long quiescence.

Table 1. pCA (vs. pLQ, RR and mixed)

	OR (95% CI)	p-value
Sex (female vs. male)	1.6 (0.4–6.7)	0.54
Age (>40 vs. ≤ 40 yrs)	1.4 (0.7–2.8)	0.32
Disease Duration	1.0 (0.9–1.1)	0.17
African American (vs. other)	2.6 (1.3–5.3)	0.007
Years of education (>12 vs. $\leq$ yrs)	0.7 (0.3–1.4)	0.27
Income		
<30000\$	Ref	
30000–65000\$	0.4 (0.2–1.0)	0.06
$\geq 65000$$	0.5 (0.2–1.2)	0.12
Smoking baseline (yes vs. no)	2.1 (1.0–4.6)	0.06
SLEDAI baseline	1.1 (1.0–1.2)	0.002
PGA baseline	1.5 (1.0–2.2)	0.04
Cytotoxic therapy ($\geq 75\%$ vs. $<75\%$ of visits)	1.1 (0.5–2.3)	0.85
Antimalaria therapy ($\geq 75\%$ vs. $<75\%$ of visits)	0.5 (0.3–1.0)	0.06
Prednisolone therapy ($\geq 75\%$ vs. $<75\%$ of visits)	1.1 (0.6–2.2)	0.82

Conclusions: In this large SLE cohort, African American ethnicity and high disease activity at the time of diagnosis are predictors of chronic activity, regardless of treatment, even after adjustment for education years and income, while higher education and low disease activity at baseline predict long-term quiescence.

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OP0046 RISK FACTORS FOR ADVERSE PREGNANCY OUTCOME IN ANTIPHOSPHOLIPID ANTIBODIES CARRIERS: RESULTS FROM A MULTICENTER ITALIAN COHORT OVER 20 YEARS OF EXPERIENCE

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Background: Antiphospholipid antibodies (aPL) are risk factors for Adverse Pregnancy Outcome (APO). In particular, for aPL carriers (patients with aPL positivity with no thrombotic or obstetric history) pregnancy outcome and treatment are still undefined.

Objectives: To review pregnancy outcome in a large multicenter cohort of aPL carriers patients, according to different serological profile and treatment protocols.

Methods: We reviewed 69 pregnancies in 61 patients, prospectively followed in 3 Italian centers (1994–2015). Patients with any complication in previous pregnancies or concomitant autoimmune diseases were excluded. aPL profile was defined as the combination of the 3 criteria tests for aPL (Lupus Anticoagulant, anti-cardiolipin, anti-Beta2 Glycoprotein I). APO was defined as: miscarriage ($<10w$), fetal death ($\geq 10w$), severe preterm delivery ($\leq 34w$) with or without preeclampsia (PE), HELLP syndrome or perinatal death.

Results: Regarding aPL profile: 44 (64%) were single positive, 16 (23%) were double and 9 (13%) were triple. aPL non-criteria manifestations were present in 6 (9%) and lupus-like manifestations in 5 (7%). Eight pregnancies had a combination treatment with prophylactic low molecular weight heparin (LMWH) plus low dose aspirin (LDA), 37 had LDA alone and 24 had no treatment. We observed 2 thrombotic events (3%, 1 deep venous thrombosis and 1 ischemic stroke) and 6 APO (9%): 3 fetal deaths and 3 pre-term birth $\leq 34w$ with PE. We compared 8 complicated (6 APO, 2 thrombosis) with 61 non-complicated pregnancies (Table 1). Acquired risk factors (p:0.006), non-criteria aPL (p:0.018) and lupus-like manifestation (p:0.010), triple positive aPL profile (p:0.001) were associated with APO. The combination treatment was also more frequent in APO pregnancies (p:0.005).

