EULAR 2015

Selected abstracts on SLE

[SAT0385] DISEASE ACTIVITY PATTERNS OVER TIME IN PATIENTS WITH SLE – A RETROSPECTIVE DESCRIPTIVE ANALYSIS OF THE HOPKINS LUPUS COHORT

- **Objectives**: To discern and describe SLE disease activity patterns over time by analyzing data from the Hopkins Lupus Cohort. To understand the burden of disease course over time among patients with SLE (Barr et al. 1999)

- **Methods**: Disease activity was retrospectively studied in 2386 consecutive SLE patients followed up quarterly for 1-28 years
- Activity patterns were defined using Physician Global Assessment (PGA) and SLEDAI (including serology):
  - **Long Quiescent (LQ)**, SLEDAI/PGA=0 for 1 year at all visits;
  - **Relapsing-Remitting (RR)**, periods of disease activity (SLEDAI/PGA>0) interspersed with periods of disease inactivity (SLEDAI/PGA=0) at 1 or more visits during 1 year;
  - **Chronic Active (CA)**, SLEDAI/PGA scores are >0 for 1 year at all visits.
- Disease activity at yearly intervals (“1-year blocks”). The pattern in each patient of 3 consecutive follow-up years (“3-year blocks”) was also determined

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- **Results**: The RR pattern accounted for the greatest proportion of followup time for both the SLEDAI and PGA, representing 48.3% and 51.8% of total person-years, respectively.
- The least prevalent pattern was the LQ (SLEDAI 16.1%, PGA 9.5% of total person-years). The SLEDAI was more likely to depict the LQ pattern than was the PGA.

Table 1. Frequencies of different disease activity pattern groups observed at both 1-year-, and 3-year intervals.

	1-YEAR-BLOCKS			3-YEAR-BLOCKS			
	RR	CA	LQ	pRR	pCA	pLQ	Mixed
PGA	51.8%	38.5%	9.5%	21.2%	20.6%	2.8%	55.4%
SLEDAI	48.3%	35.5%	16.1%	18.4%	20.8%	5.7%	55.1%

PGA: Physician Global Assessment ; **SLEDAI**: SLE Disease Activity Index; **RR**: Relapsing-Remitting; **CA**: Chronic Active; **LQ**: Long Quiescent; **pRR**: Persistent Remissing-Remitting; **pCA**: Persistent Chronic Active; **pLQ**: Persistent Long Quiescent

- **Conclusions**: The RR pattern appeared to be the most prevalent pattern type; Long quiescence was achieved in only a subset of patients. Over a 3-year perspective *almost half the patient maintained their disease activity pattern*

[OP0093] THE NATURAL HISTORY OF THROMBOTIC EVENTS IN SLE AND ASSOCIATED RISK FACTORS

- **Objectives:** No previous study has identified risk factors prospectively for both venous and arterial thrombosis in SLE. In this study we used a large prospective SLE cohort to assess the natural history of both arterial and venous thrombosis before and after the diagnosis of SLE

- **Methods**: 2305 SLE patients were enrolled in a prospective cohort (Hopkins Lupus Cohort Study).
- Medical records were reviewed to identify the occurrence of arterial and venous thrombosis prior to cohort entry (diagnosed by patient history, diagnostic enzymes tests and imaging, including arteriogram, and venous thrombosis by ultrasound, CT or venography).
- Calculate the rate of thrombosis per person-year in periods of follow-up defined by time since diagnosis with SLE.

[OP0093] THE NATURAL HISTORY OF THROMBOTIC EVENTS IN SLE AND ASSOCIATED RISK FACTORS

- **Results:** The highest rates of both venous thrombosis and arterial thrombosis were observed in the 2 years before and the 2 years after diagnosis. A second peak in incidence of arterial thrombosis was observed later in the course of SLE

Time since SLE diagnosis	Venous thrombosis		Arterial thrombosis	
	Rate of events per 1000 PY	Rate ratios (95% CI) adjusted for age	Rate of events per 1000 PY	Rate ratios (95% CI) adjusted for age
>5 years before SLE diagnosis	1.2	1.0 (Ref. Grp)	0.4	1.0 (Ref. Grp)
2-5 years before SLE diagnosis	2.3	1.5 (0.8, 2.7)	1.8	3.5 (1.6, 7.4)
0-2 years before SLE diagnosis	11.4	7.0 (4.7, 10.5)	8.9	15.9 (8.8, 28.8)
0-2 years after SLE diagnosis	12.5	7.4 (5.0, 11.1)	10.5	17.7 (9.9, 31.9)
2-5 years after SLE diagnosis	6.7	3.9 (2.5, 6.1)	4.5	7.2 (3.7, 13.8)
5+ years after SLE diagnosis	9.1	5.0 (3.5, 7.2)	11.8	15.8 (9.2, 27.3)

- **Conclusions**: Results suggest that the mechanism of events before diagnosis is not accelerated atherosclerosis. Accelerated atherosclerosis would not explain the increase in both arterial and venous events that occurs before and at diagnosis.

