POSTER VIEWING PRESENTATIONS

PV001 / #50

Poster Topic: ***AS01 - Adaptive Immunity***

TYPE I INTERFERON AND MITOCHONDRIAL DYSFUNCTION ARE ASSOCIATED WITH DYSREGULATED CYTOTOXIC CD8+ T CELL RESPONSES IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

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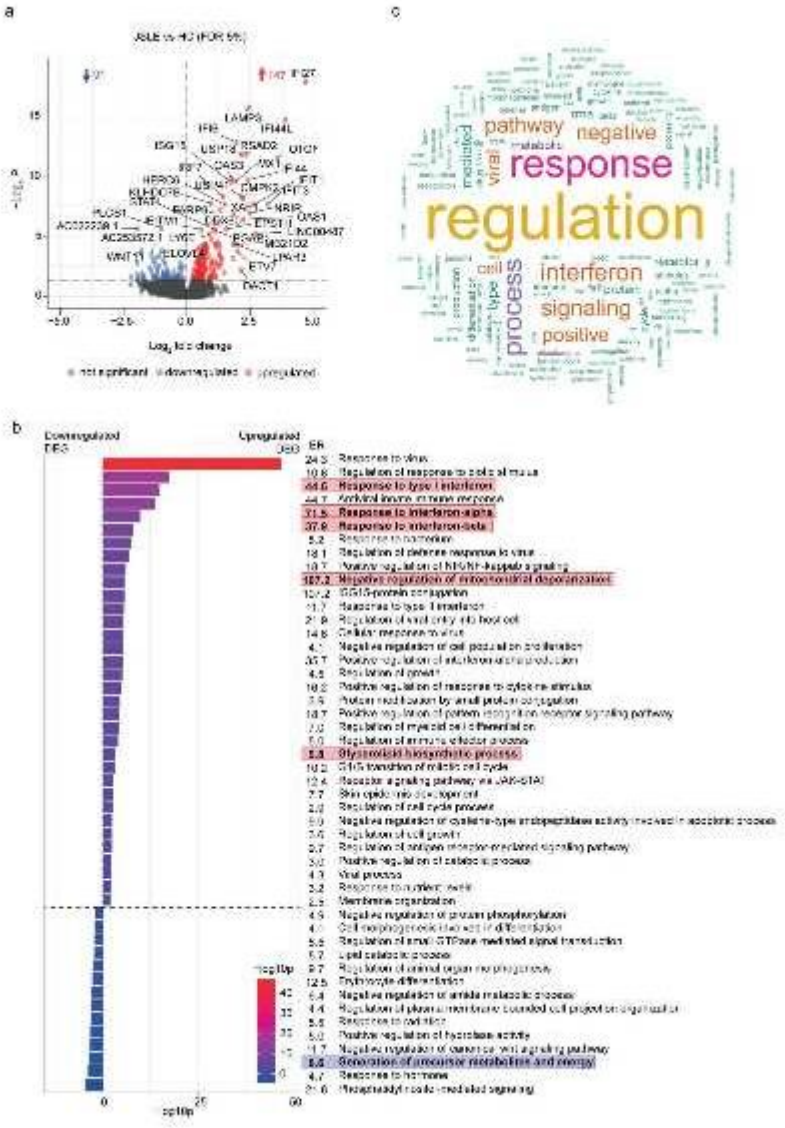
Background/Purpose: Juvenile systemic lupus erythematosus (JSLE) is an autoimmune condition which causes significant morbidity in children and young adults. While many aspects of immune dysfunction have been studied extensively in adult-onset SLE, there is limited and contradictory evidence of how cytotoxic $CD8^+$ T cells contribute to disease pathogenesis, and studies exploring cytotoxicity in JSLE are rare.

Methods: Detailed characterisation of peripheral blood $CD8^+$ T cells was undertaken in JSLE patients (n=44, median age 22 years and disease duration 9 years) and age/sex-matched healthy controls (HC, n=68, median age 20 years). Multi-parameter flow cytometric immunophenotyping, RNA sequencing, serum metabolomic profiling, cell culture assays/functional *in vitro* studies, and mitochondrial morphology studies were performed.

Results: Frequencies of $CD8^+$ T cells expressing the cytotoxic mediator perforin and effector cytokines interferon (IFN)-γ and tumour-necrosis-factor (TNF)-α were reduced in JSLE versus HC, irrespective of treatment or disease activity. Transcriptomic and serum metabolomic analysis identified that upregulated type I IFN signalling, mitochondrial dysfunction and metabolic disturbances underpinned these observations (see Figure below). Mechanistic studies demonstrated that alteration in these pathways lead to a deficiency in effector memory (EM) JSLE $CD8^+$ T cells, which are enriched for cytotoxic mediator-expressing cells, due to enhanced apoptosis of these cells selectively in JSLE versus HC. Figure: **Transcriptomic analysis reveals upregulation of IFN-α responses and potential metabolic and mitochondrial disturbances in $CD8^+$ T cells in JSLE.**



(a) Volcano plot showing differences in gene expression from RNA sequencing of CD8+ T cells from JSLE (n=26) vs HC (n=29). Blue and red points represent statistically significant differentially expressed genes below the FDR adjusted p-value threshold of 0.05. Blue and red arrows indicate number of statistically significant downregulated and upregulated genes, respectively. **(b)** Bar plot showing -log10p values and enrichment ratios (ER) of summary enriched pathway GO BP ontology terms in CD8+ T cells in JSLE vs HC using the 147 significantly upregulated and 91 significantly downregulated genes (FDR adjusted p<0.05). Statistical significance of enrichment was determined using a p-value cut-off of 0.01 and a minimum enrichment score of 1.5. Terms highlighted in red and blue represent pathways of potential interest, derived from upregulated (red) and downregulated (blue) genes in JSLE vs HC. **(c)** Word cloud representing all words taken from significantly enriched pathways in Metascape GO enrichment and GSEA analysis of DEGs in CD8+ T cells in JSLE vs HC. Text size indicates the frequency of the word.

Conclusions: Cytotoxic capacity of CD8⁺ T cells is diminished in JSLE due to a numerical deficiency in EM CD8⁺ T cells, which is linked to mitochondrial defects, dysregulated type I IFN signalling, and increased apoptosis. Future studies are needed to understand the therapeutic implications of these findings.

PV003 / #307

Poster Topic: ***AS01 - Adaptive Immunity***

PERIPHERAL BLOOD B-CELL SUBSETS IN PATIENTS WITH EARLY AND ESTABLISHED SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: To examine B-cell subsets in peripheral blood of patients (pts) with early and established systemic lupus erythematosus (SLE), and to analyze the association between the B-cell subsets and SLE activity.

Methods: Peripheral blood of 20 healthy donors, 134 patients (118 women (88%) and 16 men (12%)) with a SLE (SLICC 2012), Me(IQR) age 34 (26-41) years, disease duration 3.0 (0.3-12.0) years; 84 patients had a disease duration of more than 18 months, 50 patients had early SLE (disease duration of less than 18 months), SLEDAI-2K 7 (4-11)) were assessed for B-cell subpopulations. CD19+B cells, memory B cells (CD19+CD27+), non-switched memory B cells (CD19+IgD+CD27+), switched memory B cells (CD19+IgD-CD27+), naïve (CD19+IgD+CD27-), double negative (CD19+IgD-CD27-), transitional (CD19+IgD+CD10+CD38++CD27-) B cells and plasmablasts (CD19+CD38+++IgD-CD27+CD20-) were assessed by multicolor flow cytometry.

Results: In pts with SLE, compared to healthy donors was found the higher percentage of memory B cells, non-switched memory B cells, transitional and plasmablasts; higher absolute level switched memory B cells, transitional and plasmablasts; lower percentage and absolute level naïve B cells. In pts with early SLE, was seen the higher percentage of B cells, higher absolute level of B cells, memory B cells, non-switched and switched memory B cells, naïve, double negative, transitional B cells and lower percentage of plasmablasts, table 1. In pts with early SLE we found a significant positive correlation between the percentage of double negative B lymphocytes and SLICC (r=0.3), positive correlation between the proteinuria and B-lymphocytes (r=0.35), memory B-cells (r=0.38), switched memory B-cells (r=0.42), double negative lymphocytes (r=0.42); a negative correlation between the percentage of transitional cells and SLICC (r=0.33).

Table 1

Parameters		Pts with SLE n=134	Established SLE n=84	Early SLE n=50	Healthy donors n=20
CD19+B- cells	%	9.5 (4.1- 12.5)	6.2 (3.6-10.02)	12.5 (8.09-19.4)*	8.7 (7.2- 11.0)
	abs	0.2 (0.1- 0.2)	0.075 (0.05-0.15)	0.15 (0.06-0.33)*	0.2 (0.1- 0.2)
memory B cells	%	22.9 (12.1- 26.9)**	17.9 (12.2-26.9)	15.9 (11.98-25.8)	2.2 (1.1- 3.0)
	abs	0.03 (0.01- 0.03)**	0.015 (0.07-0.03)	0.03 (0.01-0.06)*	0.004 (0.001- 0.007)
non-switched memory B cells	%	15.8 (7.1- 20.7)**	14.46 (7.89-20.7)	12.27 (6.73-20.1)	8.4 (3.7- 11.1)
	abs	0.02 (0.004- 0.03)	0.009 (0.004-0.02)	0.016 (0.008-0.03)*	0.002 (0.005- 0.02)
switched memory B cells	%	15.7 (6.5- 21.5)	14.4 (6.21-21.9)	11.2 (8.03-19.9)	13.6 (9.3- 17.0)
	abs	0.03 (0.006-0.03)**	0.01 (0.004-0.02)	0.015 (0.009-0.04)*	0.02 (0.01- 0.04)
naïve B cells	%	55.1 (44.4- 69.0)**	57.2 (14.5-68.9)	59.02 (49.2-69.7)	64.5 (57.6- 72.4)
	abs	0.05 (0.02- 0.1)**	0.035 (0.02-0.09)	0.09 (0.03-0.2)*	0.1 (0.06- 0.1)
plasmablasts	%	3.4 (0.9-4.6)**	2.9 (1.15-4.96)	1.65 (0.53-2.9)*	0.2 (0.1- 0.2)
	abs	0.003 (0.001- 0.004)*	0.002 (0.001-0.004)	0.002 (0.001-0.004)	0.0003 (0.0001- 0.0004)
transitional B cells	%	16.2 (6.0- 19.7)**	9.97 (6.02-21.2)	11.65 (5.9-16.8)	0.08 (0.0- 0.1)
	abs	0.03 (0.01- 0.03)**	0.009 (0.004-0.02)	0.016 (0.008-0.04)*	0.0001 (0.0- 0.0003)
double negative B cells	%	13.3 (7.4- 15.3)	11.6 (7.45-15.6)	10.15 (7.1-14.9)	13.7 (7.1- 19.3)
	abs	0.02 (0.01- 0.02)	0.008 (0.005-0.016)	0.015 (0.009-0.03)*	0.02 (0.01- 0.02)

*p<0.05 between early and established SLE groups; **p<0.05 between patients with SLE and healthy donors

Conclusions: Pts with early SLE have higher levels of B cells, non-switched and switched memory B cells, naïve, double negative, transitional B cells and lower levels of plasmablasts. The level of memory B-cell, switched memory cells, and double negative cells correlates with the level of autoantibodies, the development of nephritis, and the SLICC index.

PV004 / #575

Poster Topic: ***AS01 - Adaptive Immunity***

GLOBAL IMMUNE REPERTOIRE PROFILING SUGGESTS MULTIFACETED UNRESOLVED DYSREGULATION UPON SYSTEMIC LUPUS ERYTHEMATOSUS IMMUNOSUPPRESSANT THERAPY

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Background/Purpose: Objective Examination of cross-treatment immune dynamics and its potential contribution to the relapse of systemic lupus erythematosus (SLE) in the real clinical setting.

Methods: Methods We performed single-cell RNA and VDJ profiling on 31 samples from 24 individuals in total, consisting of 20 naive SLE patients, 7 matched standard-of-care-treated SLE patients, and 4 health control samples. Along with published SLE data, we compiled a comprehensive SLE immune atlas of ~1.6 million cells.

Results: Results While the treatment did lead to the suppression of global immune overactivity, we discovered for the first time its failure to effectively restore several undocumented abnormalities in treatment-naïve patients, including the drop in somatic hypermutation (SHM) of memory and DN B cells, and the clonal expansion of $CD4^+$ Th1 and $CD8^+$ memory T cells.

Conclusions: Conclusion Our study provides valuable data and sheds lights on the underlying multifaceted unresolved dysregulation upon SLE immunosuppressant therapy under the real clinical setting; such dysregulation may further contribute to the high post-treatment relapse rate and thus call for additional target-specific treatment strategies.

PV006 / #242

Poster Topic: ***AS01 - Adaptive Immunity***

CD8+ T CELLS AND THEIR ANTIGENS IN END-ORGAN DAMAGE IN LUPUS NEPHRITIS

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Background/Purpose: Lupus Nephritis (LN) is a severe and frequent complication of systemic lupus erythematosus (SLE). It is increasingly clear that the LN kidney hosts pathogenic mechanisms contributing to disease severity, with CD8⁺ T lymphocytes coming to the fore as relevant players. Their pathogenicity may be due to their recognition of renal (neo/modified/cryptic) antigens and consequent tissue damage.

Methods: We performed scRNASeq on flow-sorted CD8⁺ T cells from kidney, urine and blood samples at diagnosis, from two patients with active LN, using a T-cell adapted SmartSeq2 method. Three to five additional patients will be included in the future. T cell receptor (TCR) repertoire analyses were performed on the scRNASeq data. To identify antigen(s) that may be recognized by tissue-enriched TCRs, we use a functional *in vitro* screening assay: Reporter T cell lines (expressing an NFAT-responsive GFP element and a TCR of interest) are co-cultured with modified HEK293T target cells (expressing a patient HLA, and a cDNA library from the autologous kidney biopsy). Autologous EBV-transformed B cells are used as controls for TCR recognition of virally infected cells. This allows for live-cell screening for T cells recognizing antigens presented by target cells, by virtue of their expression of GFP.

Results: We identified a restricted TCR repertoire, enriched in kidney and urine as compared to blood, in both patients. This may suggest local, antigen-driven expansion. Moreover, the most repeated TCRs in kidney largely overlapped with those from paired urine (but not blood), suggesting that urine can mirror kidney CD8⁺ T cell populations. We have begun by screening for antigens recognized by the five most highly repeated TCRs from kidney and urine from one of the two patients (**Fig. 1**): a poor responder with high renal CD8⁺ T cell infiltration and renal damage (histology and clinical tests). Four of the five TCRs showed robust recognition of autologous EBV-B cells. Intriguingly, the fifth TCR (that did not show reactivity to B-EBV cells) was identified in T cells expressing a dual TCR α-chain. We hypothesize that this T cell clone may have been positively selected thanks to the reactivity of one of its TCRs to EBV-infected cells, but that its second TCR (with the same β-chain but a different α-chain) could be reactive to kidney autoantigens. Screening of the cDNA library with this (non EBV-B cell-reactive) TCR has shown promising results in the first step of the screening process; this will be repeated

with further sub-cloning in order to identify the antigenic peptide responsible for the activation.

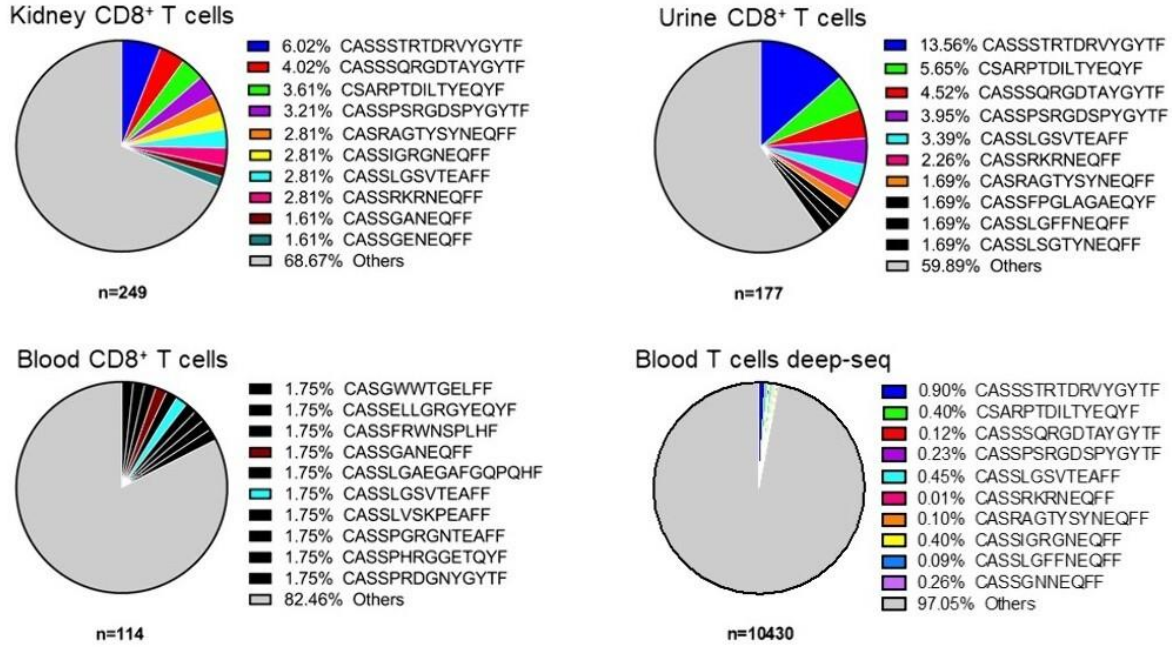

Fig 1. Clonal expansion of CD8⁺T cells as reflected by TCR repertoire in one renal biopsy, from a patient with poor outcome. Frequency of cells with identical TCR-β CDR3, by scRNA-Seq of CD8⁺ cells, or (bottom-right) deep-sequencing of blood (Adaptive Biotechnologies). Colors: specific to each clonotype, across tissues. n: Number of single-cells

Conclusions: Identifying the antigen(s) responsible for local CD8⁺ T cell expansion may be key in addressing kidney-based pathogenic mechanisms in LN. These antigen(s) may be expressed in the case of some but not all patients (or, for *e.g.*, differ in terms of abundance or spatio-temporal distribution), and may be associated with outcome. The nature of the antigen(s) may also provide information on disease-promoting cellular/molecular processes that occur in the LN kidney.

PV007 / #645

Poster Topic: ***AS02 - Animal Models***

THE ERB AGONIST, WT-IV-012, SUPPRESSES THE INFLAMMATORY RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that causes inflammation in many of the body's tissues, including the skin, joints, lungs, kidneys and heart. This inflammation causes damage to these tissues and produces significant mortality, with most complications in the early stages of the disease involving direct effects on various organs. SLE affects young women between the ages of 15 and 45 years at a 9:1 rate as compared to men. The etiology is complex and remains elusive, however the susceptibility of women during the years in which estrogen levels are at their highest may suggest a significant and critical contribution to the development of SLE. Estrogens are known to have pleiotropic effects on the immune system which is mediated through either estrogen receptor α (ERα), estrogen receptor β (ERβ) or the cell surface G-protein coupled receptor GPER1. ERα has been studied extensively in this context, however ERβ and GPER1 have received much less attention. Previously, our group and others have shown that ERα carrying immune cells are mediators of proinflammatory effects of estrogen more so than cells that lack this receptor. In the pursuit of a drug that is tailored to have a favorable selective estrogenic effect, the OSU Drug Development Institute discovered a novel carborane-based selective estrogen receptor modulator (SERM), WT-IV-012. This ERβ agonist exhibits potent binding of human ERβ (Ki = 2.0 nM) and functional selectivity for ERβ over ERα of at least 200-fold. The work presented herein describes the potential utility of WT-IV-012 in treating SLE in a humanized mouse model of the disease.

Methods: PBMC isolated from patients with active SLE were adoptively transferred into NSG mice and allowed to expand in vivo for one week. The mice were divided into 3 cohorts receiving either vehicle control, prednisone or WT-IV-012 via oral gavage on a daily basis for five weeks. Blood samples were taken at baseline, 3 and 5 weeks. Serum was analyzed for circulating cytokines using the MSD human V-PLEX Proinflammatory Panel. At 5 weeks, mice were euthanized, kidneys and hearts were harvested and processed for H&E and IHC histology and urine was collected and tested for proteinuria. Lupus patient PBMCs were isolated and stimulated under various conditions and then flow cytometry was used to identify specific cell types affected by WT-IV-012 and cytokine ELISAs were used to evaluate the cell culture supernatants.

Results: WT-IV-012 was as effective as prednisone in suppressing immune cell invasion of the kidney as well as inflammation of the heart. Furthermore, the ERβ agonist

demonstrated superior effectiveness in suppressing pro-inflammatory cytokines as compared to prednisone as well as reducing the proteinuria seen in the vehicle treated control mice. The in vitro effect of WT-IV-012 confirmed the suppression of IFNγ and TNFα and revealed the cell type specific effects of the drug.

Conclusions: WT-IV-012 is an effective inhibitor of the SLE inflammatory process and warrants additional study as a potential therapeutic in patients with SLE.

PV008 / #647

Poster Topic: ***AS02 - Animal Models***

ANTI-TRIM72 AUTO-ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AND A LUPUS MOUSE MODEL WITH MYOCARDITIS COMPROMISE MEMBRANE REPAIR IN CARDIOMYOCYTES POTENTIALLY CONTRIBUTING TO CARDIOVASCULAR DISEASE PROGRESSION

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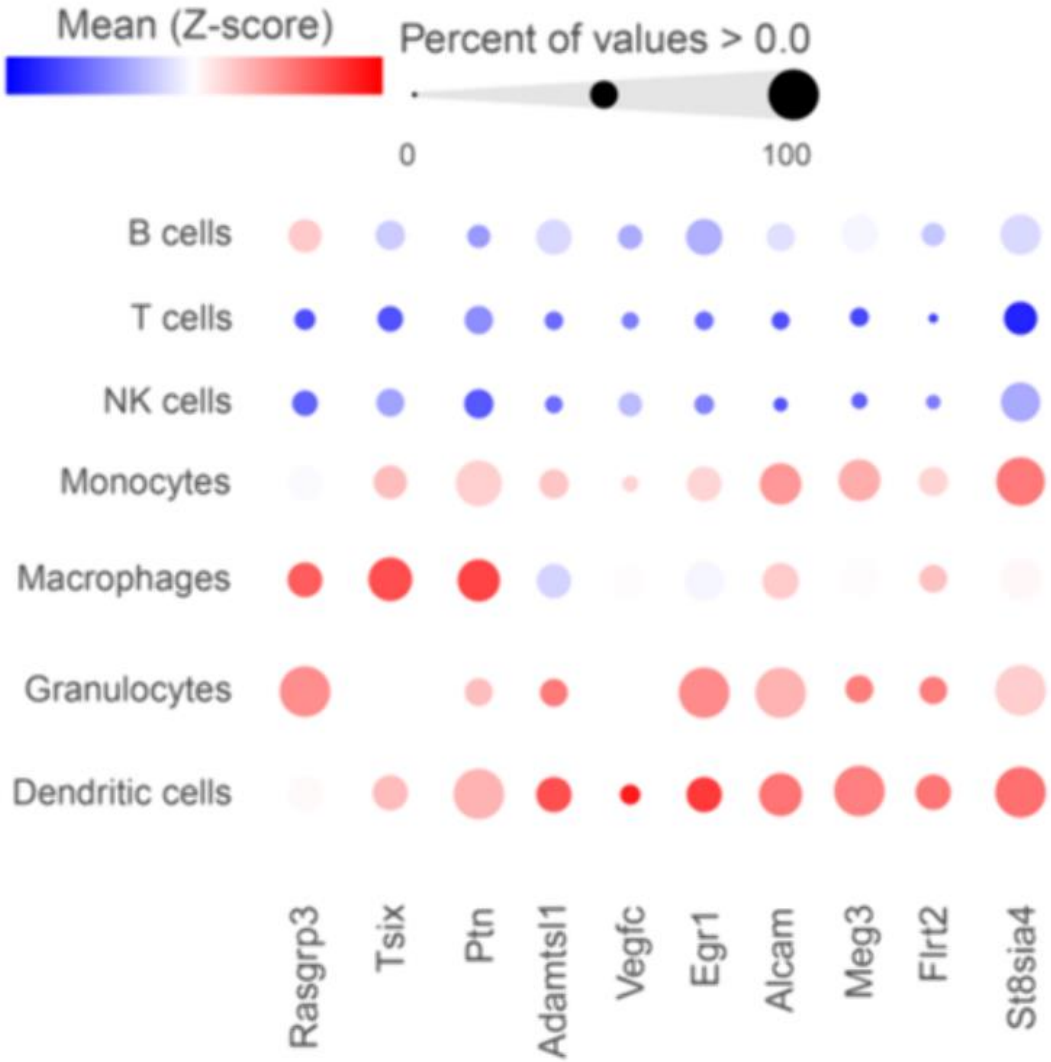
Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that causes inflammation in many of the body's tissues, including the heart. Recent studies attribute almost 50% of mortality in lupus patients to cardiovascular (CV) disease after the first 10 years. A significant prevalence of myocardial inflammation in SLE patients has been recognized across the age spectrum confirming the presence of myocarditis in up to 40% of lupus patients. Understanding the pathogenic mechanisms that drive CV disease in SLE patients is essential for its management and for developing new therapeutic approaches. Our studies and others link reduced plasma membrane repair with development of CV disease. Given the importance of the membrane barrier function in preventing exposure of intracellular antigens to the extracellular space where they could act as autoantigens, compromised membrane repair may be a contributory mechanism to SLE pathogenesis. Previous studies have linked the Tripartite Motif (TRIM) family of E3 ubiquitin ligase proteins to membrane repair and as autoantigens in lupus. Our recently published work identified TRIM72 as a new autoantigen in myositis patients and our current studies indicate this may be the case in lupus as well. Given the potential contribution of membrane repair to the development of lupus associated myocarditis and the role of TRIM72 in membrane repair, we hypothesized that defects in membrane repair are critical in the pathogenesis of lupus myocarditis leading to aberrant exposure of membrane repair proteins to the extracellular space and these autoantibodies create a positive feedback loop that causes further exposure of intracellular antigens that contributes to the progression of lupus myocarditis pathogenesis.

