cohort. Image 1 represents the Kaplan-Meier curves according to the factors affecting renal survival.

Abstract SAT0419 – Table 1. Characterisation of the UCLH cohort of Lupus Nephritis patients

		ISN/RNP 2003 classification						Total
		I	II	III	IV	V	VI	
Total, N		2	18	38	97	38	2	209
Sex								189
	F, N (%)	2	18	35	88	33	2	(90.4)
M, N (%)		0	0	3	9	5	0	20 (9.6)
Ethnicity								92 (44)
	Caucasian, N (%)	1	8	19	48	12	1	92 (44)
	Afro-Caribbean, N (%)	1	7	9	26	18	1	68 (32.5)
	Asian, N (%)	0	3	10	23	8	0	49 (23.4)
ESRD, N (%)		0	0	8	26	3	1	40 (19)
Deaths, N (%)		0	2	9	21	4	1	38 (18)
Age LN diagnosis, mean±SD		28.68±11.81						
Time FU since LN, mean±SD		12.95±8.96						

ISN/RNP: International Society of Nephrology and Renal Pathology Society; F: females; M: males; ESRD: end-stage renal disease; LN: Lupus nephritis; FU: follow-up.

Abstract SAT0419 – Table 2. Final models for predictors of shorter survival.

Multivariable COX regression	HR [95% CI] p
Overall survival	3.002 [1.461–6.171] 0.003
ESRD	
No antimalarials	2.942 [1.430–6.052] 0.003
Ethnicity (Afro-Caribbean)	2.656 [1.250–5.642] 0.011
Age at LN diagnosis	1.039 [1.012–1.067] 0.004
Renal survival	4.424 [1.542–12.695] 0.006
Histological class (III, IV or VI)	
Ethnicity (Afro-Caribbean)	3.727 [1.691–8.218] 0.001
No antimalarials	2.482 [1.237–4.982] 0.011

HR: hazard ratio; ESRD: end-stage renal disease; LN: Lupus nephritis

Conclusions: Cumulative survival rates and causes of death for this cohort are comparable with other cohorts of LN. ESRD confers the higher risk for death; African or Caribbean ethnicities and not taking antimalarials predict shorter overall and renal survival among these patients.

REFERENCE:

[1] Yurkovich M, Vostretsova K, Chen W, Avina-Zubieta JA. Overall and cause-specific mortality in patients with systemic lupus erythematosus: a meta-analysis of observational studies. *Arthritis Care Res (Hoboken)* 2014;66(4):608–16.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.2426

SAT0420 INCREASED RESISTANT HYPERTENSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE COHORT STUDY

J.S. Gandelman¹, M. Shuey², O. Khan³, J. Neal⁴, A. Dickson⁵, A. Barnado⁵, L. Wang⁴, W. Dupont⁴, C.M. Stein^{5,6}, C.P. Chung^{5,6}. ¹School of Medicine; ²Department of Pharmacology, Vanderbilt University; ³Department of Biostatistics, Vanderbilt University Medical Center; ⁴Department of Biostatistics, Vanderbilt University School of Medicine; ⁵Department of Internal Medicine; ⁶Department of Clinical Pharmacology, Vanderbilt University Medical Center, Nashville, USA

Background: Resistant hypertension (RHTN) is characterised by blood pressure that remains $\geq 140/90$ mmHg despite concurrent use of 3 antihypertensive drugs. In the general population, RHTN is associated with a 47% increased risk of cardiovascular events.¹ Patients with systemic lupus erythematosus (SLE) have increased cardiovascular risk; however, no research has addressed the incidence, prevalence, or risk factors associated with RHTN in patients with SLE.

Objectives: To compare the risk of RHTN in patients with SLE and frequency-matched controls without SLE; to define factors associated with RHTN in patients with SLE.

Methods: We used a validated algorithm (94% PPV) to identify patients with SLE from the electronic health records (EHR) at an academic medical centre.² We established a control cohort matched by age, race, and sex with a 5:1 control-case ratio. Follow-up began at first ICD9 code for SLE (cases) or first ICD9 code (controls) and continued until RHTN diagnosis or last note. RHTN diagnosis required either the simultaneous use of 3 antihypertensive drugs and a mean blood pressure $\geq 140/90$ mm Hg in the following 6 months, or the use of ≥ 4 antihypertensive drugs simultaneously. We used logistic regression and Cox proportional hazards (CPH) models to compare risk of RHTN between groups, with CPH performed on incident cases only.