[SAT0386] WHAT IS THE BEST SCREENING TEST TO IDENTIFY LUPUS PATIENTS WITH COGNITIVE IMPAIRMENT IN AN AMBULATORY SETTING?

- **Objectives:** There is an unmet need for a clinical assessment of cognitive function that can be administered in an ambulatory setting. To determine: 1) the validity of the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) as screening tests of Cognitive Impairment (CI) in SLE

- **Methods**: Consecutive patients with SLE visiting the Toronto Lupus Clinic
- Patients underwent the battery of cognitive screening tests : Hopkins Verbal Learning Test-Revised (**HVLT-R**) and Controlled Oral Word Association Test (**COWAT**) via telephone interview and **MoCA** and **MMSE** via face-to-face assessment.
- Patients completed the Perceived Deficits Questionnaire – 5-item (PDQ-5).
- Center of Epidemiologic Studies Depression Scale (CES-D), Beck Anxiety Inventory (BAI), and Reynolds Intellectual Screening Test (RIST) were completed by patients.
- Logistic regression analyses were performed to test for possible associations with CI.

[SAT0386] WHAT IS THE BEST SCREENING TEST TO IDENTIFY LUPUS PATIENTS WITH COGNITIVE IMPAIRMENT IN AN AMBULATORY SETTING?

- **Results:** 73 patients participated
- Prevalence of CI: 47% had CI using MoCA, 40% using HVLT-R, 16% using COWAT and 14% using MMSE.
- Patients with CI had marked impairment in attention, language and delayed recall in the domains of MoCA compared to normal controls
- Sensitivity was higher for MoCA (69%) compared to MMSE (21%), though MMSE was more specific (91%) than MoCA (68%).
- There was no significant difference in CES-D, BAI or RIST scores between patients with and without CI.

- **Conclusions**: Ease of use and time needed for an assessment, make the MoCA the preferential screening test for CI in patients with SLE compared to HTLV-R.

[OP0185] SIGNIFICANT CLINICAL IMPROVEMENT AND REDUCTION OF SEVERE FLARES FOLLOWING ADMINISTRATION OF AN IL-6 MONOCLONAL ANTIBODY IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) SUBJECTS WITH HIGH DISEASE ACTIVITY

- **Background:** PF-04236921 is a fully human monoclonal antibody (mAb) that binds to circulating IL-6 and neutralizes its activity. This may be beneficial in reducing the disease manifestations of active SLE.

- **Methods**: 183 subjects with active SLE (SLEDAI ≥6 and ≥1 BILAG 2004 A or ≥2 Bs)
- Received 3 doses of PF-04236921 (Pfizer) (10, 50, or 200mg) or Placebo (SQ q8 wks).
- Primary endpoint: SLE Responder Index 4 (**SRI-4**) responders **at Wk 24** using a generalized linear mixed model.
- The BILAG-based Combined Lupus Assessment (BICLA), frequency of severe flares, and SF-36 were also evaluated.

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- **Results:** The majority of subjects had musculoskeletal and mucocutaneous involvement.
- At Wk 24, there were more responders in the 10mg group vs placebo. For the 50mg group there were no significant differences vs placebo.
- Significant reduction in the frequency of severe SELENA-SLEDAI flares for the combined 10 and 50mg groups vs placebo.

Efficacy results at Week 24 (Full Analysis Set)[a]

	Broad Population		
	Placebo (n=45)	10mg (n=45)	50mg (n=47)
SRI responders,%	40.1	59.9	39.2
p-value		0.076	0.528
BICLA responders,%	25.1	49.7	40.5
p-value		0.026	0.1
SF-36 PCS[b]	3.08	6.04	5.67
p-value		0.092	0.129
Severe SFI flares, n (%)	8 (17.8)	0[c]	2 (4.5)[c]

Larger effect sizes in SLE patients with *high baseline activity* = SLEDAI ≥10, anti-dsDNA+, low C3/C4, or prednisone >7.5 mg/day

- The rate of SAEs was highest in the placebo and 200mg groups; rate of serious infections was highest in the 200mg group. There were 4 deaths; 3 in 200mg (subsequently terminated).
- **Conclusions**: An efficacy signal was apparent. Better efficacy and safety with the 10mg dosage.