Methods: A custom anti-TRIM72 antibody ELISA was used to quantify serum levels of circulating TRIM72 antibodies in mouse and human samples. Multi-photon confocal laser microscopy was used to measure the dynamics of membrane repair in vitro. Single nuclei (sn) RNAseq of NZM2410 mouse hearts was performed on young, middle and old

aged mice. Partek™ Flow™ software was used to QC, normalize and analyze the transcriptomic expression data.

Results: We demonstrate that anti-TRIM72 auto-antibodies are elevated in both SLE patient serum diagnosed with myocarditis and serum of NZM2410 mice with myocarditis. A polyclonal antibody against TRIM72, as well as both SLE patient serum and NZM2410 serum containing TRIM72 antibodies compromise membrane repair in vitro. snRNAseq revealed that cardiomyocytes are reduced and fibroblasts increase as NZM2410 mice age. Specific CV disease pathways are enriched in cells of aged hearts of NZM2410 mice as compared to young mice. Genes linked to lupus disease pathology are differentially expressed in immune cells. Subcluster analysis of specific cell populations, e.g. cardiomyocytes, fibroblasts, etc. revealed several cell types and gene expression profiles associated with development of SLE myocarditis.

Conclusions: The plasma membrane repair protein TRIM72 is an autoantigen in SLE associated myocarditis and potentially contributes to disease pathogenesis. We demonstrate the presence of TRIM72 antibodies in SLE patients that can compromise membrane repair in cardiomyocytes in vitro. Transcriptomics of cardiac tissue. Ongoing studies will examine if these defects could lead to membrane repair protein exposure to the extracellular space causing the production of additional autoantibodies which contribute to a vicious cycle that exacerbates SLE pathology.



Transcriptomic analysis of cardiac tissue reveals multiple differentially expressed genes linked to lupus. A partial list of statistically significant differentially expressed genes in immune cells is shown.

PV009 / #339

Poster Topic: *AS02 - Animal Models*

A NOVEL HUMAN IL23A-DRIVEN MOUSE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Interleukin 23, a member of the IL12 cytokine family, has been implicated in the reprogramming of immune cells by inducing and maintaining their proinflammatory state. It acts as a heterodimer composed of two subunits IL23A and IL12B and it has been shown to play a lead role in pathogenic mechanisms involved in the development of immune mediated inflammatory diseases like psoriasis, inflammatory bowel disease etc. To further explore the contribution of IL23A in disease pathogenesis we generated a transgenic mouse expressing deregulated levels of the human IL23A subunit (TghIL23A) and characterized the phenotypes developed.

Methods: To achieve deregulated levels of expression of the human IL23A subunit, we designed the TghIL23A transgene containing the complete intron-exon sequence of human IL23A gene under the human IL23A promoter, with its 3'UTR replaced with the human-beta-globin in order to abolish all posttranscriptional regulation. Signs of overt pathology included skin lesions which were assessed clinically and all affected organs, including skin, liver, lungs, spleen and lymph nodes were examined histopathologically. Biochemical and hematological analyses were used for the evaluation of blood and urine samples, while biomarkers of pathology including cytokines and anti-nuclear antibodies, were assessed at different ages by ELISA and molecular analyses. Both overt pathology signs and biological fluids analyses were assessed in crosses of TghIL23A to IL12BKO and Rag1KO mice. The response of the TghIL23A mice to human therapeutics was assessed by treating them twice weekly with guselkumab.

Results: The human IL23A subunit in the transgenic mice that we generated could form active IL23 entities by forming heterodimers with its mouse partner and resulted in the development of clinical phenotypes that involved chronic inflammatory lesions in the skin, kidney and lungs as well as enlargement of the spleen and local lymph nodes. Signs of the developing pathology also included the development of proteinuria, circulating anti-dsDNA antibodies, increased levels of circulating IgGs that were gradually found deposited in kidney glomeruli and skin. The formation of human-mouse heterodimers was supported by the abolishment of the phenotypes upon crossing the

TghIL23A to IL12BKO, while the autoimmune nature of the developing pathologies was supported by the abolishment of the pathologies upon crossing to Rag1KO mice that lack a functional immune system. The above-described pathological features exhibit significant similarities to those observed in human SLE patients supporting that the transgenic mouse that we developed can serve as novel mouse model of lupus erythematosus with cutaneous implications. Interestingly, our preliminary evidence indicates that equally to IL23A, mice expressing the human IL12B subunit show similar signs of lupus.

Conclusions: We have generated and characterized a novel genetic mouse model of SLE, providing proof-of-concept for the etiopathogenic role of hIL-23A. This new model integrate several characteristics of the human disease complexity and chronicity making it attractive preclinical tool for studying IL23-dependent pathogenic mechanisms and for the evaluation of human therapeutics targeting the human IL23 pathway.

PV010 / #583

Poster Topic: *AS02 - Animal Models*

ESTROGEN RECEPTOR ALPHA LOCALIZATION AFFECTS CYTOKINE GENE EXPRESSION AFTER TLR7 AGONISM IN LUPUS PRONE MALES

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by autoantibody production and immune complex formation, resulting in inflammation and tissue damage. There are gaps in knowledge regarding the pathogenesis of SLE, including female sex as a risk factor. It has also been suggested that male patients diagnosed with SLE have increased disease severity (organ-threatening disease) compared to women. It is known that estrogen contributes to SLE disease expression. Estrogen exerts its effects on the immune system via the nuclear hormone receptor estrogen receptor alpha (ERα), and ERα's function is tissue-, cell-, and localization-specific. Herein, we backcrossed mice with membrane-only ERα (MOER) function and nuclear-only ERα (NOER) function onto the lupus prone B6.Nba2 strain. This allows us to investigate the hypothesis that ERα localization to the membrane may impact SLE disease development.

Methods: Bone marrow (BM) was isolated from MOER, NOER, and wildtype (WT) male B6.Nba2 mice at 12 weeks of age. On days 0 and 3, BM cells were cultured with GM-CSF and IL-4 (10 ng/uL) to promote dendritic cell (BMDC) differentiation. On day 7, BMDCs were treated with 200 μM of loxoribine (Lox, a Toll-like receptor 7 agonist) or DMSO vehicle for 6 hours. Message levels of pro-inflammatory cytokines IL-1β, IL6, and TNF-α were assessed via qPCR.

Results: NOER BMDCs had a trend toward increased *Il1β* expression after 6 hours of Lox treatment compared to MOER (p=0.07) but not WT BMDCs (p=0.91). There was a trend toward downregulation of *Il1β* in MOER BMDCs treated with Lox compared to WT BMDCs (p=0.14). MOER BMDCs also had decreased *Il6* compared to WT BMDCs (p=0.02), while BMDCs from NOER mice trended toward increased *tnf-α* expression compared to MOER (p=0.07) BMDCs.

Conclusions: These preliminary results suggest that ERα localization to the plasma membrane impacts IL-1β, IL-6 and TNF-α expression in DCs. Non-genomic mechanisms of action by membrane ERα may be involved in anti-inflammatory signaling. Further investigation is warranted in female mice to elucidate sex differences in pro- and anti-inflammatory cytokine profiles in WT, MOER, and NOER BMDCs after TLR7 agonism.

PV011 / #383

Poster Topic: *AS02 - Animal Models*

RELATING TRANSCRIPTOMIC PROFILES OF HUMAN LUPUS NEPHRITIS AND GLOMERULONEPHRITIS IN LUPUS-PRONE MICE

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Background/Purpose: The presentation of lupus nephritis (LN) is heterogeneous, but is thought to initiate with immune complex deposition in the kidney and acute inflammation that develops into a chronic condition resulting in end-stage renal disease. We sought to better understand the molecular features of LN through gene expression profiling of human disease and its relationship to that of a well-defined murine model of LN.

Methods: Human subjects were control (CTL) patients without kidney pathology and patients with ISN/RPI class II-V LN. The NZM2328 lupus-prone mouse, an established model of human LN that progresses from pre-disease (CTL) to acute (AGN), transitional (TGN) and chronic (CGN) nephritis, was also assessed (Daamen et al. *Front Immunol.* 2023). Gene expression was analyzed from glomerular (Glom) and tubulointerstitial (TI) regions for enrichment of informative gene modules by Gene Set Variation Analysis (GSVA).

Results: GSVA and and unsupervised k-means clustering identified four subsets of LN in the human Glom and TI, which were ordered from least to most severe based on abnormalities in molecular profile as compared to CTL subjects. In the Glom, subset specific changes in metabolism, kidney tissue, immune, endothelial cell and podocyte modules were noted (**Fig. 1a**). Mouse orthologs of the human gene modules were applied to analysis of the Glom from lupus-prone mice (**Fig. 1b**). In the mouse Glom, progression from CTL to AGN and TGN was accompanied by an increase in immune/inflammatory modules and decreases in metabolism and tissue modules. CGN mice were divided between Subsets 2-4 with some mice that exhibited an inflammatory profile and others that were de-enriched for all modules indicative of a post-inflammatory state. Analysis of the human and mouse TI revealed progressive abnormalities (**Fig. 2**). The TI samples from human CTL patients were clustered in Subset 1 and exhibited minimal immune module enrichment, whereas metabolism and kidney tubule modules were prominent (**Fig. 2a**). Subsets 2-3 had increased of immune and decreased metabolism and kidney tubule modules. Subset 4 had minimal inflammation, but decreased kidney tubule expression. The progression of disease severity in the TI of lupus-prone mice from pre-disease to chronic disease was highly aligned with the molecular subset of each mouse and consistent with changes in human disease (**Fig. 2b**).

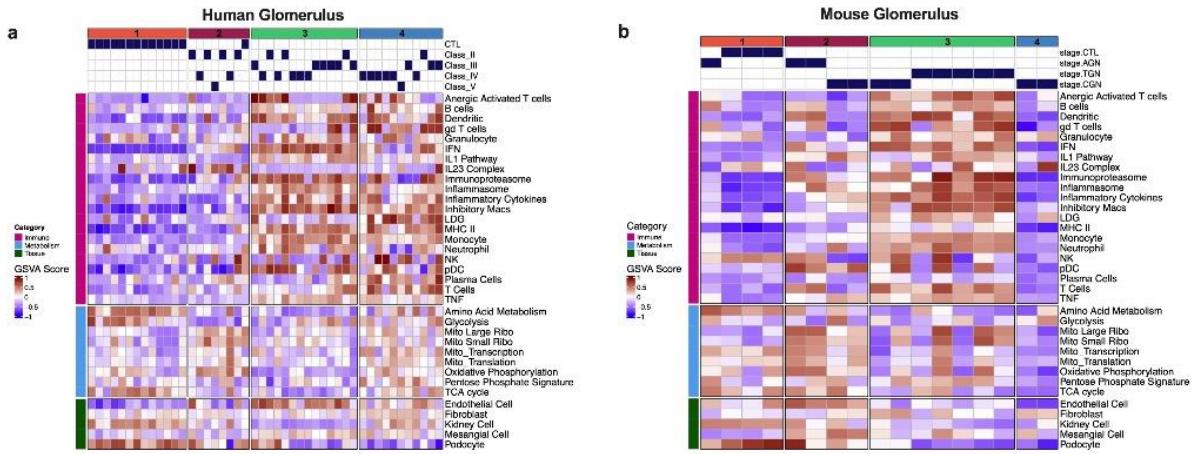

Figure 1: Clustering of GSVA enrichment scores from human and mouse lupus kidney glomeruli. (a) GSVA heatmap of kidney glomeruli from human CTL and LN patients (GSE32591) with ISN/RPI classification for enrichment of immune, metabolism, and kidney tissue gene modules. (b) GSVA heatmap of kidney glomeruli from NZM2328 mice (GSE206806) with pre-defined disease stage annotation for enrichment of mouse orthologs of the modules in (a).

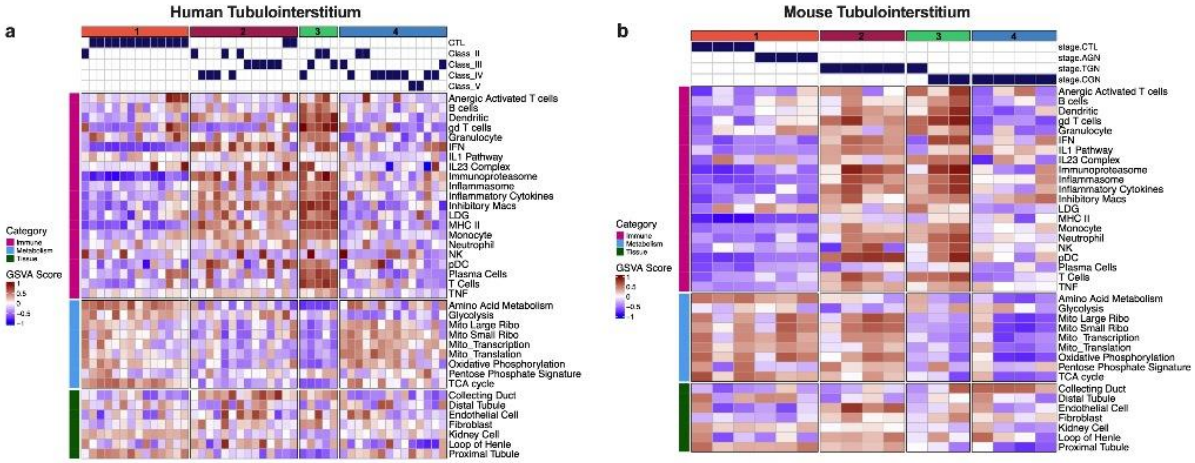

Figure 2: Clustering of GSVA enrichment scores from human and mouse lupus kidney tubulointerstitial tissue. (a) GSVA heatmaps of kidney tubulointerstitium from human (a) NZM2328 mice (b) as in Figure 1.

Conclusions: Human and mouse LN transcriptomic profiles were strikingly similar, such that the progression in human could be related to that of murine LN. Class II patients resembled CTL and AGN mice. Class III patients were akin to AGN and TGN mice. Class IV-V patients shared profiles of TGN and some CGN mice. Alignment of the transcriptomic profiles of human and mouse LN provides new evidence on the nature of progression of human disease and also confirms the utility of the NZM2328 model of LN in defining the molecular pathogenesis of human LN.

PV012 / #474

Poster Topic: *AS02 - Animal Models*

IMIQUIMOD-INDUCED ONSET OF DISEASE IN LUPUS PRONE NZB/W F1 MICE

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Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous disease and onset of the disease in lupus-prone NZB/W F1 mice are typically between weeks 20 to 25. Kidney failure in female mice normally develops within 9 months. Here, we wanted to study if we could accelerate disease onset and possibly induce a more homogenous disease by topical treatment of imiquimod (IMQ), a toll like receptor (TLR) 7 agonist. Activation of TLRs, especially TLR7 and TLR9 by nucleic acids, have been linked to one of many mechanisms contributing to the development and aggravation of autoimmune diseases such as SLE.

Methods: We applied IMQ to the ears of five weeks old NZB/W F1 mice three times per week for five weeks with endpoints set at experimental weeks six and ten. We used age-matched C57BL/6J and NZB/W F1 as control mice. Disease progression was closely monitored by weekly measurements of proteins in urine, serum levels of anti-dsDNA antibodies, and hematological analysis using IDEXX ProCyte Dx. At endpoint, spleen, lymph nodes and kidney were collected for flow cytometric analysis on lymphocyte activation, macrophage, and dendritic cell populations. IgG deposition in glomeruli and tubules was analyzed by immune electron microscopy. Classification of kidney damage was performed according to the 2003 ISN/RPS criteria on zinc-fixated paraffin embedded kidney sections stained with Periodic acid–Schiff staining. Cellular composition and tissue changes were assessed using immunohistochemistry and immunofluorescence, and mRNA gene expression of genes related to disease progression was analyzed using qPCR.

Results: In this study, none of the mice developed full-blown proteinuria. At experimental endpoints, at week six and ten after treatment start, IMQ treated mice had elevated production of autoantibodies against dsDNA, RNA, and cardiolipin compared to control mice. Hematological analysis revealed hemolysis, thrombocytopenia, neutrophilia, and lymphocytopenia. Immune complex deposition in the kidneys was observed at both endpoints. Increased infiltration of activated lymphocytes into the kidneys was observed by both histological and flow cytometric analyses. An increase in CD8+ tissue residential memory cells (CD69+CD44+), monocytes and CD11c+ monocyte derived dendritic cells, CX3CR1+ M2 macrophages, and CX3CR1+ dendritic cells was observed. In contrast, a decrease in plasmacytoid dendritic cells and XCR1+

conventional dendritic cells were seen. In addition, we detected a rise in regulatory immune mechanisms such as an increase of FoxP3+CD4+ Tregs in kidneys, spleen and lymph nodes.

Conclusions: IMQ treatment in young NZB/W F1 mice induced breakage of tolerance against nuclear antigens, but failed to induce nephritis in these mice. The highest disease burden was in general seen after five to six weeks following treatment initiation. However, anti-dsDNA antibodies production increased after four to five weeks and eight to ten weeks post-treatment onset. The age-matched controls did not manifest disease within the experimental time frame.

PV013 / #145

Poster Topic: *AS02 - Animal Models*

A NOVELLA OF MICE AND MEN: IMMUNOLOGICAL AND REPRODUCTIVE ALTERATIONS IN A PRISTANE-INDUCED MOUSE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS AFTER HORMONAL THERAPY

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by an aberrated immune response against nuclear, cytoplasmic and cell-surface antigens. Symptoms often aggravate in females during their active reproductive years, indicating a significant interaction between the reproductive and immune systems. Given the urgency of understanding how SLE can influence female fertility and the role of hormones in disease manifestation, this study aims to investigate these questions. Notably, we utilize mouse models of SLE, a unique and valuable tool for studying the interactions of different systems and the impact of lupus development on oogenesis.

Methods: Methods: We successfully induced lupus-like symptoms in healthy Balb/C mice through intraperitoneal injection of the hydrocarbon oil pristane. The mice were randomly assigned to four groups (10 animals per group). One group of pristane-injected and another group of intact, healthy Balb/C mice were subjected to hormonal stimulation. Following standardized procedures of *in vitro* stimulation in humans, an exemplary short protocol was adapted to a prospective mouse model. One group of pristane-injected and another group of intact, healthy Balb/C mice were subjected to hormonal stimulation. The initial stimulation included 9 days of using products with a follicle-stimulating function. From day 7th to the final 11th day, the mice were subjected to stimulation with a Gonadotropin-releasing hormone antagonist, combined on the final day with human chorionic gonadotropin with luteinizing function. The dose conversion of the corresponding doses of all hormones was calculated using Equivalent Dose (HED) calculation based on the Km ratio. Control groups of pristane-injected mice and healthy animals were treated with PBS only. To follow up on the immune status of these experimental animals, we utilized flow cytometry, ELISpot, and ELISA. The diversity of autoantibodies, histological changes, and oocyte quality were meticulously examined using fluorescent microscopy.

Results: A single intraperitoneal injection of pristane sparked the production of autoantibodies and led to the deposition of IgG-containing immune complexes in the kidneys, resulting in proteinuria. Notably, hormonal stimulation in the lupus-model mice significantly increased the percentage of pro-inflammatory immune cell subtypes, changed ANA immunofluorescence imaging patterns, and elevated the number of plasmacytes producing anti-dsDNA IgG antibodies. The ANA immunofluorescent staining was described according to the corresponding ANA patterns in humans, according to the International Consensus on ANA Patterns (ICAP). Additionally, depositions of IgG-containing immune complexes were detected in both the kidneys and ovaries of treated mice, alongside observable structural abnormalities in isolated oocytes.

Conclusions: The observed oocyte impairments in pristane-treated mice are compelling evidence of a disrupted local microenvironment due to disease activity. They underscore the critical interplay between autoimmunity and reproductive health, and their significance could influence future research and clinical practice in this field.
This study was supported by National Science Fund, Bulgaria, grant number [KP-06-H53/8/2021] and the European Fund for regional development through Operational Program Science and Education for Smart Growth 2014 - 2020, Grant BG05M2OP001-1.002-0001-C04 “Fundamental Translational and Clinical Investigations on Infections and Immunity”.

PV014 / #607

Poster Topic: ***AS02 - Animal Models***

PRISTANE-INDUCED LUPUS MICE PRESENT INCREASED MEGAKARYOCYTE COUNTS ALONGSIDE OTHER HISTOPATHOLOGICAL FEATURES IN THE SPLENIC TISSUE

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Background/Purpose: Pristane-induced lupus (PIL) mice develop an autoimmune response to a single intraperitoneal (i.p.) injection of pristane oil. Consequently, there is the production of autoantibodies, leading to the deposition of immune complexes in tissues. Splenic involvement is observed in this model, especially as splenomegaly and histopathological features. One of these features is the increased proliferation of hematopoietic cells such as megakaryocytes (MKs). Although its impact on lupus splenic pathology remains unclear, vitamin D (vitD) has potential immunomodulatory effects. This study examined the effects of vitD supplementation on splenic alterations in a PIL model.

Methods: Thirty-eight BALB/c mice were randomized into three groups: control (CO, n = 12), PIL (n = 13), and PIL supplemented with vitD (VD, n = 13). PIL and VD received an i.p. injection of 500 µL of pristane; VD received 2 µg/kg of 1α,25-dihydroxycholecalciferol subcutaneous injections every two days for 180 days. After euthanasia, spleens were weighed and paraffin embedded. Spleen index was calculated as the proportion of spleen-to-body weight (mg/g). H&E slides were produced and analyzed for histopathological features. MKs were counted in ten random fields. IgM and IgG expressions were determined via immunofluorescence. One-way ANOVA followed by Tukey's or Kruskal-Wallis followed by Dunn's tests ($p \leq 0.05$) were used and results expressed as mean ± SD or median (IQR).

Results: PIL mice demonstrated significant higher spleen index (CO: 2.63 mg/g ± 0.3; PIL: 3.42 ± 0.59; VD: 3.56 ± 0.84; PIL vs. CO: p = 0.009; VD vs. CO: p = 0.002), elevated MK counts (CO: 0.15 cells/field (0.02-0.28); PIL: 0.6 (0.35-0.8); VD: 0.9 (0.3-1.7); PIL vs. CO: p = 0.04; VD vs. CO: p = 0.003), and characteristic histopathological features such as the presence of foam cells, disorganization of red and white pulps, and fibrous capsule expansion. VitD supplementation did not reduce spleen size (VD vs. PIL: p = 0.84), splenic MK counts (VD vs. PIL: p > 0.99) nor did it prevent histological alterations. Either, it has not altered immunoglobulins expression – PIL and VD groups showed similar IgM (CO: 0.06 (0.0-0.16); PIL 0.09 (0.06-0.17); VD: 0.06 (0.01-0.18); p = 0.46) and IgG (CO: 0.55 ± 0.59; PIL: 1.6 ± 1.8; VD: 1.24 ± 1.21; p = 0.15) fluorescence intensity.