Results: We studied 1044 patients with SLE and 5241 controls (median age 42, [31–54] 90% female and 70% Caucasian). Of the total cohort, RHTN developed in 106 SLE patients (10%) and 278 controls (4%). The incidence rate of RHTN was 14.7 cases/1000 person-years in SLE patients compared to 7.4 in controls [HR 1.66, 95% CI, 1.25–2.21] (figure 1). In logistic regression models, RHTN was associated with older age, black race, male gender and end stage renal disease (ESRD). Patients with SLE had a higher risk of RHTN when adjusted for age, sex, race, calendar year, and ESRD [HR 1.53, 1.15–2.05]. In an analysis among SLE patients, RHTN was associated with mortality in an unadjusted model [HR 3.38, 2.20–5.18]. This association remained when age, sex and race were added to the model [HR 2.58, 1.65–4.03], but when ESRD, calendar year and creatinine were included, the association was no longer significant [HR 1.51, 0.91–2.51].

Abstract SAT0420 – Figure 1. Cumulative Incidence of RHTN in SLE versus Control Cohort

Log rank test: $p=0.000391$

Conclusions: Patients with SLE have a higher risk of RHTN compared to frequency-matched controls. RHTN is an important comorbidity for clinicians to recognise in SLE, as it is associated with a 3.3-fold higher risk of mortality.

REFERENCES:

[1] Muntner P, et al. *Hypertension* 2014;64(5):1012–1021.
[2] Barnado A, et al. *Arthritis Care Res* 2017;69(5):687–693.

Acknowledgements: VUMC's Synthetic Derivative supported by institutional funding and by the CTSA grant ULTR000445 from NCATS/NIH. CTSA awaUL1TR000445 from NCATS, The Rheumatology Research Foundation, Lupus Research Alliance and K-23 award from the NIAMS.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.3947

SAT0421 LONG-TERM IMMUNOGENICITY OF A QUADRIVALENT HUMAN PAPILLOMAVIRUS VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C.C. Mok¹, L.Y. Ho¹, C.H. To². ¹Medicine, Tuen Mun Hospital; ²Medicine, Pok Oi Hospital, HK, Hong Kong

Objectives: To report the 5 year immunogenicity of a quadrivalent human papillomavirus (HPV) vaccine (GARDASIL) in patients with systemic lupus erythematosus (SLE).

Methods: Female SLE patients and healthy controls, aged 18–35 years, who received GARDASIL in the year 2011 and sero-converted 12 months post-vaccination were followed for the persistence of immunogenicity at 5 years. Antibodies to HPV serotypes 6,11,16,18 were repeated at 5 years using an IgG immunoassay developed on a Luminex microsphere platform (total IgG LIA; Merck Research Laboratory). The rate of sero-reversion was compared between

patients and controls. Factors associated with sero-reversion of the anti-HPV antibodies were studied by statistical analyses.

Results: 50 SLE patients (age 25.8 ± 3.9 years) and 50 controls (25.8 ± 3.9 years) were vaccinated with Gardasil in 2011. The sero-conversion rates of anti-HPV serotypes 6, 11, 16 and 18 in patients and controls were 82%, 89%, 95%, 76%, and 98%, 98%, 98%, 80%, respectively, at month 12 post-vaccination. Among those subjects who sero-converted and were available for follow-up, persistence of the antibodies to HPV serotypes 6, 11, 16 and 18 at 5 years was present in 24/27 (89%), 26/31 (84%), 32/34 (94%), 24/25 (96%) of the SLE patients and 32/33 (97%), 32/33 (97%), 32/32 (100%) and 23/24 (96%) of the controls, respectively. Moreover, antibody titers to HPV serotypes 6 and 16 at 5 years were significantly lower in SLE patients than controls. Seven (21%) SLE patients had sero-reversion of any one of the four anti-HPV antibodies (6, 11, 16 or 18) at year 5 post-vaccination. Patients who sero-reverted had received a significantly higher cumulative dose of prednisolone (13.0 ± 5.34 vs 4.63 ± 4.59 grams; $p=0.002$), mycophenolate mofetil (1050 ± 1180 vs 238 ± 49.5 grams; $p=0.007$) and tacrolimus (375 ± 580 vs 268 ± 1180 mg; $p=0.03$) during the 5 year follow-up than those with persistence of immunogenicity. These sero-reverted patients had also received a non-significantly higher cumulative dose of cyclophosphamide (1.97 ± 5.22 vs 0.43 ± 2.24 grams; $p=0.27$). In addition, sero-reverted patients had more SLE flares in the 5 year follow-up period compared to those with persistence of immunogenicity (3.14 ± 1.21 vs 1.89 ± 1.28 ; $p=0.03$). Among 64 flares in patients with persistent anti-HPV antibodies and 26 flares in those with sero-reversion, renal flares occurred more frequently in the latter group of patients (16% vs 38%; $p=0.02$).