[OP0184] EFFICACY AND SAFETY OF TABALUMAB IN PATIENTS WITH SLE: RESULTS FROM 2 PHASE 3, 52-WEEK, MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED TRIALS

- **Background:** Tabalumab is a human IgG4 monoclonal antibody that binds and neutralizes membrane and soluble BAFF.
- Two trials, involving >2000 SLE patients, evaluated the efficacy and safety of SQ tabalumab + standard of care (SoC) *versus* placebo + SoC at 52 weeks

- **Methods**: ANA+ pts with active, moderate-to-severe SLE (SELENA-SLEDAI score ≥6).
- Pts with severe active renal or CNS disease were excluded.
- Loading dose (240 mg) at Wk 0, followed by 120 mg tabalumab q2 wks (120 Q2W), 4 wks (120 Q4W), or pbo.
- **Primary endpoint**: SLE Responder Index 5 (SRI-5) response at Wk 52.
- Key **secondary endpoints**: time to severe flare, corticosteroid sparing, and worst fatigue over last 24 hours (hrs).

[OP0184] EFFICACY AND SAFETY OF TABALUMAB IN PATIENTS WITH SLE: RESULTS FROM 2 PHASE 3, 52-WEEK, MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED TRIALS

- **Results:** SRI-5 was not met in Trial 1, but was met in Trial 2 for the 120 Q2W dose
- Reduction in anti-dsDNA; also, increases in C3/C4 and reduction in total B cells and immunoglobulins (Ig).
- The safety profile of the tabalumab and pbo groups was similar across both trials.

	Trial 1			Trial 2		
	120 Q2W	**120 Q4W**	**Pbo**	**120 Q2W**	**120 Q4W**	**Pbo**
	(n=387)	**(n=389)**	**(n=388)**	**(n=372)**	**(n=376)**	**(n=376)**
SRI-5, %[a,b]	31.8	35.2	29.3	38.4	34.8	27.7
	p=0.409	p=0.052[†]		p=0.002	p=0.051[†]	
Corticosteroid sparing, %[c]	23.4	17.5	18.9	22.5	17.5	13.9
	p=0.280	p=0.747		p=0.051[†]	p=0.342	
Time to severe flare, HR[d]	0.94	0.79		0.88	0.98	
	p=0.724	p=0.204		p=0.480	p=0.911	
Worst fatigue in last 24 hrs, LSM[e]	−1.31	−1.38	−1.01	−0.73	−0.66	−0.57
	p=0.163	p=0.081		p=0.957	p=0.779	

- **Conclusions**: Tabalumab had biologic activity consistent with BAFF inhibition. The primary endpoint was met in 1 of 2 trials for the 120 Q2W dose.

[OP0188] IMPACT OF HYDROXYCHLOROQUINE TREATMENT ON PREGNANCY OUTCOME IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES

- **Objectives:** Despite current management, rates of maternal, fetal, or neonatal complications in APS women range 20-30%.
- To assess the pregnancy outcome in women with antiphospholipid antibody (aPL) treated with hydroxychloroquine (HCQ) during pregnancy

- **Methods**: Observational, retrospective, single centre clinical study
- 170 pregnancies in 96 women with persistent aPL (many with SLE).
- 65 consecutive pregnancies in 31 women treated with HCQ for ≥6 months prior to pregnancy. HCQ was continued throughout gestation (**group A**).
- 119 consecutive pregnancies in 65 women who had not been treated with HCQ prior to conception acted as controls (**group B**).

[OP0188] IMPACT OF HYDROXYCHLOROQUINE TREATMENT ON PREGNANCY OUTCOME IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES

- **Results:** HCQ was associated with higher rate of live births (66.7% in group A vs. 57.1% in group B, p=0.05) and a lower rate of pregnancy morbidity (47.1% in group A vs. 63.0% in group B, p=0.004).
- Pregnancy duration was longer in group A than B (27.6 [6-40] weeks vs. 21.5 [6-40], p=0.03).
- Fetal losses beyond 10 weeks gestation were less frequent in group A (2% vs 10.9%, p=0.05).
- Placenta mediated complications (pre-ecplampsia, abruption placenta, intrauterine growth restriction) were less prevalent in HCQ-treated women (2% vs. 10.9%, p=0.05).
- The association of HCQ with the absence of any complications in pregnancy was confirmed after multivariate analysis (OR 2.2; 95%CI [1.2-136.1]; p=0.04).

- **Conclusions:** Women with aPL may benefit of treatment with HCQ during pregnancy. The addition of HCQ to conventional treatment is worthy of further assessment