Conclusions: PIL led to splenomegaly and structural changes in the spleen. This highlights the spleen's altered response to inflammation in the model. Additionally, a higher presence of MKs in the splenic tissue has been previously observed in PIL mice, but to the best of our knowledge our study is the first to quantify and attest the statistical difference in MK counts. The higher values in both PIL and VD groups imply that the inflammatory process potentially reflects an immune or compensatory response in this tissue. In this study, the similar IgM intensities across groups suggest that there is stability of early immune response markers in the late stage of the model. Also, IgG presence confirms that PIL mice develop immune complex deposition in the spleen. Finally, our results imply that while vitD might have some immunological effects, it does not appear to impact spleen involvement in the PIL model. **Acknowledgements**: HCPA, UFRGS, CAPES, and SRRS, for funding of this project.

PV015 / #269

Poster Topic: *AS02 - Animal Models*

MRL-LPR MICE DISPLAY ALTERED NOCICEPTION: A POSSIBLE MODEL FOR LUPUS PERIPHERAL NEUROPATHY

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Background/Purpose: Affective disorders and cognitive abnormalities, as well as other neuropsychiatric SLE (NPSLE) manifestations, occur in 20-40% of lupus patients. Of the nineteen ACR case definitions for NPSLE, seven involve the peripheral nervous system. Treatment options for patients with NPSLE remain limited, nonspecific, and mostly non-evidenced based. Furthermore, many patients do not respond to treatment, and face significant neuropsychiatric disability. Our understanding of NPSLE is unfortunately not as advanced as for other lupus manifestations, hampered by the difficulty in obtaining human brain tissue. Therefore, animal models have added importance in investigating disease mechanisms and identifying novel therapeutic targets, especially for manifestations of disease shared between animal models and human SLE. MRL-lpr mice spontaneously develop high-titer anti-DNA and other nuclear autoantibodies, proliferative glomerulonephritis, and inflammatory skin disease, as well as depressive-like behavior and cognitive abnormalities at a young age (1). However, while peripheral neuropathy is common in human lupus patients, whether MRL/lpr mice display peripheral nervous system disease has not been carefully studied. Our goal was to determine if MRL/lpr mice display altered nociception, and could potentially be used to model lupus-associated peripheral neuropathy.

Methods: A previous study by Yan et al (2) demonstrated that female MRL/lpr mice exhibit thermal hyperalgesia and mechanical allodynia. Thermal sensitivity was measured based upon the withdrawal response of the hind paws to increased temperature generated by a radiant heat beam device. Hyperalgesia was demonstrated in 13-week-old animals, but withdrawal latencies did not change between 10 and 12 weeks and were similar to those in control mice. To better evaluate altered sensory function and develop an assay to easily monitor the effects of potential therapeutic interventions, we enhanced the standard testing protocol by incrementally raising the temperature from 40 to 52 °C within a 180-second time frame. The test focuses on observing paw licking, which signifies the behavioral reaction to the thermal stimulus. This careful modulation allowed us to accurately record the latency, or response time, for the mice to lick their fore and hind paws.

Results: We compared female MRL/lpr mice to age and sex matched control mice from the background MRL strain (separate cohorts of 8-12 week old mice). We found that

already at 8 weeks of age, MRL/lpr mice exhibit a notable increase in thermal hyperalgesia (i.e. decreased latency until withdrawal) (102+/-4.02 seconds, n=8) compared to the control MRL strain (126+/-2.34, n=7), a significant difference in the mean latencies of hind paw licking responses between the two experimental groups (p=0.02, Wilcoxon signed-rank test). Similar thermal hyperalgesia responses were observed in the MRL/lpr strain also at 10 and 12 weeks. Ongoing studies are focused on identifying the earliest detectable heightened sensitivity, and exploring how standard treatment with cyclophosphamide and other immunosuppressives influences the nociceptive response in this lupus prone strain.

Conclusions: MRL-lpr mice display heightened temperature sensitivity. Altered nociception in this strain may represent an early and sensitive tool to detect NPSLE, and if confirmed, may serve to model the involvement of the peripheral nervous system in this disease. **References:** Polis B, Cuda CM, Putterman C. Animal models of neuropsychiatric systemic lupus erythematosus: deciphering the complexity and guiding therapeutic development. Autoimmunity. 2024;57(1):2330387. Yan X, Maixner DW, Li F, Weng HR. Chronic pain and impaired glial glutamate transporter function in lupus-prone mice are ameliorated by blocking macrophage colony-stimulating factor-1 receptors. J Neurochem. 2017;140(6):963-976.

PV016 / #588

Poster Topic: *AS02 - Animal Models*

C1Q-MIMIKING SCFV FRAGMENTS BINDING ANTI-C1Q AUTOANTIBODIES HAS DISEASE-PROGRESSION EGGECT IN MRL/LPR MOUSE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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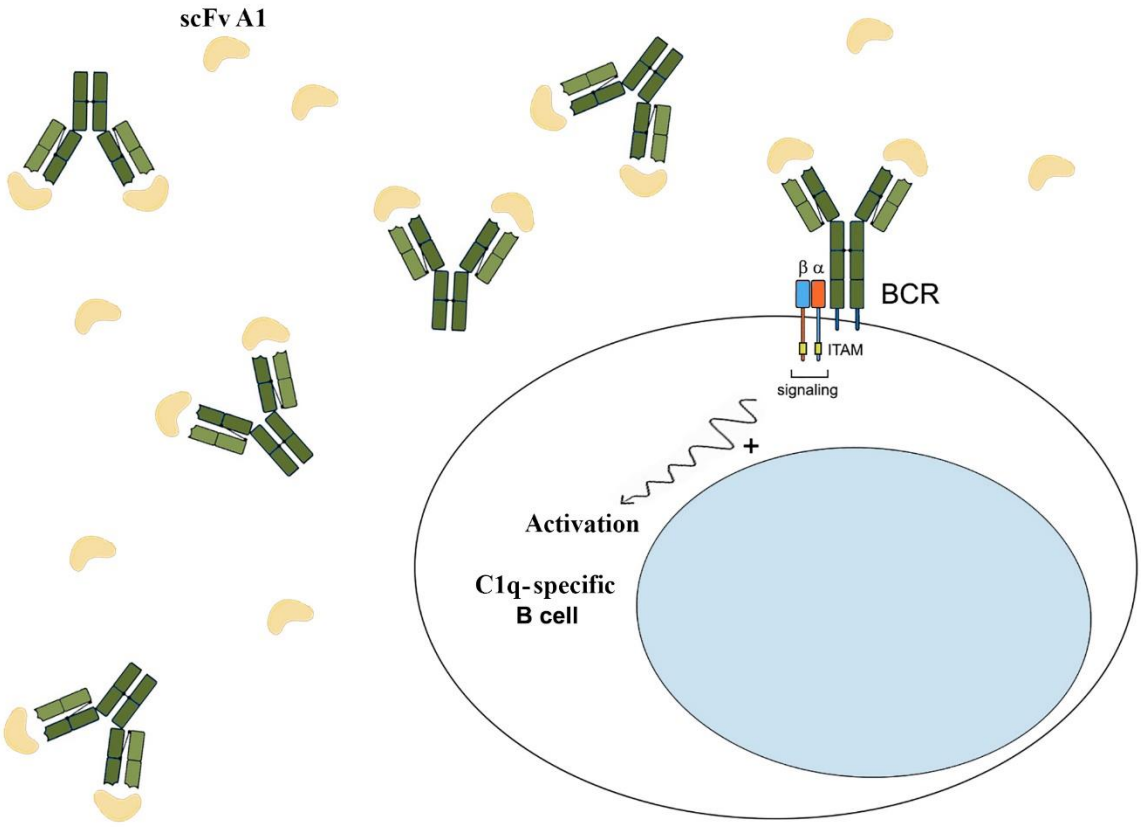
Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease characterized by tissue damage in multiple organs caused by autoantibodies and the resulting immune complexes. C1q is the first component of the classical complement pathway and primary or acquired C1q deficiencies are directly linked to development and severity of SLE. While the primary C1q deficiency is not frequent among SLE patients, 20–50% of them developed elevated levels of anti-C1q autoantibodies, which may be are responsible for low C1q levels. One possible way for complement system contribution to onset of autoimmune disorder could be realized by the impairment of C1q-mediated apoptotic clearance as part of human homeostasis. The capacity of C1q to bind early apoptotic cells could be decreased or even lost in the presence of anti-C1q antibodies which are specific for epitopes within gC1q.

Methods: A phage-displayed library expressing single-chain recombinant antibodies (scFv Ab) was screened to select scFv specific for anti-C1q autoantibodies from different sera of lupus nephritis patients. Such a monoclonal anti-idiotype scFv antibody selected from the Griffin.1 phage library was used to treat MRL/lpr mice. Two groups of MRL/lpr mice were used for *in vivo* and *ex vivo* experiments: disease free 7 weeks old mice and 16 weeks old animals with advanced disease manifestations. The mice were injected weekly with 20 µg/mouse of scFv A1 fragments binding anti-C1q antibodies. Blood samples were collected weekly and the sera were stored at -80 ºC for subsequent analyses. The number of *in vitro* and *ex vivo* studies with collected cells, sera and organs from the treated animals have been performed. The effects of therapy with the scFv A1 fragments were evaluated using flow cytometry, histology analyses, ELISpot and ELISA assays.

Results: An scFv specific for anti-C1q autoantibodies was generated and administered to MRL/lpr mice. Data show that scFv treatment changes the percentage of different B, T and NK cell subpopulations as well as plasma cells and plasmablasts in the spleen and bone marrow. An increase in the levels of splenocyte proliferation, anti-C1q antibodies, and the number of plasma cells producing anti-dsDNA and anti-C1q antibodies were

also observed in both groups of scFv-treated animals. Administration of scFv A1 fragments binding anti-C1q antibodies increase the pathological findings in kidney histology in both young and sick animals. High levels of proteinuria and hematuria combined with increased unstable levels of IL10 and IFNγ promote the development of severe lupus and shorten the survival of treated MRL/lpr mice.

Conclusions: The treatment with anti-idiotypic scFv antibodies has disease-progression effect on lupus symptoms in MRL/lpr murine model of SLE. Binding of anti-C1q antibodies by scFv fragments neutralizes their ability to contact C1q, but the scFv is also able to bind B-cell receptors on the surface of C1q-specific B cells, which enhances disease activity (Fig. 1).



PV017 / #362

Poster Topic: *AS02 - Animal Models*

EXPLORING THE ROLE OF CELLULAR SENESCENCE IN LUPUS NEPHRITIS

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Background/Purpose: Cellular senescence is a physiological process triggered by various stresses, causing cells to enter irreversible cell-cycle arrest. These cells nevertheless remain metabolically active, and undergo morphological and functional changes, such as acquisition of a pro-fibrotic and pro-inflammatory secretome. Cellular senescence has been reported in renal aging and in kidney diseases such as hypertensive nephropathy, IgA nephropathy, and diabetic nephropathy, [1.] We previously reported that lupus nephritis (LN) patients with more severe baseline disease and poor long-term outcome exhibit higher levels of cellular senescence (measured using the hallmark marker $p16^{INK4a}$), in baseline biopsy, [2.]. We assessed for the presence and time of onset of renal cell senescence in lupus-prone B6.NZM*Sle1/Sle2/Sle3* (B6.*Sle1.2.3*) mice, with a view to testing for the effects of senolytic drugs on kidney disease progression in this model.

Methods: A time-course was performed, with necropsy of 2 C57Bl/6 (B6) and 10 B6.*Sle1.2.3* mice, every 2 months from 2 to 12 months. Systemic autoimmunity was assessed by ELISA to measure total IgG and anti-dsDNA IgG in plasma. IgG deposition in kidneys was measured by immunofluorescence. Renal disease was assessed using urine albumin/creatinine ratio and kidney histology (activity and chronicity scores). Cellular senescence in the kidney was assessed by immunohistochemistry for $p16^{Ink4a}$ and senescence-associated β-galactosidase assay. We are now testing the senolytic drug combination dasatinib (5 mg/kg) plus quercetin (50 mg/kg) (DQ) *vs.* vehicle control, in two distinct settings: (i) after onset of systemic disease but before onset of any signs of renal disease or renal cell senescence (*i.e.*, from 5 months of age until necropsy at 8 months of age); (ii) after onset of renal cell senescence and overt kidney disease (*i.e.*, from 8 months of age to necropsy at 10 months of age). Treatment is administered by oral gavage bi-weekly. Systemic and renal disease, as well as cellular senescence, will be assessed as described above.

Results: We demonstrated, in aged (12-15 month old) B6.*Sle1.2.3* lupus-prone mice, that high kidney $p16^{Ink4a}$ positivity is significantly associated with increased proteinuria, histopathological scores, $CD8^+$ T cell infiltration and renal fibrosis. As in patients, $p16^{Ink4a}$-positivity was not associated with systemic disease parameters or with Ig

deposition in the kidney. A time-course showed that systemic disease parameters as well as glomerular IgG deposits increase from 4 months of age in B6.*Sle1.2.3* as compared to B6 control mice; kidney disease shows later onset (from 6-8 months of age) and greater heterogeneity. The appearance of $p16^{Ink4a}$ positive cells above B6 levels is observed at 8 months of age in B6.*Sle1.2.3* mice, [3.]. Treatment of a first cohort with DQ is currently ongoing, with preliminary results expected in January 2025.

Conclusions: Based on the time of onset of renal cell senescence and systemic vs. end-organ disease observed in the B6.*Sle1.2.3* mouse model, we are now testing the effect of senolytic therapy (drugs selectively targeting senescent cell anti-apoptotic pathways) on renal disease penetrance and severity. Should renal cell senescence (and the clearance of these cells) prove to have an impact on disease, it could provide a non-immune cell targeting strategy in LN. **References** [1.] Valentijn FA. J Cell Commun Signal 2017; 12(1):69-82 [2.] Tilman G. RMD Open 2021; 7(3):e001844. [3.] Tilman G. Lupus Sci Med 2023; 10(2):e001010.

PV018 / #802

Poster Topic: *AS03 - Antiphospholipid Syndrome*
Late-Breaking Abstract

THE CLINICAL AND IMMUNOLOGICAL SIGNIFICANCE OF ANTI-PHOSPHOLIPID ANTIBODIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune systemic disease characterized by the presence of the variety of autoantibodies. Anti-phospholipid antibodies (APL) are new criteria for classifying lupus disease and their positivity often indicates the association with secondary anti-phospholipid syndrome (APS). The aim of the study was to evaluate the frequency, the clinical and immunological associations of antiphospholipid antibodies in patients with SLE.

Methods: Our study included 156 patients diagnosed and followed up for lupus. The APL were detected by an immuno-enzyme technique (ELISA).

Results: In our study, 19% of patients (N=29) had one of the positive APL. Anti cardiolipines antibodies (aCL) were present in 12% (n=18), while anti-β2GP1 antibodies were positive in 13% of patients (n=20). The frequencies of both IgG and IgM isotypes of aCL and anti β2GP1 were 5%, 7%, 4% and 10% respectively. The study of clinical and immunological associations revealed a positive association between the presence of anti-β2GP1 and neurological involvement (25% vs 7%, P = 0.020, OR=4.70), and between anti-β2GP1 and lupus nephritis (45% vs 68%, P = 0.044, OR=0.39). Moreover, a significant association was observed between the presence of aCL and hypocomplementemia of C3 and C4 fractions (P=0.012, Or=3.48).

Conclusions: APL positivity is quite common in SLE patients. Their presence should suggest a possible association with secondary APS and monitoring of patients for thrombotic risk or obstetric complications.

PV019 / #134

Poster Topic: ***AS03 - Antiphospholipid Syndrome***

COMPARATIVE EVALUATION OF THE PERFORMANCE OF REVISED SAPPORO AND 2023 ACR/EULAR CLASSIFICATION CRITERIA IN CHILDHOOD ONSET ANTIPHOSPHOLIPID SYNDROME

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Background/Purpose: Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterised by increased risk of thrombosis and pregnancy morbidity with persistently elevated antiphospholipid antibodies (aPL). Childhood APS is usually diagnosed before age 18. Historically, APS has been classified using the Sapporo criteria, revised in 2006. The American College of Rheumatology (ACR) and European Alliance of Rheumatology Associations (EULAR) developed new classification criteria for APS in 2023 for research. Here we characterised a single-centre cohort of adolescents and young adults (AYA) with childhood-onset APS, diagnosed by expert opinion. We compared the performance of the new 2023 ACR/EULAR criteria, which have not yet been tested in childhood APS vs. the revised Sapporo criteria.

Methods: We screened our childhood-onset connective tissue disease clinical service database comprising 215 cases to identify AYA diagnosed with childhood-onset APS based on expert opinion. We collected retrospective data to assess their demographics, disease duration, clinical manifestations, serological markers, treatment, and compared the two classification criteria.

Results: We identified 12 AYA diagnosed with childhood-onset APS (see Table below), 91% of which had another associated autoimmune disease, including childhood-onset systemic lupus erythematosus (cSLE)/Sjogren and juvenile dermatomyositis (JDM). For APS manifestations, 8/12 cases were treated with aspirin and warfarin and 2/12 with direct oral anticoagulants (DOACs). One young person had previously received plasma exchange for catastrophic APS. 5/215 cases of AYA had persistently elevated aPL (four with cSLE and one with JDM) without clinical APS manifestations (fulfilling neither the Sapporo nor the 2023 ACR/EULAR criteria for APS).

Age. sex	Ethnicity	Disease duration (years)	Type of persistently positive aPL	Type of thrombotic manifestation	Pregnancy morbidity Y/N	Sapporo criteria fulfilled Y/N	ACR/EULAR criteria fulfilled Y/N
32F	Black (African)	20	Triple positive	1 Venous	N	Y	Y
35F	Middle-Eastern	20	Lupus anticoagulant, anti beta2 glycoprotein I antibodies	1 venous	N	Y	Y
32M	Asian	18	Triple positive	3 venous and 1 arterial	N	Y	Y
27M	White	10	Triple positive	3 venous and 1 arterial	N	Y	Y
26F	Asian	11	Triple positive	1 venous and 2 arterial	N	Y	Y
27F	Asian	11	Anticardiolipin antibodies	None	N	N	N
25F	Asian	10	Triple positive	None	Y	Y	Y
24F	Black (African)	8	Anticardiolipin, anti beta2 glycoprotein I antibodies	1 arterial	N	Y	N
23F	Black (African)	5	Triple positive	1 venous and 1 arterial	N	Y	Y
20F	White	3	Triple positive	1 arterial	N	Y	Y
16F	Asian	7	Anticardiolipin, lupus anticoagulant antibodies	None	N	Y	Y
19F	Asian	4	Triple positive	None	N	N	N

Table 1: Summary of persistent aPL positive cases with childhood APS

Conclusions: The 2023 ACR/EULAR classified 75%, while the revised Sapporo criteria classified 66% of AYA with APS diagnosed by expert opinion, suggesting that childhood-specific criteria may be warranted. In this small cohort, macrovascular thrombosis affected 66% of AYA diagnosed with APS, and 33% had more than one major thrombotic event. Overall, 47% (8/17) of AYA with persistently elevated aPL had thrombosis, despite previous publications suggesting low risk of thrombosis in childhood APS. This cohort was followed up for 3-20 years, allowing us to assess the clinical course of this rare disease phenotype in children. Our findings challenged some of the previous asumptions about the lack of severity of this condition in people of younger age. Future large cohort studies are required to define the natural course and outcomes of childhood APS, as well as optimal long-term management strategies.

PV020 / #573

Poster Topic: *AS03 - Antiphospholipid Syndrome*

INTRA-RENAL INVOLVEMENT IN PRIMARY ANTIPHOSPHOLIPID ANTIBODIES SYNDROME: DATA FROM TWO ITALIAN CENTERS

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Background/Purpose: Background. Antiphospholipid antibodies nephropathy (aPL-N) is defined by thrombotic microangiopathy (TMA) early lesions and late lesions such fibro-intimal hyperplasia with luminal obliteration/organized thrombi, fibrous arterial/arteriolar occlusion and focal cortical atrophy[1]. Beyond these distinct microvascular lesions, other glomerular conditions (membranous nephropathy, MN; focal segmental glomerulosclerosis, FSGS), were reported in primary APS (PAPS) patients, even without aPL-related vascular lesions. **Objectives. 1)** To evaluate clinical/laboratory features associated to intra-renal involvement in PAPS patients; **2)** to clinically and histologically characterize PAPS patients with **a)** aPL-N and **b)** non-aPL-N intra-renal involvement.

Methods: Methods. Observational retrospective multicentric study including PAPS patients regularly followed (1984-2023). **1)** Case-control study: PAPS patients with intra-renal involvement histologically confirmed vs PAPS patients without renal involvement signs. **2)** Separate analysis according to renal histologic findings: **a)** aPL-N and **b)** non-aPL-N.

Results: Results. Among 258 PAPS patients (78% females, median age at onset: 32 years, 67% thrombotic phenotype, 54% obstetric phenotype, 41% triple aPL+), 17 (7%) had histologically confirmed intra-renal involvement. It was the first disease manifestation in 10/17 (59%) patients, the main presentation was with isolated urinary abnormalities (IUAs) in 53% of the cases. At renal biopsy 35% had classic aPL-N injuries while 65% showed non-aPL-N intra-renal lesions. **1)** Patients with intra-renal involvement suffered less macrovascular thrombotic events and more catastrophic APS (CAPS), thrombocytopenia, epilepsy, and lupus anticoagulant (LA)+ (*Table 1*). **2a)** aPL-N was the first manifestation of APS in 5/6 (83%) cases, presenting with severe arterial hypertension in 17%, CAPS in 33% and IUAs in 50%. Despite therapy with anticoagulant (60%) or antiplatelet (40%) drugs in most patients, the 12-months renal response was complete in only 1/3 of the cases; half of the patients suffered subsequent aPL-related

events (3/6 thrombocytopenia; 2/6 thrombotic events). **2b)** PAPS patients with non-aPL-N intra-renal lesions had MN in 6/11 and FSGS in 5/11 cases, with some degree of non-specific vascular injury in 64%. As compared to patients with aPL-N, they presented more frequently normal serum creatinine and higher 24h-proteinuria levels (*Figure 1*) but no differences in systemic autoantibodies/complement levels. All the patients belonging to this subgroup experienced aPL-related events (8/11 thrombotic events, 5/6 obstetric events, 3/11 epilepsy, 2/11 heart valve lesions, 1/11 thrombocytopenia), that in 45% cases were preceded by the renal disease.

Patients' characteristics	All patients n=258	Intra-renal involvement n=17	No intra-renal involvement n=241	*p value*
Female sex	202/258 (78.3)	11/17 (64.7)	191/241 (79.3)	*0.218*
Age at disease onset, years	32.0 (25.0-44.0)	29.0 (24.0-28.0)	33.0 (25.0-44.0)	*0.377*
Thrombotic APS	173/258 (67.1)	6/17 (35.3)	167/241 (69.3)	***0.004***
Obstetric APS	109/202 (53.9)	5/11 (45.5)	104/191 (54.5)	*0.561*
Catastrophic APS	4/258 (1.6)	3/17 (17.6)	1/241 (0.4)	***0.001***
"Extra-criteria" APS*	19/258 (7.4)	8/17 (47.1)	11/241 (4.6)	***<0.001***
Thrombocytopenia	29/258 (11.2)	6/17 (35.3)	23/241 (9.5)	***0.006***
Heart valve lesions	21/258 (8.1)	2/17 (11.8)	19/241 (7.9)	*0.637*
Livedo reticularis	22/258 (8.5)	1/17 (5.9)	21/241 (8.7)	*1.000*
Epilepsy	17/258 (6.6)	4/17 (23.5)	13/241 (5.4)	***0.018***
Triple aPL profile	103/250 (41.2)	9/15 (60.0)	94/235 (40.0)	*0.127*
LA+	165/254 (64.9)	17/17 (100.0)	148/237 (62.4)	***0.002***
aCL+	171/257 (66.5)	11/16 (68.8)	160/241 (66.4)	*0.846*
aβ2GPI+	190/251 (75.7)	11/16 (68.8)	179/235 (76.2)	*0.548*
ANA+	125/255 (49.0)	6/17 (35.3)	119/238 (50.0)	*0.241*
anti-DNA+	0/241 (0.0)	0/17 (0.0)	0/224 (0.0)	*1.000*
C3, g/dL	101.1 (88.0-118.0)	108.5 (101.3-122.5)	101.0 (87.5-118.0)	*0.477*
C4, g/dL	19.0 (13.0 -24.0)	18.0 (12.5-23.5)	19.0 (13.0-24.0)	*0.790*

Table 1. Continuous variables are presented as median (1st-3rd quartile) and compared with Mann-Whitney test; categorical variables are presented as number/number available data (%) and compared with Chi-square test/Fisher's exact test.
*= "extra-criteria" according to Sydney APS criteria 2006.
Abbreviations: APS= antiphospholipid syndrome; aPL= antiphospholipid antibodies; LA= lupus anticoagulant; aCL= anticardiolipin antibodies; aβ2GPI= anti-beta2glycoprotein I antibodies; ANA= antinuclear antibodies.