Conclusions: Immunogenicity of the quadrivalent HPV vaccine was retained in 79% of SLE patients at 5 year post-vaccination. Antibody titers to HPV serotypes 6 and 16 were significantly lower in SLE patients than controls. Patients who had more SLE flares, especially renal flares, and had received higher cumulative doses of glucocorticoids, mycophenolate mofetil and tacrolimus were more likely to have sero-reversion of one or more anti-HPV antibodies. Re-vaccination of these patients should be considered.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4332

SAT0422

INDIRECT PATHOGENIC ROLES OF CEREBROSPINAL FLUID ANTI-U1RNP ANTIBODIES IN THE PRESENCE OF ANTI-NR2 ANTIBODIES IN PATIENTS WITH NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

T. Fujii^{1,2}, S. Kondo-Ishikawa³, N. Ishigooka², H. Yoshifuji², K. Ohmura², T. Mimori². ¹Rheumatology and Clinical Immunology, Wakayama Medical University, Wakayama; ²Rheumatology and Clinical Immunology, Kyoto University School of Medicine; ³Rheumatology, National Hospital Organization Utano Hospital, Kyoto, Japan

Background: Autoantibodies (auto Abs) and inflammatory mediators (IMs) in cerebrospinal fluid (CSF) may be involved in the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE). Previous studies indicated that anti-N-methyl D-aspartate receptor NR2 subunit (NR2) Abs have a pathogenic role in NPSLE by BBB disruption.¹Hirohata S, et al. *Arthritis Res Ther*. 2014. We also reported the association between NPSLE and CSF-anti-U1RNP Abs (Sato, et al. *A and R*, 2010).

Objectives: In the present study, synergistic effects of these auto Abs, their associated IMs, and blood brain barrier (BBB) permeability are determined in NPSLE patients.

Methods: CSF samples were collected from 69 of NPSLE patients at their acute phase and 13 of non-NPSLE control after obtaining the written informed consent. CSF anti-NR2 and anti-U1RNP Abs were determined by ELISA. CSF IL-6, IL-8, and monokine induced by IFN- γ (MIG) were measured by quantitative multiplex cytokine analysis. BBB permeability was evaluated by albumin quotient (Qalb).

Results: 1) CSF IL-6 levels were higher in CSF anti-NR2 Ab +ve (70 ± 178 pg/mL) than in -ve (11 ± 32 , $p=0.02$) patients and in controls (16 ± 40 , $p=0.003$) and positively correlated with anti-NR2 Ab titer ($r=0.42$, $p=0.003$). Anti-U1RNP Ab positivity was not associated with CSF IL6 elevation. 2) CSF IL-8 levels were higher in CSF anti-U1RNP Ab +ve than in -ve (270 ± 862 vs. 52 ± 177 pg/mL, $p=0.04$) patients. Anti-NR2 Ab positivity was not involved in CSF IL8 elevation. 3) CSF MIG levels were more elevated in both CSF anti-NR2 +ve (4483 ± 11845 pg/mL, $p=0.04$) and anti-U1RNP Ab +ve (5519 ± 13504 , $p=0.03$) patients than in controls (115 ± 125). 4) All the patients were divided into 4 groups: CSF anti-NR2 +ve/anti-U1RNP+ve (double positive [DP], n=9), anti-NR2 +ve/anti-U1RNP -ve (aNR2, n=15), anti-NR2 -ve/anti-U1RNP+ve (aU1RNP, n=9), and anti-NR2 -ve/anti-