	Complicated pregnancies (n=8)	Non-complicated pregnancies (n=61)	P-value *	OR (95% CI)
Mean age at pregnancy (mean (SD))	28.3 (5.8)	32.7(4.6)	0.015 *	
Acquired risk factors *	6 (75%)	14 (23%)	0.006	10.7 (1.55-82.4)
Congenital thrombophilia	2 (25%)	4 (7%)	0.140	
Non criteria aPL manifestations *	3 (38%)	3 (5%)	0.018	11.6 (1.37-108)
Lupus-like manifestations	3 (38%)	2 (3%)	0.010	17.7 (1.77-213)
Single positive	3 (38%)	41 (67%)	0.128	
Double positive	0 (0%)	16 (26%)	0.183	
Triple positive	5 (63%)	4 (7%)	0.001	23.7 (3.22-211)
No treatment	1 (13%)	23 (38%)	0.246	
LDA	3 (38%)	34 (56%)	0.457	
LDA+LMWH	4 (50%)	4 (7%)	0.005	14.2 (1.98-116)

Table 1. Complicated pregnancies (APO and thrombosis) compared with non-complicated pregnancies – univariate analysis
* Fisher's exact test, except otherwise indicated; p significant <0.05
§ Student's T- test
Acquired risk factors: Obesity (BMI $>30w$), hypertension ($>140/90$), hyper-cholesterolemia, hyper-triglyceridemia, hyper-homocysteinemia, diabetes mellitus
* Non-criteria aPL manifestations were defined as the presence of at least one of the followings: (livedo reticularis, thrombocytopenia, headache, hemolytic anemia, cardiac valvulopathy, epilepsy)

Conclusions: Acquired risk factors, aPL profile (triple positivity), lupus-like and non-criteria aPL manifestations could represent risk factors for pregnancy complications and could determine failure to conventional treatment. These patients may deserve additional treatment, for example LMWH at higher/anti-coagulant dose or immunomodulatory treatment (e.g. hydroxychloroquine, also considering its anti-platelet/anti-thrombotic effects).

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WEDNESDAY, 14 JUNE 2017

Osteoporosis treatment gap, new options and new strategies

OP0047 OSTEOPOROTIC HIP FRACTURE PREVENTION: ARE WE IN A CRISIS?

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Background: Osteoporotic hip fractures are a significant cause of morbidity and mortality in the elderly. With the aging of the US population, it was expected that there would be a nationwide "epidemic" of osteoporotic fractures; however, Medicare reimbursement for osteoporosis screening and the rapid uptake of bisphosphonate therapy in the late 1990s and early 2000s probably forestalled this epidemic. In fact, osteoporotic hip fractures numbers declined during this time, despite the dramatic growth of the elderly population (1). However, bisphosphonate prescriptions have dropped precipitously by over 50% from their peak in 2008 (2), likely because of concerns regarding their adverse events. In this era of "crisis" in osteoporosis prevention, has the pendulum swung back on hip fracture numbers?

Objectives: To study the number and prevalence of osteoporotic hip fractures in patients 50 years and older over the last 22 years (1993–2014) in the US?

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2014 with a primary diagnosis of non-traumatic hip fractures, and calculated age-adjusted prevalence rates. We excluded patients with concomitant diagnosis of major trauma, primary or secondary tumors locally, osteopetrosis and procedures for revision surgery or surgery for complications.

US population estimates and projections for the resident US population were obtained from the US Census Bureau.

Results: There were 407 million all-cause hospitalizations in 1.88 billion person-years of observation among people 50 years of older from 1993 to 2014 (21,626 hospitalizations per 100,000 person-years). During this time-period, there were 6.15 million hospitalizations for osteoporotic hip fractures in this population (327 per 100,000 person-years). After an initial increase in hip fractures from 1993 to 1996, there was a decline of 10.6% in total number of hip fractures from 300,154 in 1996 to 268,356 in 2010 even though population of 50 years and older increased from 69.9 million to 99.6 million in the same time. After bottoming out in 2010, the total number of hip fractures increased by 6.2% to 285,050 in 2014 (Figure, blue broken line). However, the age-standardized prevalence rate of hip fractures declined steadily (from 414/100,000 in 1996 to 269/100,000 in 2014, p<0.0001, Figure solid red line), although the rate of decline has ameliorated somewhat from 2010 onwards (not statistically significant).

Conclusions: The total number of osteoporotic hip fractures in 50 years and