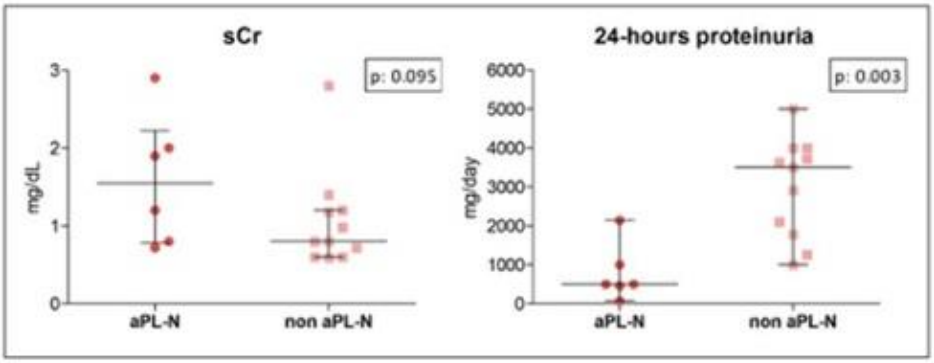

Figure 1. aPL-N vs non-aPL-N intra renal involvement: sCr= 1.9 [1.2-2.0] vs 0.98 [0.6-1.2] mg/dL; 24-hours proteinuria= 0.5 [0.4-0.5] vs 3.5 [1.9-3.9] g/24h.

Conclusions: Conclusions. The present work highlights the importance of conducting appropriate renal study in PAPS patients with renal biopsy, if needed, even in presence of mild IUAs. It underscores that aPL-N, being part of the peculiar microvascular APS subset, may require a treatment strategy beyond anticoagulation[2]. From nephrologists' perspective, routinary screening for aPL during the assessment of glomerulopathies could be relevant, given the aPL prognostic role in the development of subsequent related events. **References.** [1]Barbhaiya M. 2023.[2]Erkan D. 2021.

PV021 / #98

Poster Topic: ***AS03 - Antiphospholipid Syndrome***

TRACKING THROMBOEMBOLIC EVENTS AND ANTIPHOSPHOLIPID SYNDROME FROM ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS: A POPULATION-BASED STUDY

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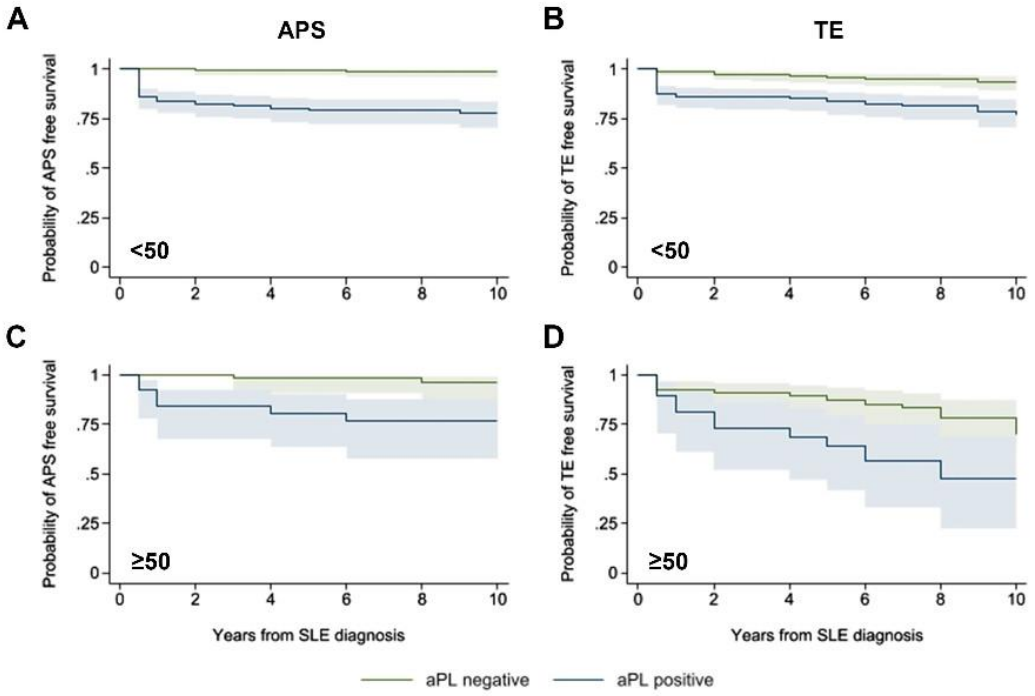
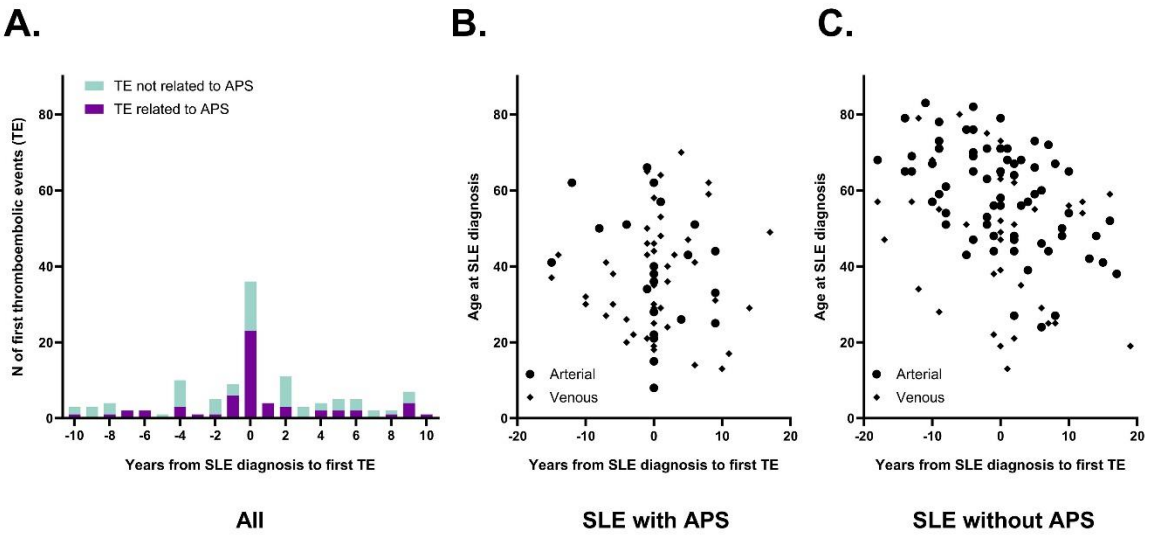
Background/Purpose: Understanding how, when and in whom Antiphospholipid Syndrome (APS) and thromboembolic events (TE) develops in Systemic Lupus Erythematosus (SLE) is important as it may facilitate risk stratification and preventive strategies. Here, we aimed to track patients from SLE diagnosis and assess relationships between APS, TE and anti-phospholipid antibodies (aPL) during follow-up.

Methods: We included all new SLE patients residing in Southeast Norway 2000-2017. All patients had chart-review confirmed diagnosis, fulfilled the 2019 European League Against Rheumatism and American College of Rheumatology SLE classification criteria and were captured within one year of diagnosis. Follow-up ended 1 January 2018. APS was defined by the 2006 Sydney classification criteria and aPL positivity referred to positive anti-cardiolipin, anti-b2glycoprotein and/or lupus anticoagulant following international guidelines. TE were defined by both arterial and venous events and included ischemic stroke, transient ischemic attack, myocardial infarction, angina pectoris or syndromes caused by occlusion of major venous vessel identified either by chart-review or by ICD-10 code (I20-22, I63, G46, R96, I26, I80-I82) in The National Cause of Death Register. We estimated APS- and TE-free survival using Kaplan-Meier methods and identified factors associated with TE with Cox regression analysis.

Results: Among 700 new SLE patients, 79 (11%) had co-occuring APS after a mean follow-up of 8 years (SD 5). Compared to non-APS patients, APS patients more frequently had thrombocytopenia (25/79, 32% versus 123/621, 20%, p-value<0.012),

neuropsychiatric lupus (6/79, 8% versus 16/621, 3%, p-value<0.016) and anti-dsDNA antibodies (66/79, 84% versus 450/621, 72%, p-value<0.035) at the time of SLE diagnosis, but mean age at SLE diagnosis (37, SD 15 versus 39, SD 17, p-value=0.309) and frequency of LN were the same (29/79, 37% versus 195/621, 31%, p-value=0.341). During follow-up, 54 SLE patient developed a new APS. At the time of SLE diagnosis, 45 of these 54 patients (83%) were aPL-positive, five (9%) were aPL-negative and four (7%) had an unknown aPL status. The 5-year APS-free survival was higher in aPL-negative (0.99, 95% CI 0.97-1.00) than aPL-positive patients (0.80, 95% CI 0.74-0.85, p<0.001). [Figure 1] By the end of follow-up, 156 (22%) patients had experienced at least one TE, with a clear clustering around SLE diagnosis. Of the 36 TEs occuring in the same year as SLE diagnosis, 26 (64%) were related to new APS. [Figure 2] Excluding those with TE or APS prior to SLE diagnosis, we found that TE developed in 45/206 (22%) of aPL-positive patients, 31/332 (9%) of aPL-negative patients and in 13/88 (15%) of patients with unknown aPL status at time of SLE diagnosis. Overall, 10-year TE-free survival was 0.84 (95% CI 0.81-0.87). TE-free survival was lower in the aPL-positive patients than in the aPL-negative already one year after SLE diagnosis (0.88, 95% CI 0.83-0.92 versus 0.98, 95% CI 0.96-0.99, p-value<0.001). Stratified by age, aPL-negative patients <50 years at diagnosis had persistently high TE-free survival, while patients ≥50 at SLE diagnosis continued to develop TE across the follow-up period, both in aPL-negative and aPL-positive patients. [Figure 2] In multivariable analyses lupus-anticoagulant, ≥2 aPLs and older age at SLE diagnosis were the individually factors with highest hazard ratios for new TE when adjusting for sex, ethnic ancestry and age.





Conclusions: This population-level study reveals a heightened risk of TE, particularly in the context of APS, around SLE onset. The elevated thromboembolic risk in new SLE requires attention and may call for preventive measures.

PV022 / #697

Poster Topic: ***AS03 - Antiphospholipid Syndrome***

OUTCOME OF PATIENTS WITH NON-CRITERIA MANIFESTATIONS OF PRIMARY ANTIPHOSPHOLIPID SYNDROME TREATED WITH IMMUNOSUPPRESSANTS -A SINGLE CENTRE STUDY

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Background/Purpose: Background: The frequency of non-criteria manifestations in Primary antiphospholipid syndrome (PAPS) is 24% . The efficacy of immunosuppressants in patients with above condition is not certain due to paucity of evidence. **Objectives:** To evaluate the outcome of patients who have been treated with immunosuppressive drugs for treatment of non-criteria manifestations of PAPS.

Methods: Methods: Patients with the diagnosis of APS or probable APS, attending our clinics between 2010 to 2024 were screened. Among these, those satisfying the APL domain of ACR/EULAR 2023 criteria and had at-least one non criteria manifestation not attributable to any other defined CTD or disease and have been treated with immunosuppressive therapy were included. The non-criteria manifestations included all the ones mentioned in ACR/EULAR criteria or autoimmune haemolytic anaemia (AIHA) and catastrophic APS (CAPS). Data regarding clinical presentation, laboratory abnormality, treatment and response were included. The primary outcome was the clinical improvement or resolution of the presenting manifestation after initiation of therapy. The results are depicted descriptively.

Results: A total of 44 patients 28 females, mean age 38±13 (SD) years satisfied the inclusion criteria. The most common non-criteria manifestation was thrombocytopenia (24, 54 %) followed by AIHA (12,27%) (Table-1). Rituximab was the most common immunosuppressant used in 19(43%) followed by mycophenolate (18 (40%). 90% received antiplatelet and anticoagulants. table 1 :

Non -criteria Manifestations	Frequency n(%)
Thrombocytopenia	24 (54%)
Autoimmune haemolytic anaemia	12(27%)
APS Nephropathy	6 (13%)
Non Healing Ulcers	5(11%)
Lupus Anticoagulant Hypoprothrombinemia Syndrome	2(4.5%)
CAPS	2(4.5%)
Diffuse alveolar haemorrhage	2(4.5%)
Thrombotic thrombocytopenia purpura	1(2%)
Choreoathetosis	1(2%)
Laboratory domain (Antiphospholipid antibodies)	
Single/ double/ triple positivity	8(18%)/7 (15%)/28 (66%)
Lupus Anticoagulant / Anticardiolipin/IgG β2 glycoprotein	41(93%), 32 (72%)/ 30 (68%)
Treatment received at initiation	
Steroid-Prednisolone equivalent (mean dose /day)	181 mg /day
Immunosuppression	
Rituximab, n (%)	19(43%)
Mycophenolate, n (%)	18(40%)
Azathioprine n (%)	7(15%)

During a median follow up of 32 months (IQR: 20-63), 80% patients responded to treatment. The response was sustained in 59% at the last follow up. The best response was noted among patients with thrombocytopenia. n=20(83%) of thrombocytopenia responded to immunosuppressive treatment including rituximab (n=9, 81%), mycophenolate (n=5,85%) and Azathioprine (n=6, 66%). Response rates of all manifestations is depicted in Table 2. Major adverse events included death in 2 patients due to sepsis and *pneumocystis carinii* pneumonia in patients receiving rituximab and 1 death due to sepsis, disseminated TB, Ca breast in patients receiving

MMF

Table 2: Comparison of response to therapy in patients receiving Rtx and mycophenolate/ azathioprine

80-100
60-79
40-59
20-39
0-19

Non criteria manifestations	RITUXIMAB (n/total no receiving Rituximab)%	MYCOPHENOLATE+ AZATHIOPRINE (n/total no receiving mycophenolate/azoran)%	Total Response
Thrombocytopenia	9/11 (81%)	11/15 (73%)	83%
AIHA	2/3 (66%)	8/9 (88%)	83%
APS Nephropathy	2/4 (50%)	1/2 (50%)	50%
Ulcers	3/3 (100%)	1/3 (33%)	66%
LAHPS	1/1 (100%)	0/2 (0%)	50%
CAPS	2/2 (100%)	-	100%
DAH	-	2/2 (100%)	100%
TTP	1/1 (100%)	-	100%
Choreoathetosis	1/1 (100%)	-	100%
Total response	80%	69%	-

Conclusions: Conclusion : Among the patients with PAPS with non-criteria manifestation, the best response to immunosuppression was observed in those presenting with AIHA and thrombocytopenia. .All manifestions except LAHPS and skin ulcers showed similar response with rituximab as well as mycophenolate/ azathioprine

PV023 / #772

Poster Topic: *AS04 – Biomarkers*
Late-Breaking Abstract

INTERLEUKIN-8 SERUM LEVEL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease characterized by the production of variety of autoantibodies that can form immune complexes and deposit in tissues, causing inflammation and organ damages. This study aimed to investigate the level of interleukin 8 (IL-8) in the serum of SLE patients.

Methods: In total, 156 SLE patients (109 active and 47 inactive patients) and 104 healthy subjects were evaluated. The serum levels of IL-8 were determined by chimiluminescent assay.

Results: In this study, a higher IL-8 serum concentration was observed in SLE patients compared to healthy controls (125.84 pg/ml vs 3.47 pg/ml, **P= 0.000**). Moreover, serum IL-8 level was also significantly higher in active SLE patients and showed positive correlation with the SLEDAI score (**P = 0.022, r = 0.324**).

Conclusions: These data suggest that IL-8 may be a useful biomarker for disease activity in SLE patients.

PV024 / #545

Poster Topic: ***AS04 - Biomarkers***

BREATHOMICS IN SYSTEMIC LUPUS ERYTHEMATOSUS: UNCOVERING NON-INVASIVE MARKERS OF DISEASE ACTIVITY AND FATIGUE

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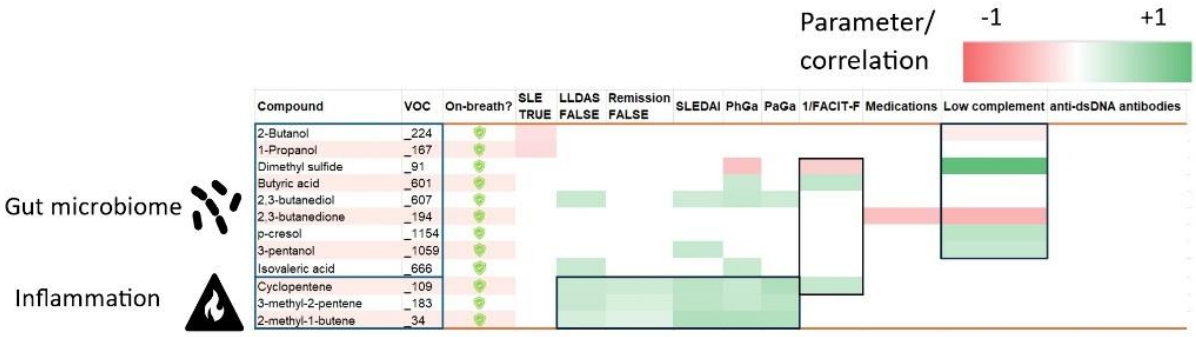
Background/Purpose: 3TR (taxonomy, treatment, targets and remission) aims to provide insights into the mechanisms of response and non-response to treatment in autoimmune diseases. The lupus arm of 3TR focuses on identifying reliable biomarkers that could serve as indicators of disease or disease severity, and molecular processes that determine patients' response to medication. Volatile organic compounds (VOCs) can be generated by metabolic processes in the body being impacted by disease pathology. VOCs diffuse from their point of origin into the blood to be emitted through breath, providing a potential non-invasive method to assess whole-body metabolism .

Methods: Sixty patients (30 SLE and 30 age- and sex-matched healthy controls) were recruited to a single-site, case-control observational study. Breath VOC sampling was performed using the ReCIVA® breath sampler, linked to a clean air supply (CASPER®). Collected samples were analyzed by thermal desorption gas chromatography-mass spectrometry (TD-GC-MS) by Owlstone Medical. VOCs were chemically identified in alignment with the Metabolomics Standards Initiative (MSI) criteria, with blank air samples analyzed to discern VOCs genuinely present in patients' breath. Univariate analyses were performed by linear regression modeling for categorical variables and by Spearman's rank correlation coefficient for continuous variables, including physician/patient global assessments (PhGA/PGA) and FACIT-F scores.

Results: Patients had a median disease duration of 14 years (IQR: 6–21), with a mean (SD) SLEDAI-2K score of 3.6 (3.3). Twenty subjects (70%) were in LLDAS and 14 (46.7%) in DORIS remission. The mean PhGA and PGA scores were 19.7 (19) and 40.3 (33.7). Fourteen patients (46.7%) tested positive for anti-dsDNA. The mean serum C3 and C4 levels were 90 (20) and 8.6 (9.5) mg/dL, with 17 patients (56.7%) hypocomplementemic. The mean FACIT-F score was 37.9 (11.9). After quality control, 1,433 VOCs were

observed. Of these, 539 were classified as “on-breath,” appearing at significantly higher levels than background. VOC identities were assigned based on pure analytical standards or matches to third-party databases, with on-breath statistically significant VOCs further interpreted for their biological relevance. Three main themes emerged from the analysis (Figure). First, a strong link was found between SLE and gut microbiome, with significant decreases in gut microbiome fermentation products (e.g., 2-butanol and 1-propanol) in SLE. Additionally, elevated levels of 2,3-butanediol correlated with greater disease severity. Notably, differences in gut microbiome products were also observed in SLE according to complement levels. Second, there was a positive correlation between VOCs with potential links to oxidative stress and inflammation (i.e. cyclopentene, 3-methyl-2-pentene, and 2-methyl-1-butene) and disease severity indicators, including SLEDAI-2K, LLDAS, DORIS remission and both PhGA and PGA. Third, there was evidence of a correlation between an altered gut microbiome and fatigue. Results pointed toward a decrease of sulphate-reducing bacteria that may eventually promote inflammation via a loss of degradation of cyclopentene, coupled with a syntropic compensatory production of butyrate.



Conclusions: These data demonstrate, for the first time, the potential of breath-based VOC analysis in detecting pathophysiological changes in SLE patients. They align with recent findings that highlight gut microbiome dysbiosis as central in SLE and suggest a potential link with complement levels. Our data demonstrate the functional nature of gut dysbiosis with significant correlation with fatigue. These data reveal possible markers of inflammation, which correlate with disease severity and patient’s perception of fatigue and offer an exciting prospect for non-invasive disease assessment. Future work should focus on validating these markers and their associations with additional inflammatory indicators.

PV025 / #639

Poster Topic: ***AS04 - Biomarkers***

ANTI-NEUTROPHIL EXTRACELLULAR TRAPS (NET) ANTIBODIES AND THEIR ASSOCIATION WITH DISEASE ACTIVITY AND SYSTEMIC LUPUS ERYTHEMATOSUS CLINICAL PHENOTYPES

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Background/Purpose: Anti-neutrophil extracellular traps (NETs) antibodies have been observed in patients with lupus nephritis and may contribute to the pathogenic production and degradation of NETs in patients with lupus. However, the relationship of anti-NETs antibodies with clinical features of SLE patients have not been studied.

Methods: 87 patients fulfilled the ACR/EULAR 2019 classification criteria for SLE. Using ELISA, we quantified the plasmatic neutrophil elastase-DNA complexes as NETs remnants and the IgG anti-NETs antibodies in the same sample. 23 healthy controls were included to establish the cut-off point for anti-NETs antibodies, (0.076 arbitrary units), corresponding to two standard deviations above their mean optic density. We compared medians using Mann-Whitney U test. Associations between qualitative variables were assessed with Chi-square test. Correlations between quantitative variables were performed using Spearman's rho.

Results: 35.6% of patients had positive anti-NETs antibodies. The median of IgG anti-NETs antibodies was 0.30 AU (0-0.163 AU). Patients with anti-NETs antibodies were younger at disease onset and had prominent serological disease activity, with a higher prevalence of anti-double stranded (ds)-DNA antibodies, at higher titers (148.2 mg/dl vs 35.6 mg/dl, p=0.015) and lower levels of C3 and C4. The positivity for anti-NETs antibodies was associated with lupus serositis (8 (25.8%) vs 6 (10.7%), P=0.022). Anti-NETs antibodies were positively correlated with the SLEDAI score (r=0.245, p <0.05) as well as titers of anti-dsDNA antibodies (r=0.290, p <0.01). **Table 1. Clinical and laboratory features of SLE patients**

Variable	n (%)/Median (IQR)

Women (n)	77 (88%)
Age (years)	31.13 (24.6 - 42.5)
Disease duration (years)	8.11 (3.78 – 14.98)
Hydroxychloroquine use (n)*	45 (51.7%)
Prednisone use (n)*	49 (56.3%)
SLEDAI (points)	8 (4 – 16)
C3 (mg/dl)	73 (42 – 112)
C4 (mg/dl)	12 (8 - 24)
Lymphocytes (cells/µl)	1010 (510-1800)
Anti-dsDNA levels (UI/ml)	51.4 (6.7 – 366)
Anti-NETs IgG levels (AU, OD)	0.30 (0 – 0.163)
Anti-NETs antibodies positivity (n)*	31 (35.6%)
Secondary antiphospholipid syndrome (n)*	14 (16.1%)

Table 2. Comparison of clinical and laboratorial characteristics between patients with positive vs negative anti-NETs antibodies.