U1RNP -ve (double negative [DN], n=36). In comparison between DP and aNR2 groups, anti-U1RNP Abs had a synergistic effect on CSF IL-6 elevation (150 ± 260 vs. 18 ± 44 pg/mL, $p=0.03$) that is not directly associated with anti-U1RNP Ab positivity. In comparison with aNR2 group, both CSF IL-8 (543 ± 1198 vs. 43 ± 102 pg/mL, $p=0.04$) and MIG ($10104 \pm 17\,748$ vs. 1111 ± 2584 pg/mL, $p=0.03$) levels, which were positively correlated with CSF anti-U1RNP Ab titer, were more elevated in DP group. 5) Qalb was positively correlated with CSF IL-8 ($r=0.51$, $p<0.0001$) and MIG ($r=0.44$, $p=0.0003$), suggesting that CSF anti-U1RNP Ab positivity is involved in the BBB disruption. Actually, Qalb ($\times 10^3$) tended to be higher in DP than in aNR2 group (13 ± 9 vs. 9 ± 8 , $p=0.06$) and CSF anti-NR2 Ab titer appeared to be more elevated in DP than in aNR2 group (81 ± 47 vs. 57 ± 21 , $p=0.06$).

Conclusions: The present study suggested that anti-NR2 and U1RNP Abs have synergistic effects on CSF IL-6 elevation in patients with NPSLE. CSF IL-6 level was associated with anti-NR2 Ab titers, which depend on BBB permeability. CSF anti-U1RNP Ab-mediated IL-8 and MIG elevation may induce BBB disruption followed by anti-NR2 Ab penetration into CSF.

REFERENCES:

- [1] Sato T, Fujii T, et al. *Arthritis Rheum* 2010;62:3730.
- [2] Yokoyama T, Fujii T, et al. *Lupus* 2014;23:635.

Acknowledgements: The present study is supported by the Japanese Ministry of Education, Culture, Sports, Science, and Technology.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3033

SAT0423

MOLECULAR PROFILES ASSOCIATE WITH CLINICAL DISEASE ACTIVITY AND INFORM PATIENT SUBSETTING IN ADULT SYSTEMIC LUPUS ERYTHEMATOSUS

J.M. Guthridge, R. Lu, C. Arriens, T. Aberle, S. Kamp, M.E. Munroe, T. Gross, W. DeJager, S.R. Macwana, R.L. Bourn, S. Apel, H. Chen, E.F. Chakravarty, A. Thanou, J.T. Merrill, J.A. James. *Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, USA*

Background: Systemic lupus erythematosus (SLE) is characterised by remarkable clinical and pathophysiological diversity, hindering diagnosis, treatment and treatment development. Subsetting of patients based upon clinical presentations alone has not identified homogeneous groups of patients best treated with a directed therapeutic.

Objectives: To cluster SLE patients into more homogeneous subsets with common molecular pathway signatures, and to assess the clinical, therapeutic, and demographic features enriched in each cluster.

Methods: Serial or single plasma, serum and RNA samples (n=290) were collected from 198 SLE patients who met ACR classification. Disease activity was assessed by modified SLEDAI-SLEDAI at an average of 17 visits per patient. Transcriptional co-expression signature module scores were calculated from Illumina Beadchip Microarray gene expression data for 29 immune pathway related modules. Plasma soluble mediators (n=23) and 12 antinuclear autoantibodies (anti-dsDNA, chromatin, ribosomal P, Sm, Sm, SmRNP, RNP, Ro/SSA, La/SSB, centromere B, Scl-70 and Jo-1) were assessed by multiplex bead-based assay and ELISA. Spearman correlations were used for univariate and multivariate analysis using R. Patients were clustered on module signature scores and soluble mediators using random forest and tSNE.

Results: SLEDAI scores strongly correlated with interferon modules and were modestly correlated with plasmablast and select cell cycle signatures in this adult lupus collection. SLEDAI scores also correlated with soluble levels of IFN α , IL21, IL1 α , IL17A, IP10 and MIG. Random forest defined seven clusters of SLE patients with unique molecular phenotypes based upon gene co-expression module signatures and soluble mediators. Inflammation and interferon (IFN) signatures were elevated in Clusters 1 (moderately) and 4, with decreased T cell signatures in Cluster 4. The other clusters had lower IFN and inflammation signatures, but differed in their monocyte, plasmablast and T cell signatures. Clusters 1 and 4 had the highest SLEDAI scores, with high rates of anti-dsDNA, low complement, proteinuria and hematuria; these features were also prominent in Cluster 3, which lacked the IFN and inflammation signatures. Cluster 6 had the highest plasmablast module score, highest IL1 α levels, and SLEDAI scored rashes, but only moderate IFN and inflammation module scores. Cluster 2 had higher rates of SLEDAI scored alopecia, a slightly elevated inflammation signature, but lower interferon signature and lower soluble mediator levels.