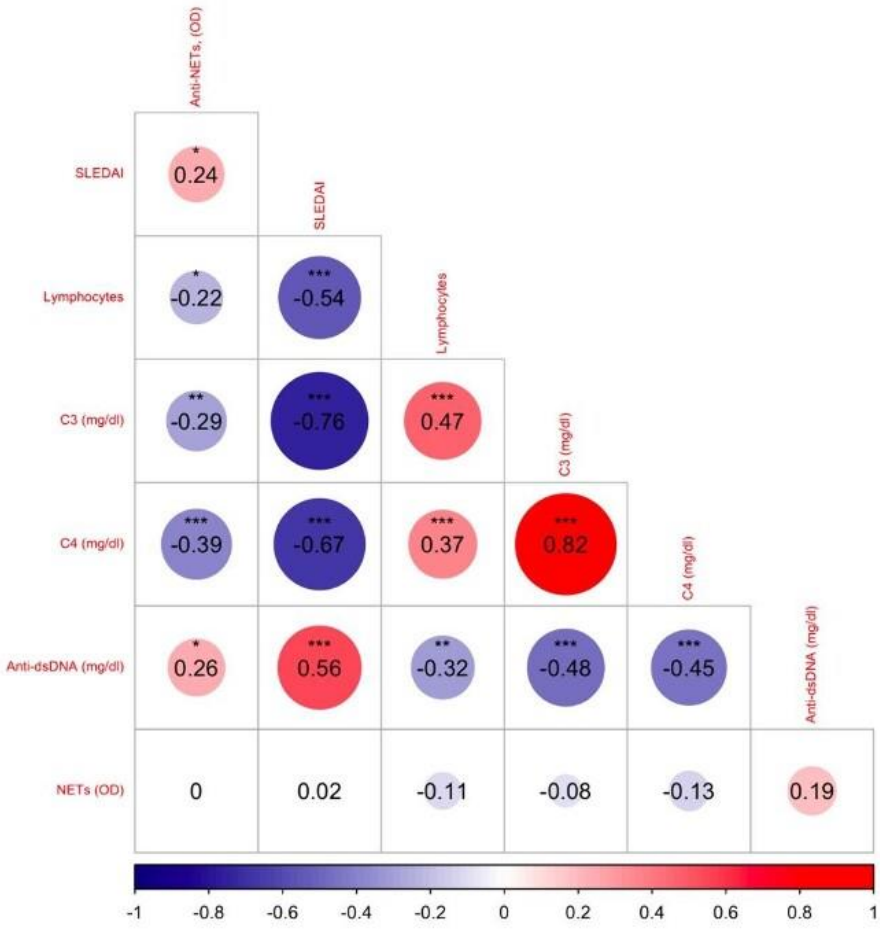
	Positive anti-NETs antibodies, n=31 Median (IQR)/ n(%)*
Age, years	28.7 (23.8-33.2)
Serositis (n)*	8 (25.8%)
Prednisone use (n)*	23 (74.2%)
SLEDAI (points)	13 (6.5 – 18)
Anti-NETs AU (OD)	.207 (.135 – .301)
NETs levels AU (OD)	0.115 (.102-.135)
Anti-dsDNA, (UI/dl)	148.2 (26.1 – 957.9)
C3 (mg/dl)	58 (37 – 85.5)

C4 (mg/dl)	**8 (8 – 12.5)**

Table 3. Anti-NETs antibodies levels according to the clinical features of SLE patients.

	Anti-NETs antibodies AU (OD) Median (IQR)		
Activity	**Present**	**Absent**	***p* value**
Lupus nephritis	.045 (.000-.172)	.002 (.000-.133)	0.301
Hematologic	.000 (.000-.054)	.043 (.000-.173)	0.077
Mucocutaneous	.044 (.000-.197)	.028 (.000-.128)	0.753
Serositis	.086 (.000-.190)	.017 (.000-.131)	0.068
Serological activity	.045 (.000-.178)	.000 (.000-.045)	**0.023**

Figure 1. Correlations of IgG anti-NET antibodies and SLEDAI, C3, C4, lymphocyte count and anti-dsDNA.



Conclusions: IgG anti-NET antibodies were found in one third of SLE patients. Higher prevalence was found in SLE patients with global and serological activity. This is the first description of the association between IgG anti-NET and clinical features of SLE. Their characterization might address their role as novel biomarkers.

PV026 / #271

Poster Topic: ***AS04 - Biomarkers***

DERMATOLOGIC INDICATORS OF RHEUMATIC DISEASES: INSIGHTS FROM ANTINUCLEAR ANTIBODY TESTING IN OUTPATIENT SETTINGS

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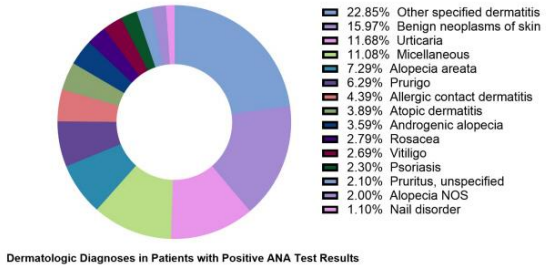
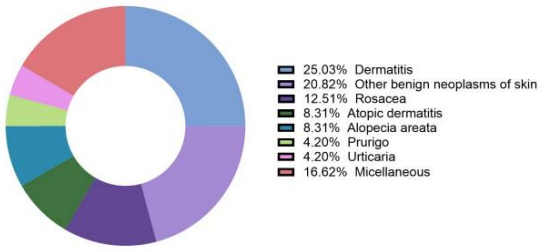
Background/Purpose: Cutaneous symptoms frequently signal rheumatic diseases, sometimes presenting early in their course. This study assesses the prevalence of anti-nuclear antibody (ANA) positivity in dermatology patients, the frequency of rheumatic disease diagnoses made via ANA testing, and the associated dermatological presentations and antibody patterns in a single-center tertiary care setting.

Methods: Data were collected retrospectively from dermatology outpatient visits between January 1, 2013, and December 31, 2023, at a national tertiary hospital. ANA titers and patterns were analyzed for patients with positive ANA results, excluding those with prior rheumatology visits or known rheumatic diseases. Patients with positive ANA were further examined for rheumatologic and dermatologic diagnoses.

Results: Of 8,347 dermatology patients who underwent ANA testing, 1,054 (12.7%) had positive results and were referred to rheumatology. Positive ANA titers included 1:80 in 332 patients (31.5%), 1:160 in 167 patients (15.8%), and 1:1280 or higher in 33 patients (3.1%). Among those referred, 59 patients (5.6%) were diagnosed with rheumatic diseases: 32 patients (55.9%) with Sjögren's syndrome, 24 (39.0%) with systemic lupus erythematosus (SLE), 2 (3.4%) with systemic sclerosis, and 1 (1.7%) with mixed connective tissue disease. Dermatologic diagnoses in Sjögren's syndrome patients included dermatitis (24.2%), urticaria (15.1%), benign skin tumors (15.1%), pruritus (15.1%), and alopecia (9.0%). ANA titers were 1:1280 in 24.2% and 1:160 or higher in 72.6% of Sjögren's syndrome cases. For SLE patients, dermatologic conditions included dermatitis (25.0%), benign skin tumors (20.8%), rosacea (12.5%), and alopecia (8.3%), with ANA titers of 1:1280 in 25.0% and 1:160 or higher in 83.3% [Figure 1].



Dermatologic Diagnoses in Patients with Positive ANA Test Results



Initial Dermatologic Diagnoses in Patients
Later Diagnosed with Systemic lupus erythematosus

Conclusions: This study underscores the value of ANA testing in dermatologic settings, revealing a noteworthy prevalence of rheumatic diseases in patients presenting with ANA positivity. Sjögren's syndrome and SLE were the most frequent diagnoses, with distinct dermatologic manifestations and ANA titer patterns. Positive antinuclear antibody results, along with certain skin presentations, may prompt dermatologists to consider possible underlying rheumatic diseases.

PV027 / #769

Poster Topic: *AS04 – Biomarkers*
Late-Breaking Abstract

PREDICTION OF SLE FLARES BY MEASURING AUTO-ANTIBODY DYNAMICS: A NOVEL APPROACH FOR EARLY DETECTION AND MONITORING

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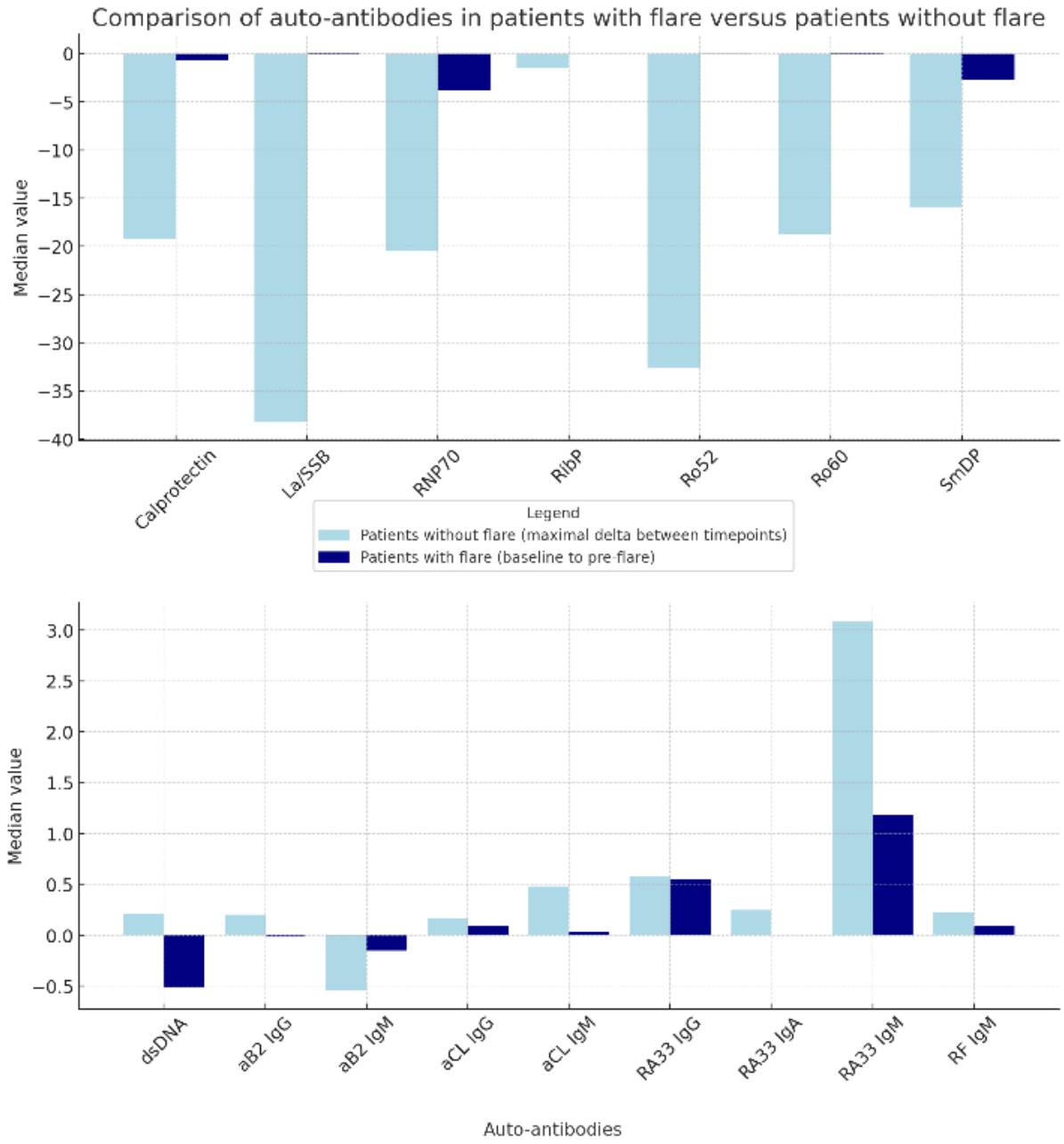
Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by a highly variable disease course, including unpredictable flares that can lead to significant morbidity. Early identification of impending flares could improve patient management and outcomes. This study investigates whether measuring dynamic levels of auto-antibodies can predict the occurrence of SLE flares.

Methods: A cohort of 100 SLE patients was prospectively followed for two years, with visits scheduled every three months at the outpatient clinic of the University Medical Center, Utrecht, the Netherlands. At each visit, clinical parameters were recorded, including the presence or absence of a flare, assessed with the SELENA-SLEDAI Flare Index. Additionally, blood samples were collected, and blood biomarker levels, including antibodies associated with SLE as well as calprotectin as a marker of neutrophil activation, were semi-quantitatively measured using the EliA™ technology (Phadia AB, Sweden) on citrate plasma. To assess whether changes in these auto-antibodies predicted the occurrence of a flare three months later, binary logistic regression analysis was performed. For patients who experienced a flare during follow-up, changes (Δ) in biomarker levels were calculated between baseline and the pre-flare time point. For patients without flares, the highest Δ value observed between any two time points was used.

Results: The cohort consisted of 100 SLE patients with a median age of 50 years (IQR 39-57); 88 women and 12 men. Regarding ethnic distribution, 77 patients were White, 9 Asian, and 4 Black. Median disease duration was 18 years (IQR 8-28). Median SLEDAI score at baseline was 4 (IQR 2-6). During follow-up, 132 flares were registered, of which 119 moderate and 13 severe.
In the binary logistic regression analysis changes in La/SSB (OR 1.48, 95%CI 1.026-2.129), Ro52 (OR 1.03, 95%CI 1.004-1.047), and Ro60 (OR 1.04, 95%CI 1.007-1.076) were identified as significant predictors of a flare occurring within the following three months. RA33 IgA was inversely associated with flare risk (OR 0.20, 95%CI 0.053-0.757).



For no-flare patients, change in auto-antibody values was calculated between all consecutive visits and the maximum Δ (i.e. the maximum background dynamics in patients with stable disease) used. For flare patients, Δ between baseline and the visit prior to flare was calculated to assess dynamics pre-flare. aB2: anti-beta-2-glycoprotein-1; aCL: anti-cardiolipin.

Table 1: Results of binary logistic regression analysis assessing whether changes in autoantibody titers predict the occurrence of flares three months later.

Antibody	**OR**	**p-value**	**95%CI Lower**	**Upper**

dsDNA	1.01	0.175	0.994	1.032
aB2 IgG	0.80	0.168	0.582	1.098
aB2 IgM	0.91	0.279	0.775	1.076
aCL IgG	0.89	0.083	0.774	1.016
aCL IgM	0.95	0.447	0.836	1.082
RA33 IgG	0.96	0.537	0.846	1.091
RA33 IgA	**0.20**	**0.018**	**0.053**	**0.757**
RA33 IgM	0.99	0.607	0.966	1.020
RF IgM	1.05	0.604	0.869	1.273
Calprotectin	1.00	0.682	0.999	1.002
SmDP	1.09	0.052	0.999	1.190
La/SSB	**1.48**	**0.036**	**1.026**	**2.129**
RibP	1.30	0.469	0.638	2.648
RNP70	13.64	0.996	0.001	29.425
Ro52	**1.03**	**0.018**	**1.004**	**1.047**
Ro60	**1.04**	**0.017**	**1.007**	**1.076**

$p<0.05$ statistically significant

Conclusions: These findings suggest that the dynamics over time of specific autoantibody levels, particularly La/SSB, Ro52, and Ro60, can serve as predictors for impending disease flares in SLE patients. Additionally, the inverse association of RA33 IgA with flare risk indicates a potential modulatory role in disease activity. Further research is needed to elucidate the underlying mechanisms of this findings and explore their clinical applicability in personalized disease management.

PV028 / #749

Poster Topic: *AS04 – Biomarkers*
Late-Breaking Abstract

VITAMIN D LEVEL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS ASSOCIATION WITH BONE TURNOVER MARKERS

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Background/Purpose: According to scientific sources, vitamin D insufficiency has been detected in two-thirds of patients with systemic lupus erythematosus (SLE), while the deficiency is observed in one of five individuals. Hypovitaminosis D in SLE patients can be caused by kidney damage, chronic administration of glucocorticoids and, possibly, hydroxychloroquine, use of sunscreens, formation of antibodies to vitamin D, etc. It is also known that SLE patients demonstrate a tendency to rapid bone loss caused by impaired differentiation and decreased activity of osteoblasts, increased maturation and activity of osteoclasts, and accelerated apoptosis of osteocytes in chronic inflammations. Here, serum bone turnover markers may play a role in assessing synthesis and resorption progress. At the same time, the information about vitamin D influencing bone metabolism requires further study.The study is intended to determine vitamin D levels in SLE patients and assess their relationship with bone turnover markers.

Methods: We examined 65 SLE patients (mean age 48.95±1.46 years) and 30 the control group subjects of the corresponding age and sex. The main group consisted of 54 (83.08%) women and 11 (16.92%) men. The average duration of the disease was 12.05±1.09 years. We used ELISA to determine vitamin D concentration and characterized it as optimal (30–50 ng/ ml), insufficient (20–30 ng/ml) and deficient one (<20 ng/ml). The blood serum osteocalcin, procollagen type I C-terminal propeptide and C-terminal telopeptide of type I collagen were determined using ELISA.

Results: Blood serum vitamin D concentration in SLE patients was 18.58±0.97 ng/ml, while the one in the control group subjects was 27.44±1.28 ng/ml. Vitamin D deficiency and insufficiency was diagnosed in 43 (66.15%) and 16 (24.62%) patients, respectively, while only 6 (9.23%) subjects had the optimal vitamin D level. The control group presented normal 25(OH)D concentration, vitamin D insufficiency, and deficiency in 11 (36.67%), 11 (36.67%), and 8 (26.66%) subjects, respectively. Vitamin D levels were associated with the metabolic state of bone tissue, as indicated by a proportional change in the concentration of synthesis markers, such as osteocalcin (OC), procollagen type I C-terminal propeptide (PICP) and a resorption marker, C-terminal telopeptide of type I collagen (CTX). For example, patients with vitamin D deficiency had

average OC and PICP 21.45% and 25.72% lower, accordingly, than had the patients of the group with optimal vitamin D concentration ($p < 0.05$). The average CTX in patients with vitamin D deficiency was 38.71% higher than the one in the group of patients that presented no hypovitaminosis D ($p < 0.01$). The results of the correlation analysis confirmed the close relationship between the vitamin D concentration and OC ($r = 0.32$; $p = 0.01$), and CTX ($r = -0.25$; $p < 0.05$). A reliable direct correlation was also established between CTX and the total dose of glucocorticoids ($r = 0.48$; $p < 0.001$).

Conclusions: Our study has demonstrated a significant prevalence of vitamin D deficiency and insufficiency in the Ukrainian population of SLE patients, as well as close association of hypovitaminosis D with changes in bone turnover markers (OC, PICP, CTX).

PV029 / #143

Poster Topic: ***AS04 - Biomarkers***

ANTI-NEUTROPHIL EXTRACELLULAR TRAP ANTIBODIES IN AUTOIMMUNE RHEUMATIC DISEASES: A SUITABLE BIOMARKER OF THROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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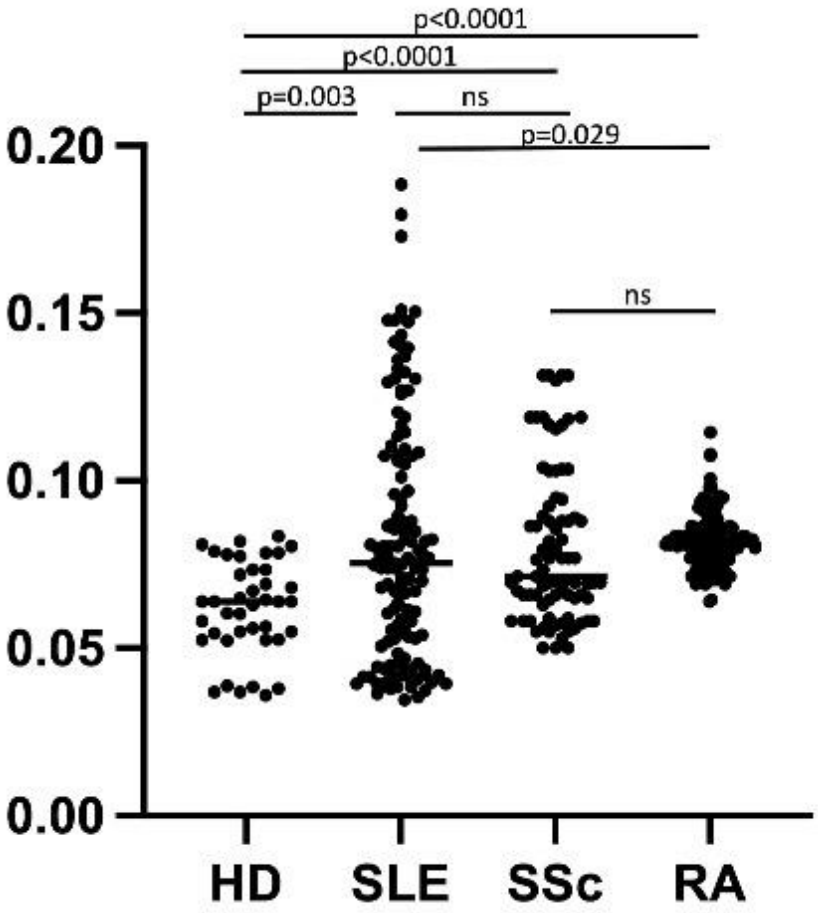
Background/Purpose: The release of intracellular material during neutrophil extracellular trap (NET) formation – NETosis – could have a role in breaking immunological tolerance to self-components. When NETs are formed in an uncontrolled manner or are not cleared properly, the immune system might recognize NETs and trigger an autoimmune reaction against NET components, giving rise to anti-NET antibodies. To date, limited information is available regarding the prevalence and the clinical significance of anti-NET antibodies in Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SSc) and Rheumatoid Arthritis (RA) patients. This study aimed to elucidate the prevalence and the potential role as biomarker of anti-NET antibodies in SLE, SSc and RA patients.

Methods: Serum samples from SLE, SSc, RA and healthy donors (HD) were evaluated for anti-NETs IgG, using an ELISA home-made coated with phorbol myristate acetate (PMA)-induced NET. Based on a positivity threshold set at the 99th percentile for HD sera we calculated the positive samples.

Results: We enrolled 349 patients with autoimmune rheumatic diseases (ARD), founding a prevalence of anti-NETs of about 40% (Figure 1). Of the 136 SLE patients (Table 1) 50 (36.8%) were anti-NETs positive, revealing an association between anti-NETs and Antiphospholipid Syndrome (APS) (OR 3.37 [95% CI 1.22-9.36], p = 0.02) and with an history of arterial thrombosis regardless of coexisting Secondary APS (SAPS) (OR 5.52 [95% CI 1.07-28.52], p = 0.032). In RA patients 52 out 131 (39.7%) tested positive for anti-NETs and we found a significant difference in the anti-NETs OD between seronegative (33/131) and seropositive patients (median 0.079 OD [IQR 0.04] vs median 0.084 OD [IQR 0.05] respectively; p = 0.04). Almost all RA patients (88.6%) with a positive anti-NETs test were ACPA-positive. Indeed, our results revealed a significant association between testing positive for anti-NETs and the presence of ACPA (p = 0.049). In addition, the anti-NETs OD was significantly greater in RA patients than in those with SLE (p = 0.016). Of the 82 SSc patients enrolled 33 (40%) were anti-NETs positive, and we found a direct correlation with CCL-18 (r 0.289 [CI 95% 0.04-0.50], p = 0.02), a biomarker of worst prognosis and mortality in ILD- SSc patients.

Figure.1 Levels of anti-NET in autoimmune rheumatic disease (ARD) patients and healthy donors (HD)



	HD (n 40)	SLE (n 136)	SSc (n 82)	RA (n 131)
Median (IQR)	0.0640 (0.047)	0.0750 (0.154)	0.0770 (0.019)	0.0810 (0.051)

Anti-NET IgG were measured in Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SSc), Rheumatoid Arthritis (RA) and healthy donor (HD). Levels of anti-NET IgG at 450-m optical density (OD) were compared between the groups.

Table 1. Clinical and demographic features of Systemic Lupus Erythematosus patients

Clinical and demographic features	**SLE n=136**
Age (years), mean (SD)	46 (12.6)

Female, n (%)	125 (91.9)
Disease duration (years), median (25^{th}-75^{th}percentile)	13 (8-23.5)
SAPS, n (%)	19 (14)
SLEDAI mean (SD)	1.4 (2.1)
Neurological manifestations, n (%)	6 (4.4)
Cutaneous manifestations, n (%)	77 (56.6)
Renal manifestations, n (%)	35 (25.7)
Cytopenia, n (%)	54 (39.7)
Serositis, n (%)	19 (14)
Arthritis, n (%)	84 (61.8)
Thrombosis, n (%)	17 (12.5)

SAPS= Secondary Antiphospholipid Syndrome; SLEDAI= Systemic Lupus Erythematosus Disease Activity Index.

Conclusions: Anti-NETs are highly prevalent in ARD patients. In SLE patients, they are associated with APS and arterial thrombosis, a major cause of mortality in SLE. Their association with ACPA further highlighted the possible role of NETosis in RA.

PV030 / #282

Poster Topic: ***AS04 - Biomarkers***

SERUM BIOMARKERS AND INTERFERON ALPHA CONCENTRATION AND THEIR CORRELATION TO DISEASE ACTIVITY IN 62 ESTONIAN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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Background/Purpose: SLE is a rare chronic autoimmune disease with polymorphic clinical manifestation. With a complex disease in pathoetiology and heterogenicity in organ involvement, understanding disease activity and treating patients can be difficult. Identifying certain cytokine profiles in different disease states can give additional information in characterizing SLE and relieving the burden of disease.

Methods: Consecutive outpatient and inpatient patients with rheumatologist diagnosed SLE (≥20 years) were enrolled. Evaluation for disease activity, current treatment, organ involvement, immunological findings and comorbidities were done. In addition, data from medical records were collected: organ involvement and immunological findings at the time of diagnosis and initial treatment. SLE disease activity was measured using SLEDAI 2K (Systemic Lupus Erythematosus Disease Activity Index 2K) score. Blood tests were taken to measure interferon levels using Simoa (Single Molecul Array) method and Olink proximity extension assay was used to measure inflammatory proteins. To evaluate the extent of the deviation of IFNα and marked protein levels in patients compared to non-autoimmune individuals, age and gender matched control group was used. Interferon score was calculated according to interferon induced gene expression in blood cells collected to RNA stabilizing tubes. Principal component analysis, volcano plot and analysis of variance (ANOVA), Kruskal and Wilcoxon test were used to evaluate significant differences between controls and patients, different disease activity groups and glycocorticosteroid dosage in serum protein pattern. Heatmap to visualize different SLE clusters in relation to organ involvement, biomarker pattern and used treatment was done.

Results: Among 62 patients (mean age 49 (SD ±12.4) years, mean disease duration 12 (±10.1) years, mean SLEDAI 2K at diagnosis 11 (±5.5)) 90% were females. Mean SLEDAI 2K value at study visit was 4 (±4.0), 39% of patients had SLEDAI 2K >4 and 42% of patient were positive for anti-dsDNA antibodies and 48% had hypocomplementemia. Glucocorticosteroids were used in 71% of patients and 29% had Rituximab treatment. Olink assay highlighted 25 upregulated biomarkers for patients in comparison to controls with IL-10 and IL15RA upregulated in inactive patients (SLEDAI 2K=0) versus controls. We found significant differences in cytokine levels for patients in

methylprednisolone treatment groups high dose (>4mg/day), low dose (1-4mg/day) and no treatment in SLEDAI high (SLEDAI 2K>4) group for IL18R1, PD-L1, FGF5; in SLEDAI low group (SLEDAI 2K £4) for FGF-5 and SLEDAI inactive group for IL-12B. With identifying four different disease clusters, it was highlighted that CXCL10 and CXCL11 were related with more active disease while MCP-1 could predict arthritis in patients with low cytokine activity.

Conclusions: With measuring biomarkers activity in Estonian SLE patients, we have identified four disease clusters, confirming CXCL10 and CXCL11 role in more active disease and giving additional insight to low cytokine activity driven disease with MCP-1 as a potential predictor for arthritis as it has been highlighted in rheumatoid arthritis studies. However further studies are needed to provide insight to changes in FGF-5 levels in relation to glucocorticosteroids. [1]Reynolds JA, McCarthy EM, Haque S, Ngamjanyaporn P, Sergeant JC, Lee E, Lee E, Kilfeather SA, Parker B, Bruce IN. Cytokine profiling in active and quiescent SLE reveals distinct patient subpopulations. Arthritis Res Ther. 2018 Aug 9;20(1):173. [2]Ellingsen T, Buus A, Stengaard-Pedersen K. Plasma monocyte chemoattractant protein 1 is a marker for joint inflammation in rheumatoid arthritis. J Rheumatol. 2001 Jan;28(1):41-6.

PV031 / #294

Poster Topic: ***AS04 - Biomarkers***

GALECTINS-1,3 AND 9 IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: ARE THERE ANY LINKS WITH DISEASE ACTIVITY OR IRREVERSIBLE ORGAN DAMAGE?

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Background/Purpose: To compare serum concentrations of galectins -1, 3 and 9 in patients with systemic lupus erythematosus (SLE) and healthy women, and to identify the relationship of these biomarkers with disease activity and damage index.

Methods: Seventy-nine women with SLE (according to the criteria of SLICC/ACR 2012) were included in the study. The median age was 32 [26;40] years, the median disease duration was 24 [1;144] months. High SLE activity (SLEDAI-2K>10) was recorded in 18 (22.8%), moderate (SLEDAI-2K= 5-10) – in 34 (43.0%), low activity or remission (SLEDAI-2K = 0-4) – in 27 (34.2%) patients. The SLICC damage index ranged from 0 to 6 (median [IQR] = 0 [0-1]). Glucocorticoids (GC) were received by 62 (78.5%) with median daily dose of prednisone 10 [5-20] mg, hydroxychloroquine – 60 (75.9%), immunosuppressants – 24 (30.4%) (cyclophosphamide – 2 (2.5%), mycophenolate mofetil – 16 (20.3%), azathioprine – 3 (3.8%), methotrexate – 3 (3.8%)), biological agents – 7 (8.9%) (rituximab – 5 (6.3%), belimumab – 2 (2.5%)), immunoglobulin – 3 (3.8%) patients. The control group included 21 women without immune-inflammatory rheumatic diseases, matched by age with patients with SLE. Serum concentrations of galectins-1,3,9 were determined by enzyme-linked immunosorbent assay (Cloud-Clone Corp., China).

Results: Galectins-1,3 and 9 levels in SLE and in the control group are shown in Table 1. The use of GC, hydroxychloroquine, immunosuppressants and biological agents did not affect galectins levels. Table1. Galectins-1,3 and 9 levels in SLE and in the control group

Biomarkers	SLE (n=79)	Control (n=21)	p (Mann-Whitney U Test)
Galectin-1, ng/ml	1,3 [0,91-1,89]	0,51 [0,006-0,97]	<0,0001
Galectin-3, ng/ml	1,13 [0,91-1,42]	0,88 [0,69-1,27]	0,057

Galectin-9, pg/ml	0,001 [0,001-0,005]	0,001 [0,001-0,002]	0,33

In SLE, galectin-1 correlated with SLEDAI-2K (r = 0.24, p = 0.033), hemoglobin (r = -0,23, p = 0,039), platelet count (r = -0,22, p =0,049), anti-Sm (r = 0,3, p = 0,007). Galectin-3 correlated with damage index (r = 0,29, p = 0,03), C-reactive protein (r = 0,37, p = 0,0046). Galectin-9 correlated with hemoglobin (r = -0,24, p = 0,034), anti-dsDNA (r = 0,31, p = 0,006). Clinical manifestations that occurred in the SLE group with a frequency of >10% were increased a-ds-DNA – in 54 (68.4%) patients, hypocomplementemia – in 52 (65.8%), rash - 34 (43.0%), arthritis – in 32 (40.5%), alopecia – in 24 (30.4%), nephritis – in 20 (25.3%), serositis – in 14 (17.7%). Galectin-1 levels were higher in patients with pleuritis or pericarditis than without serositis (2.5 [0.98-6.65] ng/ml vs 1.27 [0.91-1.67] ng/ml, p = 0,048). Similar results were obtained also for galectin-3 (1.63 [0.41-2,38] ng/ml vs 1.07 [0.87-1,33] ng/ml, p = 0,003).There were no differences in galectins levels for other common manifestations of SLE.

Conclusions: SLE patients had higher serum galectin-1 levels and a trend toward elevated galectin-3 levels, while galectin-9 concentrations were similar to healthy women. Galectin-1 levels were linearly related to disease activity, and galectin-9 levels were linearly related to irreversible organ damage, although the associations were weak. Of the most common clinical manifestations of SLE, only serositis was associated with an increase in galectins-1 and 3. Both galectin-1 and galectin-9 were also correlated with some hematological and immunological parameters.

PV032 / #459

Poster Topic: ***AS04 - Biomarkers***

TYPE I INTERFERON GENES SIGNATURE AND GALECTINS-1,3,9: ARE THERE A RELATIONSHIPS?

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Background/Purpose: To find out whether galectins-1,3,9 levels are related to the type I interferon genes signature (IFNGS) in patients with systemic lupus erythematosus (SLE).

Methods: A total of 43 patients (38 women and 5 men) with SLE (31[23-41] years old) were enrolled in the study. The median SLE duration was 24 [1-96] months, SLEDAI-2K was 8 [4-14]. SLE pts were treated with glucocorticoids (GC) (72,12%), hydroxychloroquine (69,8%), immunosuppressive drugs (35,9%) and biological agents (4,7%). Type I interferon status was assessed as «low» or «high» by the average expression of interferon-inducible three selected genes (MX1, RSAD2, EPSTI1) using real-time polymerase chain reaction. IFNGS was considered «high» if the average genes expression value in patients exceeded that in donors (20 healthy donors comparable in sex and age with the SLE patients). Serum galectins-1,3,9 levels were determined by enzyme—linked immunosorbent assay (Cloud-Clone Corp., China).

Results: «High» IFNGS was detected in 33 of 43 patients with SLE. Patients with «high» and «low» INFGS did not differ in age, gender, disease duration, SLE activity according to SLEDAI-2K (p>0,05 for all). Galectins-1 and 3 levels were comparable in patients with «high» and «low» IFNGS, but the galectin-9 levels were higher in patients with elevated gene expression (table 1).

Table 1. Galectins levels depending on IFNGS status in patients with SLE

Biomarkers	«High» INFGS (n=33)	«Low» INFGS (n=10)	p (Mann-Whitney U Test)
Galectin-1, ng/ml	1,37 [0,91-3,13]	1,31 [0,96-1,57]	0,77
Galectin-3, ng/ml	1,37 [1,07-1,81]	1,17 [0,98-1,3]	0,26
Galectin-9, pg/ml	0,004 [0,001-0,22]	0,001 [0,001-0,001]	0,028

Conclusions: The serum concentrations of galectin-9, but not galectins-1 and 3, depend on interferon-inducible genes expression in SLE patients. Increased galectin-9 may be a surrogate serological biomarker of elevated type I interferon status.

PV033 / #298

Poster Topic: ***AS04 - Biomarkers***

ANTI-DFS70 ANTIBODIES AS A MARKER FOR EXCLUSION OF SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES

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Background/Purpose: The DFS70 pattern, which is rare in patients (pts) with systemic autoimmune rheumatic diseases (SARDs), has been described as the second most common in serum healthy individuals (HI). The purpose of our study was the frequency of detection of anti-DFS70 in HI, pts with undifferentiated SARDs and systemic lupus erythematosus (SLE).

Methods: A total of 45 HI, 17 undifferentiated SARDs pts and 81 SLE pts were included in the study. Groups were comparable in gender and age among themselves. The diagnosis of SLE was performed according to the ACR/EULAR 2019 classification criteria. Serum samples were tested for anti-DFS70 (ANA HEp-2 ELITE/DFS70 knock-out indirect immunofluorescence assay (IFA), “Trinity Biotech”, Ireland). Fluorescence titers ≥1:160 were considered as positive for ANA HEp-2 cell patterns.

Results: Positive results of the ANA study were found in 81 (100.0%) pts with SLE, in 16 (94.0%) pts with undifferentiated SARDs and 7 (15.6%) HI. Isolated antibodies to DFS70 detected in 4 (57.1%) HI, in 9 (56.2%) undifferentiated SARDs, but were not detected in SLE pts. Classical HEp-2 cell patterns (homogeneous AC-1, speckled AC-4,5, homogeneous+speckled AC-1,4,5, cytoplasmic AC-19,20,21) without anti-DFS70 were determined in 3 (42.9%) HI, in 7 (43.8%) pts with undifferentiated SARDs and in 81 (100%) pts with SLE (Table 1). Therefore, monospecific anti-DFS70 were detected in the HI and undifferentiated SARDs groups, but were not detected in pts with a reliable diagnosis of SLE.

Table 1. Detection rate of patterns in ANA-HEp-2-positive pts

HEp-2 cell patterns	**HI, n=7 (%)**	**SLE, n=81 (%)**	**Undifferentiated SARDs, n=16 (%)**
Nuclear dense fine speckled - DFS70 (AC-2), n (%)	4 (57.1)	0 (0.0)	9 (56.2)

Nuclear homogeneous (AC-1), n (%)	0 (0.0)	26 (32.1)	0 (0.0)
Speckled (AC-4,5), n (%)	1 (14.3)	14 (17.3)	1 (6.2)
Nuclear homogeneous+speckled (AC-1,4,5), n (%)	2 (28.6)	35 (43.2)	3 (18.8)
Cytoplasmic (AC-19,20,21), n (%)	0 (0.0)	6 (7.4)	3 (18.8)

Conclusions: The presence of monospecific DFS70 pattern in IFA without concomitant SARD-associated antibodies could be an exclusion biomarker for SARDs and a sign of benign autoimmunity.

PV034 / #275

Poster Topic: ***AS04 - Biomarkers***

URINARY PROTEOMIC ANALYSIS PROVIDES DIFFERENT PATTERNS BETWEEN LUPUS PATIENTS WITH AND WITHOUT NEPHRITIS: RESULTS OF A MULTICENTER STUDY IN 124 PATIENTS

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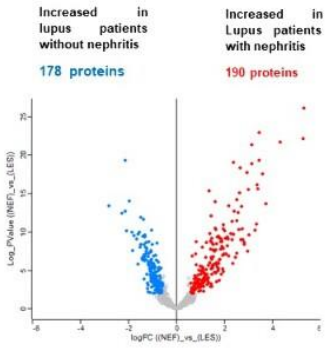
Background/Purpose: Lupus nephritis is a common and serious manifestation in lupus patients. Biopsy is the gold standard to identify different patterns of disease, being not always accessible and with potential complications. A need emerges to identify biomarkers that reflect disease pathology in a non-invasive manner. Urine investigation by proteomics could in theory provide new biomarkers to better classify these patients. The objective of the study is to compare urine from lupus patients with and without nephritis usin proteomics in order to find potential biomarkers of the disease

Methods: Multicentric and prospective proteomics study was conducted in 24-hour urine samples from SLE patients with and without renal involvement. The analysis has been performed by label free nLC MS/MS in two batches that included class I, II, III, IV and V nephropathology,. SLE patients has been diagnosed according to the 2019 EULAR/ACR Classification Criteria. Limma test statistics were made using Prostar v.1.34.6

Results: 124 samples of patients from 5 hospitals were collected and from those 109 was analyzed. There were no differences between groups according to race, gender and age (Table 1).

	Nº Samples	Males	Females	SLE With Renal Involvement	SLE Without Renal Involvement
Basurto University Hospital	85	8	77	57	28
Donostia University Hospital	14	2	12	6	8
Araba University Hospital	8	1	7	0	8
Sierralllana Hospital	10	1	9	6	4
Fundació PuigVert	7	2	5	3	4
	124	14	110	72	52

803 proteins were identified. 178 proteins were increased in lupus without nephritis and 190 in patients with nephritis. Making a different analysis by batches, results, it is confirmed that there is a linear correlation between proteins in patients with and without renal involvemet (figure 1).



Proteins increased in urine of nephritis patients includes transport proteins as afamin but also others involved in B cell activation: Fc receptor-like protein 5, enzimes like beta-ala-his dipeptidase, immunoglobulin heavy constant gamma 4 involved in antibacterial humoral response and complement activation (table 2).

T. Fasta headers	logFC ((NEF)_vs_((LES)) 317	P_Value ((NEF)_vs_((LES)) 317	Log_PValue ((NEF)_vs_((LES)) 317	Adjusted_PV C: alue ((NEF)_vs_((LES)) 317	isDifferential ((NEF)_vs_((LES)) 317	logFC ((NEF)_vs_((LES)) 429	P_Value ((NEF)_vs_((LES)) 429	Log_PValue ((NEF)_vs_((LES)) 429	Adjusted_PV C: alue ((NEF)_vs_((LES)) 429	isDifferential ((NEF)_vs_((LES)) 429
spP43652|AFAM_HUMAN Afamin OS=Homo sapiens OX=9606 GN=AFM PE=1 SV=1	3,671	4,48E-05	4,349	0,001033	Up	6,13	1,01E-20	20	1,57E-18	Up
spQ96RD9|FCRL5_HUMAN Fc receptor-like protein 5 OS=Homo sapiens OX=9606 GN=FCRL5 PE=1 SV=3	3,287	2,69E-06	5,571	0,000224	Up	5,283	5,57E-18	17,25	1,97E-16	Up
spQ96KN2|CNDP1_HUMAN Beta-Ala-His dipeptidase OS=Homo sapiens OX=9606 GN=CNDP1 PE=1 SV=4	1,796	0,004708	2,327	0,01713	Up	5,052	1,40E-20	19,85	1,57E-18	Up
spQ8NE71|ABCF1_HUMAN ATP-binding cassette sub-family F member 1 OS=Homo sapiens OX=9606 GN=ABCF1 PE=1 SV=2	3,01	4,98E-05	4,303	0,001033	Up	4,859	4,20E-19	18,38	2,52E-17	Up
spP01861|IGHG4_HUMAN Immunoglobulin heavy constant gamma 4 OS=Homo sapiens OX=9606 GN=IGHG4 PE=1 SV=1	2,166	0,003302	2,481	0,01371	Up	4,624	4,13E-13	12,38	6,39E-12	Up
spP04217|A1BG_HUMAN Alpha-1B-glycoprotein OS=Homo sapiens OX=9606 GN=A1BG PE=1 SV=4	2,642	7,32E-05	4,136	0,00136	Up	4,125	1,30E-19	18,89	1,05E-17	Up
spP02750|A2GL_HUMAN Leucine-rich alpha-2-glycoprotein OS=Homo sapiens OX=9606 GN=LRG1 PE=1 SV=2	2,064	0,0004159	3,381	0,003711	Up	4,09	1,59E-13	12,8	2,96E-12	Up
spP19652|A1AG2_HUMAN Alpha-1-acid glycoprotein 2 OS=Homo sapiens OX=9606 GN=ORM2 PE=1 SV=2	3,027	1,97E-05	4,706	0,00064	Up	3,861	6,34E-15	14,2	1,70E-13	Up
spP08185|CBG_HUMAN Corticosteroid-binding globulin OS=Homo sapiens OX=9606 GN=SERPINA6 PE=1 SV=1	2,323	0,0001882	3,725	0,002215	Up	3,846	3,87E-21	20,41	9,35E-19	Up

Conclusions: This study shows different patterns of proteomic profile in lupus patients with renal involvement and opens a new field of investigation for better understanding of the disease and find potential biomarkers of different types and severity of nephritis. - GSK-funded study

PV035 / #122

Poster Topic: ***AS04 - Biomarkers***

EFFECT OF COMORBIDITY AND STANDARD THERAPY ON INTERFERON STATUS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Type I interferon (IFN-I) play a central role in the pathogenesis of Systemic lupus erythematosus (SLE). Overexpression of IFN-I occurs in 60-80% patients with SLE. Type I IFN-inducible gene expression, measured using the IFN gene signature (IFGNS), provides a method to asses IFN-I pathway activation in individual patients. Against a background of genetic predisposition, a trigger stimulus, possibly microbial, induces the production of IFN-I and autoantibodies leading to inflammation. Can only the clinical and immunological manifestations of SLE affect on IFNGS? The aim of our study was to describe any conditions, comorbidities and standard therapy of SLE depending on IFN gene signature.

Methods: This observational retrospective-prospective study included 76 patients (86% women, median aged 33 [25;43] years (median [interquartile range 25;75%]), with a definite diagnosis of SLE (SLICC 2012) attending a routine visit at our Clinic between February 2021 and June 2024. Baseline demographics, family history of immune-inflammatory rheumatic diseases among the first-line relatives, triggers, body mass index, smoking status, cardiovascular disease/stroke risk factors, renal disease, cancer, standard therapy (glucocorticoids, antimalarial, immunosuppressants) and IFNGS status (high/low) were analysed in SLE patients. IFN status was assessed by the expression of IFN-inducible genes (MX1, RSAD2, EPSTI1) using real-time polymerase chain reaction. IFNGS was calculated as the average expression value of three selected genes. In patients, IFNGS was considered high when the average value of gene expression exceeded the average value of gene expression in donors. The control group consisted of 20 healthy donors comparable in sex and age with the SLE patients.

Results: The median disease duration was 2.3 [0.2;11.0] years, SLEDAI-2K 7 [4;11] score, SDI 0 [0;2] score. At the time of inclusion in the study, SLE patients had the following manifestations: hematological disorders - 49%, most commonly leucopenia –

45%, inflammatory arthritis - 39%, nephritis - 33% (most commonly class IV), cutaneous lupus - 28%, serositis -18%, mucosal ulcers - 8%, nervous system involvement - 7%. Among 'non-criteria' symptoms the most common were: livedo – 20%, Raynaud's phenomenon - 12%, interstitial lung disease - 12%, lymphadenopathy - 8%, unexplained fever - 7%. Concomitant APS and Sjogren's syndrome were found in 12% and 38% of patients, respectively. The majority of patients at the time of inclusion were taking glucocorticoids (83%) at low doses (10.0 [7.5; 20.0] mg/day prednisolone) in combination with hydroxychloroquine (80%) at a dose of 200 mg/day. Immunosuppressants were used less frequently (in 36% of patients), mainly - mycophenolate mofetil (18%), cyclophosphamide, methotrexate and azathioprine in single cases. In addition, 13/76 (17%) patients were not receiving any therapy. Anti-B-cell biologic (mainly rituximab) according to the inclusion criteria were used more than 2 years ago in 8% of patients. IFNGS-high was detected in 72% of SLE patients. IFNGS-high patients were younger at the time of inclusion (31 [25; 41] and 40 [32; 49] years, $p<0.05$). We identified less hypertension (24% and 52%) and dyslipidaemia (13% and 38%) in IFGNS-high patients versus IFNGS-low patients with SLE. No effect of standard therapy for SLE on IFN-inducible genes expression was found.

Conclusions: In SLE patients, IFN-I is independent of family history of autoimmune disease, any provoking factors, gender, weight, smoking, and any comorbidity. The lower incidence of hypertension and dyslipidemia in IFNGS-high patients is due to the younger age of them. Standard therapy has no significant effect on the expression of certain IFN-inducible genes.

PV036 / #672

Poster Topic: ***AS04 - Biomarkers***

TYPE I INTERFERON STATUS AND CLINICAL MANIFESTATIONS IN A LARGE COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Type I interferons (IFN) are pivotal in the pathogenesis of SLE, with studies showing high IFN gene signature (IGS) status associated with certain organ manifestations, autoantibody profiles, and disease severity. With novel medications targeting the interferon pathway, an enhanced understanding the IGS in patients with SLE is necessary. In this study, we investigated the differences between IGS levels in relation to clinical characteristics in a large cohort of patients with SLE.

Methods: Patients meeting 2019 EULAR/ACR classification criteria for SLE from a single centre were included. Whole blood collected cross-sectionally was analyzed for IGS by the DxTerity assay, categorizing patients into IFN high or IFN low status. The SLICC/ACR damage index (SDI), antibody status, glucocorticoid use, and use of immunosuppressives were analyzed according to IFN status. Additionally, the SLEDAI-2K, SLEDAI-2KG, and clinical SLEDAI-2K were characterized cumulatively from 5 years prior to whole blood collection to last available visit, with adjusted mean SLEDAI (AMS) and AMS-G calculated from the previous 10 years and stratified based on IFN status.

Results: In total, 506 patients with a median age of 49.5 years (IQR 37.26-60.49) were included, with 91.5% female. Overall, 291 (57.5%) were IFN high and 215 (42.5%) were IFN low. The median disease duration was longer in the IFN low group (22.7 years, IQR 11.58-21.05) than in the IFN high group (14.06 years, IQR 7.90-24.71) ($p<0.001$). The median SLEDAI-2K score was higher in the IFN high group (2.0, IQR 0.00-4.00) then in the IFN low group (0.0, IQR 0.00-4.00) (<0.001), as was the SLEDAI-2KG (8.0, IQR 0.00-3.75 vs. 6.0, IQR 0.00-2.00) ($p<0.001$) though the clinical SLEDAI-2K was not significantly different. Similar trends were seen with the cumulative AMS (3.94, SD=2.61 vs. 3.27, SZD 2.47) ($p=0.004$) and AMS-G (5.36, SD=3.53 vs. 4.41, SD=3.25) ($p=0.002$). There was no difference in the proportion of the SLEDAI-2K organ domains between the IFN high and low groups, other than the hematologic domain (IFN high 82.8% vs. IFN low 73.0% [$p=0.011$]). The SDI was similar between the two groups. More patients in the IFN high vs. low group had positive autoantibodies (79.7% vs. 67% [$p=0.002$]), including Smith (56.7% vs. 32.6% [$p<0.001$]), RNP (66.7% vs. 49.3% [$p<0.001$]), Ro (67.4% vs. 47.0% [$p<0.001$]), La (30.9% vs. 17.2% [$p=0.001$]), chromatin (75.6% vs. 41.9% [$p<0.001$]), dsDNA (61.2% vs. 38.1% [$p<0.001$]) and ribosomal P (27.1% vs. 7.9%

[p<0.001]) autoantibodies. There were no differences in levels of C3 or lupus anticoagulant, but more patients in the IFN high group had low C4 and positive anti-cardiolipin. More patients with high IFN were on glucocorticoids (38.5%) then were patients with low IFN low status (27%) (p=0.009). More IFN high status patients were on immunosuppressive agents (185; 63.6%) vs. the IFN low group (98; 45.6%) (p<0.001). Similar trends were seen in our inception cohort, defined as those patients evaluated within one year of diagnosis.

Conclusions: In this large cohort of patients with SLE, IGS status may help to predict overall disease severity as per SLEDAI-2K, SLEDAI-2KG, AMS, and AMS-G (though not the clinical SLEDAI-2K), use of glucocorticoids, and overall use of immunosuppressive therapy, and is associated with more autoantibody positivity. IFN level did not reliably predict presence of specific SLEDAI-2K organ domains or damage. More studies are needed to assess those clinical characteristics associated with an elevated IGS and to determined who may respond best to type I IFN targeted therapies.

PV037 / #22

Poster Topic: ***AS04 - Biomarkers***

NOVEL DIAGNOSTIC BIOMARKER OF SYSTEMIC LUPUS ERYTHEMATOSUS: ANTI-CHAPERONIN CONTAINING T-COMPLEX POLYPEPTIDE 1 ANTIBODY

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Background/Purpose: Systemic lupus erythematosus (SLE) is diagnosed with several clinical and immunological criteria. To find a diagnostic biomarker of SLE, microarray technique was used to find SLE-specific autoantibodies and to provide a clear diagnosis.

Methods: Autoantibodies were discovered by analyzing sera of SLE patients and normal controls (NCs) using a human proteome microarray containing 21,000 purified proteins. This analysis revealed the presence of 63 SLE-specific autoantibodies. Notably, the anti-chaperonin containing t-complex polypeptide 1 (TCP1) antibody exhibited higher expression in patients with SLE. To validate the specificity of anti-TCP1 antibody expression in SLE, Dot blot analysis and enzyme-linked immunosorbent assay (ELISA) were conducted using sera from patients with SLE, NCs, and patients with rheumatoid arthritis, Behçet's disease, and systemic sclerosis.

Results: Dot blot analysis was conducted using sera from patients with SLE and NCs, as well as patients with rheumatoid arthritis, Behçet's disease, and systemic sclerosis. The results confirmed the detection of anti-TCP1 antibody in 79 out of 100 patients with SLE, with significantly elevated expression compared to both NCs and patients with other autoimmune diseases. We performed enzyme-linked immunosorbent assay (ELISA) to determine the relative amounts of anti-TCP1 antibody. ELISA analysis revealed markedly elevated anti-TCP1 antibody levels in the sera of patients with SLE (50.1 ± 17.3 AU, n=251) compared to those of NCs (33.9 ± 9.3 AU, n=50), RA (35 ± 8.7 AU, n=25), BD (37.5 ± 11.6 AU, n=28), and SSc (43 ± 11.9 AU, n=30).

Conclusions: These data suggest that anti-TCP1 antibody is a potential diagnostic biomarker of SLE.

PV038 / #485

Poster Topic: *AS04 - Biomarkers*

ANTI-DSDNA ANTIBODY ISOTYPES IN SYSTEMIC LUPUS ERYTHEMATOSUS: THE NEGLECTED DIAGNOSTIC PARAMETERS

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Background/Purpose: In systemic lupus erythematosus (SLE) many different organs are affected by an immune response including the skin, blood, muscles, heart, lung or kidneys making the range of symptoms vary widely. SLE occurs in about 0.1% of the general population and is predominant in females, especially in the age between 20 and 40 years, and may be linked to the hormone estrogen. Anti-double stranded DNA (dsDNA) antibodies are highly specific for the disease and can be found in 30-40% of patients. Perform a comprehensive literature search to identify all relevant available published data for demonstration of the State-of-the-Art (medicine and technology, SOTA), the Scientific Validity (SV) of the analyte and the Clinical Performance (CP) of anti-dsDNA autoantibodies.

Methods: Systematic literature search, evaluation and documentation was done by applying PRISMA method. The search strings are assembled with the use of Boolean operators and search was restricted to peer-reviewed literature and systematic reviews.

Results: In total 22 publications have been identified as significant for SOTA, SV and CP of anti-dsDNA antibodies. The reviewed literature concludes that anti-dsDNA antibodies are specific and pathogenic biomarkers for monitoring SLE. IgG anti-dsDNA antibodies are the gold standard for diagnosing and monitoring SLE, especially in patients with kidney involvement (Lupus Nephritis) being the most common and severe organ manifestation. These antibodies can bind to self-antigens or immune complexes and accumulate in the glomerular and tubular basement membranes. Defective clearance of apoptotic cells may trigger the production of anti-dsDNA antibodies. Anti-dsDNA IgA and IgG show a strong association with disease activity, and the IgA isotype is additionally associated with several symptoms of skin involvement. However, the IgA isotype has no association with nephritis and arthritis and may therefore define a distinct subset of SLE patients. The presence of IgM anti-dsDNA antibodies shows a negative correlation with various parameters indicating Lupus Nephritis. Due to the contrary roles of IgG and IgM anti-dsDNA Isotypes in the pathogenesis of Lupus Nephritis, there is strong scientific evidence to use the IgG/ IgM Isotype ratio for prediction of nephritis (IgG/IgM >0.8 nephritis; IgG/IgM <0.8 no nephritis) also considered as replacement for kidney biopsy. Anti-dsDNA isotype evaluation in ELISA

might indeed improve diagnostic accuracy, and multiple isotype detection (IgG, IgA, IgM) could enhance sensitivity in detecting the disease.

Conclusions: Almost all patients with renal problems show anti-dsDNA antibodies and they are also suitable for disease monitoring, since anti-dsDNA antibody concentration increases before disease flares but there is still some controversy. But even though anti-dsDNA antibodies have been established as one of the American College of Rheumatology (ACR) and Systemic Lupus International Collaborating Clinics' criteria for diagnosing SLE, IgA and IgM anti-dsDNA isotypes are not included in follow-up routine of the patients. The combination of analysis of different anti-dsDNA isotypes (IgG, IgA, IgM) provides a more nuanced perspective on SLE disease. It not only enables more precise diagnosis, but also better monitoring of disease activity and progression, especially when distinguishing between organ involvement and tracking treatment courses. Overall, the analysis of anti-dsDNA antibody isotypes could provide a tailored and more precise diagnostic strategy in clinical practice, which may be particularly important in the monitoring of Lupus Nephritis and the specific treatment of SLE patients.

PV039 / #308

Poster Topic: ***AS04 - Biomarkers***

GLYCOSYLATION OF ANTI-DSDNA IGG CORRELATES WITH ORGAN INVOLVEMENT IN TREATMENT-NAÏVE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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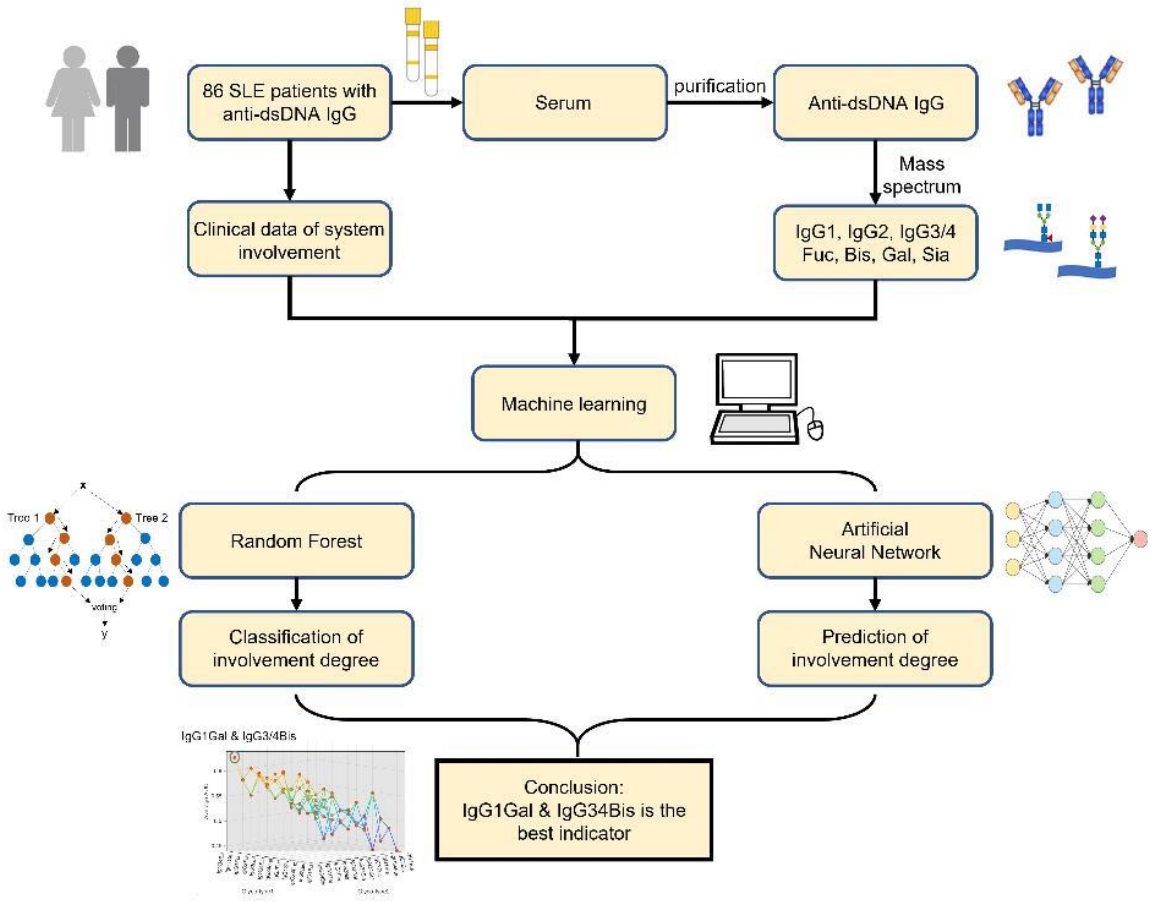
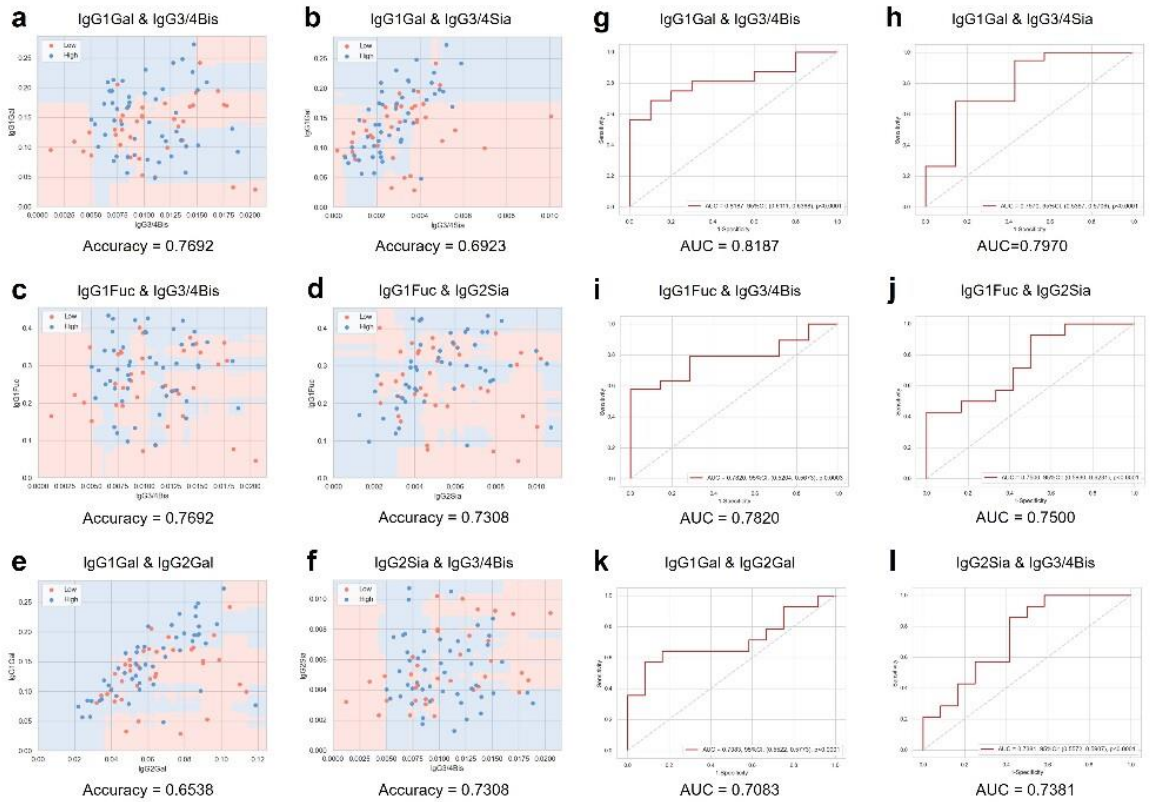
Background/Purpose: Background: Anti-double-stranded DNA (anti-dsDNA) antibodies are important antibodies in systemic lupus erythematosus (SLE). Glycosylation is one of the most commonly post-translational modifications of antibodies, and anti-dsDNA antibodies glycosylation is related with SLE disease activity. However, the association of anti-dsDNA antibodies glycosylation and SLE organ involvement is still unclear.

Methods: Methods: We enrolled 86 consecutive treatment-naïve SLE patients with positive anti-dsDNA antibodies from the Department of Rheumatology and Immunology at Ruijin Hospital, Shanghai, between 2017 and 2022. Serum samples were used in this study. We quantified and classified the organ involvement degree of SLE patients according to the number of organ systems involved in each patient. Then we analyzed each glycoform and combination of glycoforms based on the involvement degree. Random Forest Classifier and Artificial Neural Network were applied to evaluate the correlation between combinations of glycoforms and the organ involvement degree. Fig 1 Workflow of classifying and predicting the involvement degree of organ systems in SLE patients by leveraging glyco-pairs.



Results: Results: Pearson correlation analysis presented a strong connection between involved organs compared with uninvolved organs in SLE patients. The bisection(Bis) of IgG3/4, galactosylation (Gal) of IgG1, fucosylation (Fuc) of IgG1, and sialylation (Sia) of IgG2 displayed high Area under Curve (AUC) values when combined with other glycoforms for classifying the involvement degree. The result of Random Forest showed that the combination of IgG1Gal&IgG3/4Bis had the highest accuracy (0.7692) and AUC value (0.8187). In terms of predicting the involvement rate using Artificial Neural Network, IgG3/4Bis&IgG1Gal had the lowest MSE (0.0244). Fig2. The results of the RF classification model on glyco-pairs. In a-f, the dots on the figure represented the original samples and the grid-like background colors represented the output of the model. Dots sharing the same color with the back ground color were correctly classified by the RF model. The accuracy might seem smaller than the intuition as it was derived solely from the test set's samples. In g-l, ROC of the RF models were plotted. AUC, 95%CI and p-value all reflected the performance of a an RF model. A larger AUC value and a wider gap between the 95%CI and 0.5 suggested a better classification ability of the glyco-pair. In both evaluation metrics, glyco-pair IgG1Gal&IgG3/4Bis performed the best. Abbreviations: AUC: Area under Curve; ROC: Receiver Operating Curves; CI: confidence interval.



Conclusions: Conclusions: Our study showcased the effectiveness of combining glycotypes to classify and predict SLE organ involvement degree. Different glycotypes were correlated with the involvement degree to different extents, and the combination of IgG3/4Bis&IgG1Gal had best correlation with SLE organ involvement.

PV040 / #601

Poster Topic: ***AS04 - Biomarkers***

SERUM PROTEOME PROFILING IDENTIFIES SEROLOGICALLY ACTIVE, CLINICALLY QUIESCENT LUPUS ENDOPHENOTYPES WITH DISTINCT DISEASE TRAJECTORIES

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Background/Purpose: Serologically active clinically quiescent (SACQ) refers to a subset of systemic lupus erythematosus (SLE) patients with elevated serological markers but no apparent clinical symptoms. The variability within SACQ complicates disease management. This study aims to identify serum proteomic markers that characterize SACQ subgroups and predict clinical outcomes.

Methods: SLE patients were consecutively recruited from Peking Union Medical College Hospital (January 2018 - June 2024), including 58 SACQ patients and 25 controls (13 in remission, 12 in active phase). Clinical data and serum samples were collected during follow-ups. Primary endpoints were flares and new organ damage. Serum protein profiling used Olink PEA with three panels ('Target 96 Inflammation', 'Cardiovascular III', 'Immune Response') measuring 269 proteins. Differentially expressed proteins (DEPs) were identified via generalized linear models, and SACQ subtypes were classified using unsupervised clustering. Associations between proteins and outcomes were analyzed using Cox models and LASSO regression.

Results: SACQ patients and controls were comparable in demographics and past SLE manifestations. Seventy-four proteins showed differential abundance between SACQ and controls. SACQ patients were classified into three distinct endophenotypes, with significant differences in organ involvement and prognosis. Type 1 had higher rates of lupus nephritis (66.7%) and neurological involvement (33.3%), Type 3 had elevated lupus nephritis (47.8%), while Type 2 had fewer major organ involvements. These groups exhibited significant differences in flare rates, with Type 1 showing the highest flare rate (86.7%), severe flares (40.0%) and organ damage accumulation (46.7%). Key proteins distinguishing these subtypes included IL18, PCSK9, TNFRSF14, MILR1, and BTN3A2. IL18 was significantly elevated in Type 1 compared to Type 2 (coef = 6.175, SE = 2.218, p = 0.0054). For Type 3 versus Type 2, PCSK9 (coef = 2.005, SE = 0.899, p = 0.026), TNFRSF14 (coef = 2.521, SE = 0.954, p = 0.008), MILR1 (coef = 1.472, SE = 0.721, p = 0.041), and BTN3A2 (coef = -1.378, SE = 0.611, p = 0.024) showed significant differences. Clinical correlation analysis confirmed these proteins' association with flare and organ damage accrual.

Conclusions: Serum proteome analysis in SACQ identifies distinct subgroups with differing clinical outcomes, offering potential biomarkers for personalized prognosis and targeted therapy in SLE management.

PV041 / #676

Poster Topic: *AS05 - CNS Lupus*

MAGNETIC RESONANCE IMAGING BY DIFFUSION TENSOR IMAGING-MICROSTRUCTURAL THALAMIC CHANGES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Neuroimaging plays a crucial role in identifying neurological abnormalities in patients with Systemic Lupus Erythematosus (SLE), particularly in those with central nervous system involvement. Diffusion Tensor Imaging (DTI) is an advanced magnetic resonance imaging (MRI) technique that maps the brain's microstructure by measuring fractional anisotropy (FA) and mean diffusivity (MD), providing additional insights beyond conventional MRI. DTI is especially useful when conventional MRI does not reveal significant findings, and it aids in both early disease detection and monitoring progression.

Methods: The study involved 58 childhood-onset SLE (cSLE) patients, 68 adult-onset SLE (aSLE) patients, and 60 healthy controls (HC). All participants underwent clinical, neurological, and laboratory evaluations, including disease activity and damage assessments using the SLE Disease Activity Index (SLEDAI) and Systemic Lupus International Collaborating Clinics (SLICC) scales. Mood and anxiety disorders were evaluated using the Beck Inventory, while cognitive function was assessed with the Montreal Cognitive Assessment (MoCA) (table 1). MRI scans were performed using a Philips 3 Tesla scanner, with thalamus segmentation on T1-weighted images using FreeSurfer. Diffusion-weighted images (DWI) were analyzed using the FSL tool, and DTI scalar maps of FA, MD, Axial Diffusivity (AD), and Radial Diffusivity (RD) were generated. Mean and standard deviation values for these parameters were calculated for each thalamic region. A p-value ≤0.05 was considered statistically significant.

Results: No significant difference in thalamic volume was found between cSLE (mean volume 12641.4mm^3, SD=1571.9) and aSLE patients (mean volume 12521.3mm^3, SD=1582.9). However, both groups showed significantly reduced thalamic volumes compared to the HC group (mean volume 13990.8mm^3, SD=1621.8, p<0.001). DTI analysis revealed significant differences in FA, MD, RD, and AD values between the SLE groups and HC. We observed significantly lower FA values between the cSLE and HC groups in the following regions: left intralaminar (p=0.034), right anterolateral (p=0.09), right lateral caudal (p=0.005), right intralaminar (p=0.02) and right posterior (p=0.04). Significantly higher MD values between the cSLE and HC groups in the left anterolateral (p=0.047) and right anterolateral (p<0.001) regions; between the cSLE and aSLE groups

in the right anterolateral region (p=0.02); and between the aSLE and HC groups in the left medial (p=0.038) and left posterior (p=0.05) regions. Significantly higher RD values between the cSLE and HC groups in the left anterolateral (p=0.046), right anterolateral (p<0.001), right caudal lateral (p=0.016), and right medial (p=0.037) regions; between the cSLE and aSLE groups in the right anterolateral region (p=0.03); and between the aSLE and HC groups in the left medial (p=0.039) and left posterior (p=0.01) regions. Significantly higher AD values between the cSLE and HC groups in the left medial region (p=0.047); and between the aSLE and HC groups in the left posterior region (p=0.006).

Table 1. Demographic data, laboratory findings, neuropsychiatric manifestations, and treatment in cSLE, aSLE, and the controls.

Demographic Data	cSLE N=58	aSLE N=68	Controls N=60
Sex- female	52 (89.6%)	61(89.7%)	44 (73.3%)
Current age	20.36 (SD ±4.73)	33.65 (SD ±8.59)	24.73 (SD ±5.11)
Disease duration	7.62 (SD ±4.77)	8.16 (SD ±6.41)	
Clinical Data			
Malar Rash	46 (79.3%)	37 (54.4%)	
Discoid Injury	1 (1,7%)	6 (8.8%)	
Photosensitivity	25 (43.1%)	41 (60.3%)	
Oral injury	22 (37.9%)	11 (16.2%)	
Arthritis	47 (81%)	56 (82.3%)	
Serosite	17 (29.3%)	26 (38.2%)	
Nephritis	43 (74.1%)	11 (16.2%)	
Hematological alteration	40(68.9%)	51 (75%)	
Laboratorial Data			
↓C3	18 (31%)	24 (35.3%)	
ANA	58 (100%)	68 (100%)	
dsDNA	18 (31%)	27 (39.7%)	
Anti-Ro	10 (17.2%)	25 (36.7%)	
Anti-Sm	19 (32.7%)	21 (30.9%)	
Anti-La	1 (1.7%)	8 (11.7%)	
Lupus anticoagulant	12 (20.7%)	15 (22%)	
Anticardiolipin antibodies	21(36.2%)	18 (26.5%)	
NPSLE			
Overt NPSLE manifestations	45 (77.6%)	60 (88.2%)	
Anxiety	22 (37.9%)	37 (54.4%)	
Depression	21 (36.2%)	23 (33.8%)	
Cognitive impairment	31(53.4%)	38 (55.9%)	
Headache	14 (24.1%)	11 (16.2%)	
Convulsion	10 (17.2%)	11 (16.2%)	
Psychosis	4 (6.9%)	2 (2.9%)	
Treatment			
Corticosteroids	49 (84.5%)	56 (82.3%)	
Immunosuppressive	41 (70.7%)	44 (64.7%)	
Antimalarials	41 (70.7%)	41 (60.3%)	

Conclusions: SLE patients exhibit reduced thalamic volume compared to HC, with more pronounced microstructural changes observed in cSLE patients compared to aSLE. These findings suggest that cSLE is associated with greater thalamic involvement and microstructural alterations. Longitudinal studies are needed to determine whether these microstructural changes are transient or permanent.

PV042 / #281

Poster Topic: *AS05 - CNS Lupus*

PSYCHOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Neuropsychiatric (NP) events are a major cause of morbidity in patients with systemic lupus erythematosus (SLE) and are associated with high mortality. The infrequent occurrence of psychosis has limited the number of clinical studies conducted on this condition, leaving the development of SLE with psychosis poorly defined. We aimed to identify clinical and genetic factors associated with psychosis in SLE patients through a genome-wide association study (GWAS) conducted within a prospective lupus cohort.

Methods: This study included 960 Korean patients diagnosed with SLE, all meeting the 1997 American College of Rheumatology (ACR) classification criteria. The neuropsychiatric SLE (NPSLE) was defined using a modified version of the 19 ACR criteria excluding minor neuropsychiatric events. Clinical features were collected annually, and genotyping was performed on all SLE patients. A generalized mixed model within the SAIGE was conducted to assess the association of SLE with psychosis, compared to SLE patients without neuropsychiatric manifestations (non-NPSLE), adjusting for age, sex, and 10 genetic principal components.

Results: Of the cohort, 26 patients (2.71%) exhibited psychosis, with a mean onset-age of 24.5 years, a mean disease duration of 13.5 years, and a predominance of females (96.2%). The SLE patients with psychosis had more clinical manifestations based on the 1997 ACR criteria compared to 934 non-NPSLE patients (7.1 vs. 5.8, $p = 1.21 \times 10^{-5}$), as shown in Table 1. A higher SLICC/ACR Damage Index score was observed in patients with psychosis compared to non-NPSLE patients ($p = 0.03$). We identified nine genetic variants significantly associated with psychosis compared to non-NPSLE at a suggestive significance level ($p < 5 \times 10^{-6}$), with a notable variant on chromosome 19 ($p = 1.13 \times 10^{-6}$) showing eQTL effects in the brain cortex based on the GTEx v8 dataset.

Table 1. Association between clinical manifestations and psychosis in SLE patients[a]

	Non-NPSLE [a]	SLE with psychosis	*P*

	(n = 934)	(n = 26)	
Demographics b			
Female	91.6%	96.2%	0.64
Age (year)	41.4 (±12.4)	38.1 (±9.6)	0.15
Onset-age age (year)	27.0 (±10.4)	24.5 (±8.9)	0.38
Child-onset SLE (<16 year)	13.1%	19.2%	0.53
Disease duration	14.4 (±7.1)	13.5 (±7.2)	0.63
Clinical manifestation c			
Number of ACR criteria d	5.8 (±1.4)	7.1 (±1.7)	**1.21×10-5**
Immunologic disorder	93.1%	92.3%	0.78
Adjusted mean SLEDAI-2K (except NP e)	3.9 (±2.2)	4.8 (±2.3)	0.09
SLICC/ACR Damage Index score (total)	0.7 (±1.1)	1.7 (±2.1)	**4.20×10-5**
SLICC/ACR Damage Index score (except NP)	0.7 (±1.1)	1.1 (±1.5)	**0.03**

[a] Neuropsychiatric (NP) manifestations: a revised version that did not include minor NP event of American Colleague of Rheumatology (ACR) case definitions for 19 NP syndromes. [b] Demographic variables are analyzed by Wilcoxon rank sum test and Chi square test for continuous and categorical variables, respectively. [c] P values are derived from logistic regression analysis adjusting for age and sex. [d] Clinical manifestation based on the 1997 revised American College of Rheumatology (ACR) criteria for SLE [e] SLEDAI-2K NP: seizure, psychosis, organic brain syndrome, cranial nerve disorder, cardiovascular events, lupus headache Mean (±SD) and percentage were used for continuous and categorical variables, respectively.

Conclusions: SLE patients with psychosis exhibited more diverse clinical phenotypes and increased organ damage. Our identification of genetic risk variants provides valuable insights into the pathogenesis of psychosis in SLE.

PV043 / #685

Poster Topic: *AS05 - CNS Lupus*

FACTORS INFLUENCING SUBJECTIVE MENTAL ALTERATIONS: UNRAVELING THE LUPUS BRAIN FOG

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Background/Purpose: Brain fog is a common symptom in systemic lupus erythematosus (SLE) patients that refers to a “clouding of mental functions”. Its prevalence is probably underestimated due to the fact that a universal definition of “lupus fog” does not exist. The aim of the study was to evaluate in a cohort of SLE patients the prevalence of subjective mental alterations, named “lupus fog” (LF) and objective mental alterations (depression, cognition, fatigue) adopting screening tools validated in SLE. The second objective was to investigate which factors are associated with LF.

Methods: A cross-sectional study was conducted enrolling adult SLE patients (ACR/EULAR 2019 criteria). LF referred to the presence of mental alterations (i.e. memory, concentration, attention impairment) as reported by participants. Demographic, clinical, clinimetrics, therapeutic data were collected (Table). Serum anti-ribosomal P antibodies (anti-Rib P) were quantified using ELISA kits. Cognitive deficits were screened using the Montreal Cognitive Assessment (MoCA) test performed by certified personnel (using the standard cut-off of <26/30 and a more sensitive cut off <28/30 [1]) and assessed by a neuropsychologist exploring deficits in 8 cognitive domains with a battery of neuropsychological tests. Depressive symptoms were evaluated using the Center for Epidemiologic Studies Depression Scale (CES-D) and adopting a more sensitive cut off (>15) and the cut off suggested by Kwan et al (>25) [2]. Fatigue was measured using the The Functional Assessment of Chronic Illness Therapy (FACIT-F) (cut off <30 and a more sensitive cut off <34) [3]. Chi-squared and the Mann-Whitney test were used for univariate analysis; multivariate analysis was performed building logistic regression models including variables showing p values of <0.10.

Results: 114 SLE patients were enrolled (Table), 105 female (92.1%), mean age 43.7 years (+-12.2). LF was found in 54/100 patients (54%). CES-D >15 was altered in 56/105 pts (53.3%), CESD >25 in 26 (24.7%), MoCA <26 in 45/100 pts (45%), MoCA <28 in 75 (75%), FACIT <30 in 31/69 (44.9%) and FACIT <34 in 36 (52.9%). At univariate analysis, an association emerged between the presence of LF and CES-D alterations (CES-D >15

p=0.014; CES-D >25 p=0.010, CES-D score p<0.001) , FACIT (FACIT <30 p=0.039, FACIT <34 p=0.042, FACIT score p=0.012), fibromyalgia (p<0.001), the neuropsychiatric involvement (NPSLE) (p=0.015), anti-Ribonucleoprotein RNP (p=0.014), anti Rib-P (p=0.018) and disease duration (p=0.045). No association was found with MoCA test, the battery of neuropsychological test, disease activity scores or treatment. Two different models of logistic regression were built. Model 1 including fibromyalgia, showed independent association between LF and fibromyalgia (OR=34.6; 95%CI 2.3-523.1, p=0.011), CES-D score (OR=1.1 per unit, 95%CI 1.0-1.2, p=0.033) and disease duration (OR=1.1 per year, 95%CI 1.0-1.2, p=0.038). Model 2 excluding fibromyalgia showed independent association between LF and FACIT score (OR=0.93 per unit, 95%CI 0.88-0.99, p=0.013), anti-Rib-P (OR=5.2 per unit, 95%CI 1.0-1.2, p=0.033).

Conclusions: Lupus fog is frequent. Our study also confirms the high prevalence of cognitive impairment, depressive symptoms and fatigue in SLE. A longer disease duration, depressive symptoms and the diagnosis of fibromyalgia were factors independently associated with lupus fog. Our findings suggest that SLE patients frequently have a negative perception about proper cognitive performances, without having a real impairment, supporting the multifactorial etiology of clinical issues in SLE, related to direct and indirect factors. References [1] Raghunath S. Lupus Sci Med. 2021 Dec;8(1):e000580. [2] Kwan A. Semin Arthritis Rheum. 2019 Oct;49(2):260-266. [3] Kawka L. RMD Open 2023;**9**:e003476

Variables	Lupus fog present N=54	Lupus fog absent N=46	P (*<0.05)
Female (%)	52 (96.3%)	40 (86.9%)	
Age, mean (SD)	44.8 (11.6)	43.3 (13.1)	
Education ≤8 years, N (%)	18 (33.9%)	12 (26.7%)	
Disease duration years, median (IQR)	11.7 (6.7-19.9)	7.4 (2.4-14.5)	0.045
Neuropsychiatric Lupus, N (%)	15 (27.8%)	4 (8.7%)	0.015
Dyslipidemia, N (%)	13 (24.6%)	8 (17.4%)	
Hypertension, N (%)	19 (57.6%)	14 (42.4%)	
Smoking, N (%)	11 (20.4%)	8 (17.8%)	
MoCA test <26	24 (47.1%)	20 (47.6%)	
MoCA test mean (DS)	25.3 (2.8)	25 (3.5)	
CES-D altered (>15), N (%)	32 (64.0%)	17 (38.6%)	0.014
CES-D altered (>25), N (%)	17 (34%)	5 (11.4%)	0.010
CES-D, mean (DS)	20.9 (11.5)	12.9 (9.8)	<0.001
FACIT altered (<30), N (%)	17 (54.8%)	9 (29.0%)	0.039
FACIT altered (<34), N (%)	19 (61.3%)	11 (35.5%)	0.042
FACIT, mean (DS)	28.3 (12.4)	36 (10.8)	0.012
Fibromyalgia, N (%)	21 (38.9%)	2 (4.3%)	<0.001
SLEDAI-2K, median (IQR)	2 (0-6)	2 (2-5.75)	
PGA, median (IQR)	0.2 (0-1)	0.2 (0-0.775)	
SLICC-DI, median (IQR)	0 (0-1.75)	0 (0-1)	
LLDAS, N (%)	30 (55.6%)	25 (56.5%)	
Anti-dsDNA, median (IQR)	6.8 (1.8-30.3)	13.9 (2.9-42.1)	0.063
Remission	25 (46.3%)	17 (36.9%)	
C3, median (IQR)	86.8 (20.4)	85.4 (23.4)	
Anti-phospholipids, N (%)	16 (31.4%)	12 (28.6%)	
Anti-RNP	20 (37.7%)	7 (15.6%)	0.014
Anti Rib-P, N (%)	15 (30%)	4 (9.8%)	0.018
PDN dose mg/die, median (IQR)	4.3 (2.5-7.1)	4.5 (2.5-7)	
Hydroxychloroquine, N (%)	41 (51.3%)	39 (48.8%)	
csDMARDs, N (%)	43 (79.6%)	37 (80.4%)	

Legend: MoCA: Montreal Cognitive Assessment test; CES-D: Center for Epidemiologic Studies Depression Scale; FACIT: The Functional Assessment of Chronic Illness Therapy; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index; PGA: Physician lobal Assessment; SLICC-DI: Systemic Lupus International Collaborating Clinics/ Damage Index; LLDAS: Lupus Low Disease Activity State; csDMARDs: conventional synthetic disease

PV044 / #345

Poster Topic: *AS05 - CNS Lupus*

SERUM NEUROFILAMENT LIGHT TO DISTINGUISH AND MONITOR ACTIVITY IN A COHORT OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Neuropsychiatric systemic lupus erythematosus (NPSLE) is a poorly recognized entity leading to diagnostic and therapeutic delays. This is likely due to heterogeneity of manifestations complicating recognition, and the lack of markers that portend neuropsychiatric activity, with conventional serology, neuroimaging studies and CSF analysis often yielding unremarkable results. Serum levels of neurofilament light (NfL), a neuronal cytoskeletal protein, have been associated with other neurological conditions, e.g., multiple sclerosis, suggesting utility as a non-invasive biomarker in neuroinflammatory pathologies. Studies to-date assessing its utility in SLE have been limited by heterogeneously defined study populations of NPSLE. [1. Emerson J. Front Neurol 2023; 14:1111769]. We present serum NfL concentrations in an NPSLE cohort, highlighting the need for more novel modalities for assessment of neuropsychiatric involvement by SLE.

Methods: Subjects: 83 patients (70 female, 13 male) under the Department of Immunology at Blacktown and Westmead Hospitals, Sydney, Australia. All fulfilled the European League Against Rheumatism / American College of Rheumatology (ACR) 2019 Classification Criteria for SLE and were recruited at various treatment time points between 2014-2024 (disease duration 0-41 years). Seven were reassessed at a second time point (range: 0.2-3 years) due to a change in clinical activity or treatment. NPSLE: Classification based on 1999 ACR nomenclature and case definitions for NPSLE and Italian Society of Rheumatology 2015 attribution model for neuropsychiatric manifestations to SLE. [2. Bortoluzzi A. Rheumatology (Oxford) 2015;54(5):891-8]. Classified at onset of neuropsychiatric manifestations, independent of activity during study recruitment. Serum NfL: Performed using Single Molecular Array technology, units expressed as pg/mL. Normal values increase with age, [3. Khalil M. Nat Rev Neurol 2018;14(10):577-89] therefore age-adjusted reference ranges were not utilized, rather comparing mean differences MRI: The following considered abnormal – atrophy, cerebrovascular disease or infarction, multiple high signal changes in white matter, demyelinating lesions, myelitis. Statistical analysis: Mann-Whitney U test. P values less than 0.05 considered significant.

Results: Sixty-five patients with non-NP SLE (ages 18-81 years [mean ± SD: 42 ± 14 years]) and 18 NPSLE (ages 21-60 years [37 ± 13 years]) were included. Six NPSLE

patients had active whereas 12 had inactive neuropsychiatric manifestations. Serum NfL levels trended 2.5 times higher in NPSLE than non-NP SLE cohorts (mean ± standard error of mean: 64.28 ± 25.63 pg/mL versus 24.03 ± 4.543 pg/mL; p = 0.41) (Figure 1). NfL levels trended higher in those with active than inactive NPSLE (103.7 ± 55.18 pg/mL versus 44.58 ± 26.91 pg/mL; p = 0.7) (Figure 2). There was a trend toward a younger age in both NPSLE than non-NP SLE cohorts and active than inactive NPSLE cohorts, suggesting that patient age did not contribute to the measured difference between groups. Abnormal MRIs were seen in 45% of patients with NPSLE and 24% non-NP SLE (p = 0.4). There were no differences in seropositivity for anti-dsDNA nor antiphospholipid antibodies, nor in hypocomplementemia between the NPSLE and non-NP SLE groups. Six patients with NPSLE and 1 with non-NP SLE were followed up, 3 of whom improved with treatment with corresponding reductions in serum NfL concentrations, 2 of whom who had persistent active disease due to inadequate treatment with an increasing serial NfL concentrations, and 1 of who developed new neuropsychiatric involvement with a corresponding rise in serum NfL concentration.

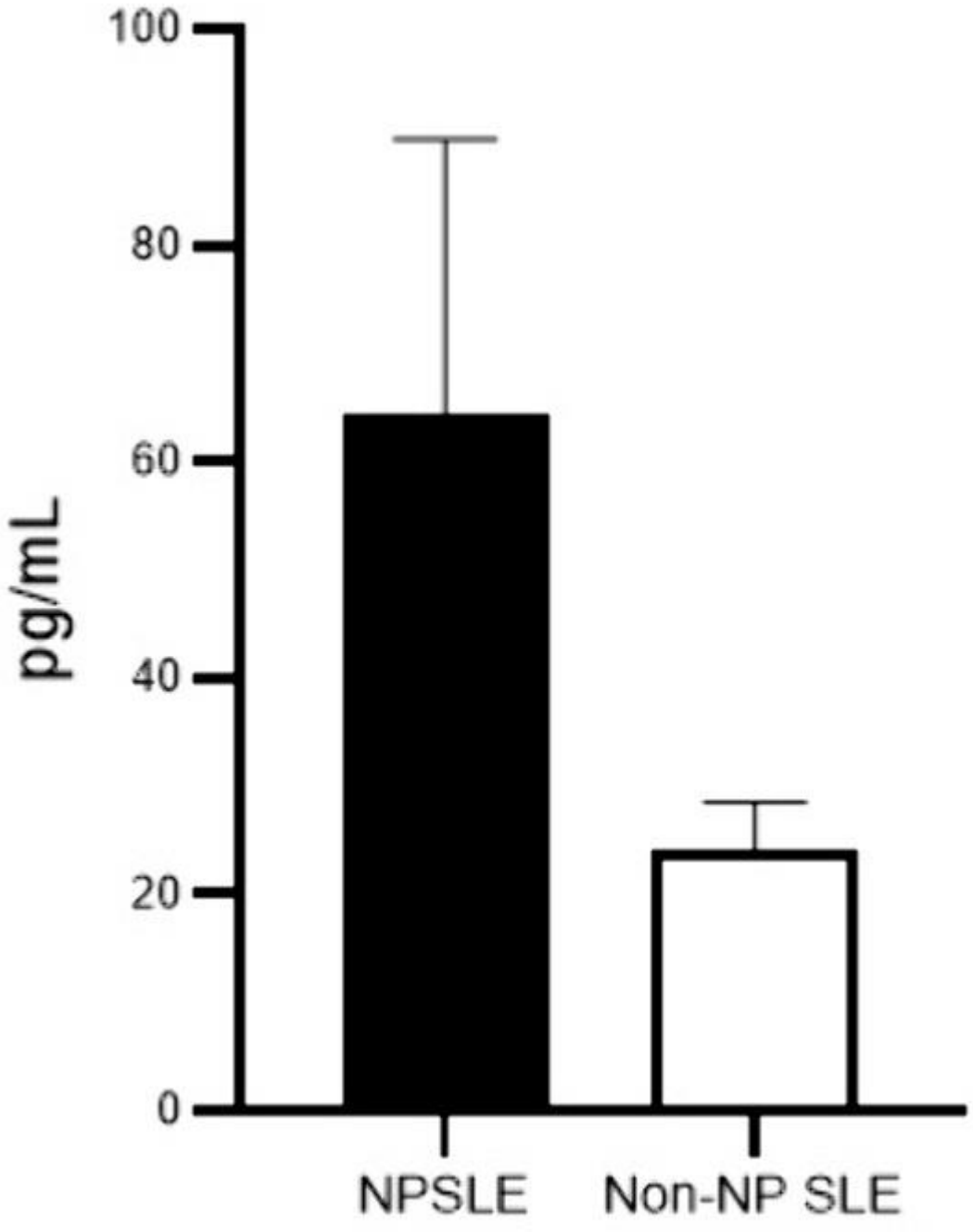

Figure 1. Serum NfL levels in NPSLE and non-NP SLE (mean & SEM pg/mL).

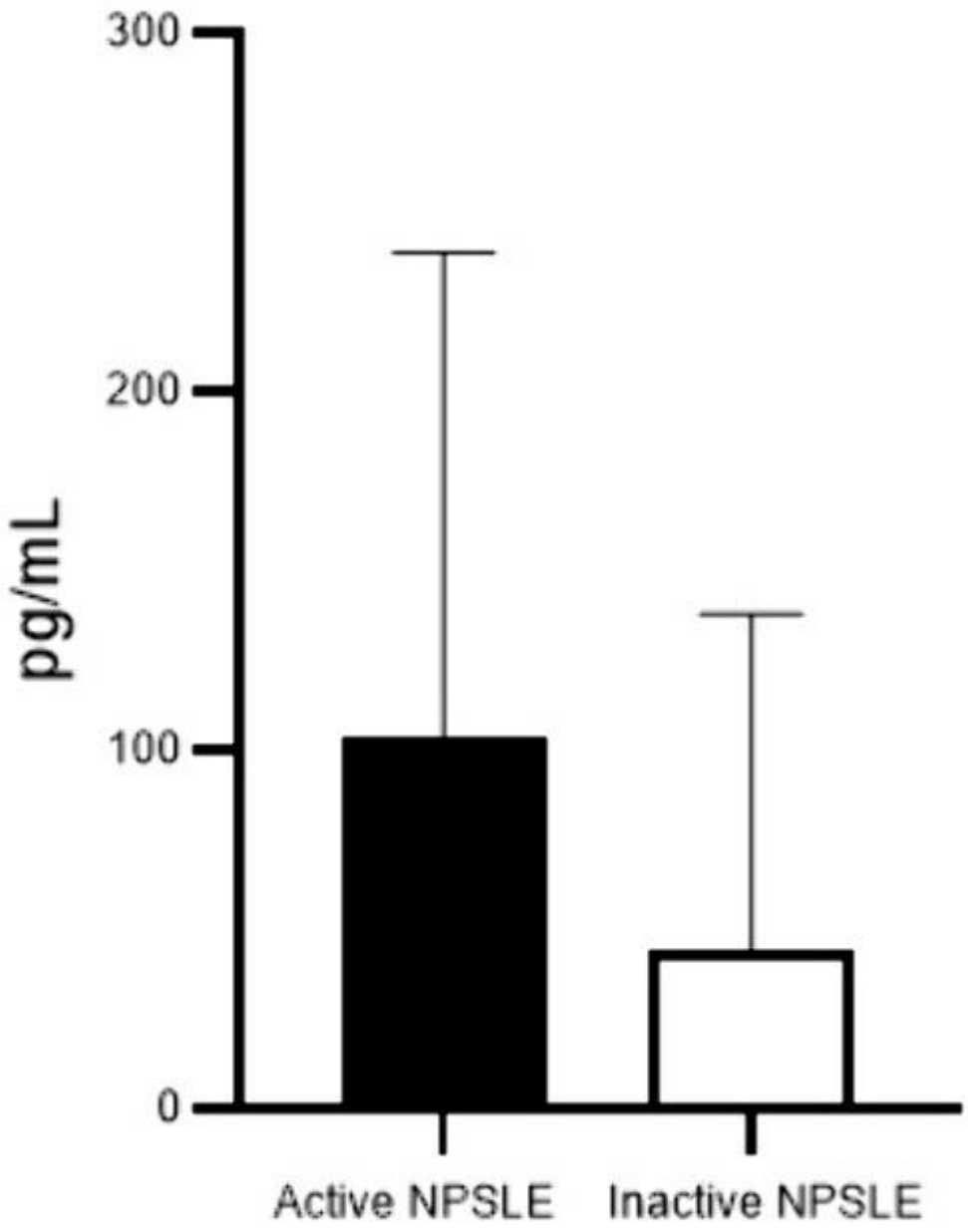

Figure 2. Serum NfL levels in NPSLE patients with active neuropsychiatric manifestations and those with inactive neuropsychiatric manifestations (mean & SEM pg/mL).

Conclusions: Serum NfL levels may be a useful method for diagnosing, monitoring and prognosticating patients with NPSLE.

PV045 / #321

Poster Topic: *AS05 - CNS Lupus*

CLINICAL, LABORATORY CHARACTERISTICS AND OUTCOMES OF NEUROPSYCHIATRIC LUPUS ATTENDED IN LUPUS CLINICS: A PROSPECTIVE STUDY

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Background/Purpose: About half of SLE patients have neuropsychiatric symptoms at some point, although it's rare as an initial presentation. Early diagnosis and treatment may lead to early remission and lower mortality. Present study aims to describe clinical and laboratory characteristics and outcomes of neuropsychiatric lupus

Methods: This is a prospective study ongoing at the lupus clinics of the National Institute of Neurosciences and Hospital and Popular Medical College Hospital in Dhaka. The study included all cases of SLE presenting with neuropsychiatric symptoms as per the ACR/EULAR nomenclature of CNS lupus and the 2019 classification criteria for SLE. The SLE DAI 2K scoring system was used to determine the disease activity. Standard treatments were administered, and patients are regularly following up in the respective sites. Outcomes are assessed in terms of remission, treatment failure, and death.

Results: In this study, a total of 32 patients were enrolled with a mean age of 24 and a male-female ratio of 1:8. The most common presentations were migrainous headache 19 (60%), convulsion 12 (38%), hemiparesis 5 (20%), and psychosis 5 (20%). The most prevalent neuroimaging characteristics of the brain were micro-hemorrhages 8 (38%), hemorrhagic infarct 7 (28%), and ischemic infarct 5 (20%). Additionally, the MR angiogram (MRA) of the cerebral artery revealed a beaded appearance in the middle cerebral artery (MCA) or its branches 9 (36%). MR venogram showed a filling defect, narrowing, and irregularity of the superior sagittal and transverse sinuses 5 (20%). Upon admission, the mean SLE DAI was 24 (± 9). After receiving standard treatment, complete remission occurred in 24 (72%) and partial remission in 7 (28%), with a median SLE DAI of 2 [1-4.5] at a minimum follow up of 120 days. However, one patient expired while on treatment.

Conclusions: Migrainous headaches, convulsions, stroke, and psychosis are important neuropsychiatric manifestations of SLE. MRA helps to confirm vasculitis. Patients generally have a satisfactory outcome with standard treatment at 4 months.

PV046 / #490

Poster Topic: *AS05 - CNS Lupus*

CHARACTERISTICS OF LUPUS PATIENTS WITH PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)-LITERATURE REVIEW

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Background/Purpose: Progressive multifocal leukocencephalopathy (PML) is a potentially fatal degenerative condition caused by reactivation of the human polyomavirus 2 (John Cunningham-JC virus) in immunodeficient individuals. It has been observed in patients receiving Rituximab, but those treated with other immunosuppressants, such as systemic lupus erythematosus (SLE) patients, may be at risk as well.

Methods: A review of various online databases was conducted, with publications ranging from 1986 to 2024. 14 cases were selected for further analysis.

Results: Sex-12 female and 2 male; **age**-youngest 28 years, oldest 83 years
Initial SLE treatment: glucocorticoids (Prednisone, Prednisolone, iv Methylprednisolone)-all 14 patients; chloroquin/hydroxychloroquin (HCQ)-4/14; Mycophenolate mofetil (MMF)-6/14; Azathioprin (AZA)-5/14; iv Cyclophosphamide (CYC)-1/14; 6-mercaptopurin-1/14; Cyclosporin-2/14; Belimumab-2/14; anti interleukin 2 agent-1/14; Synachten-1/14; Dapsone-1/14; Plasmapheresis-1/14
Neurological symptoms: muscle weakness-5/14; hemiparesis-3/14; dysarthria-5/14; apraxia-3/14; gait disturbance-5/14; visual disturbances-4/14; cognitive disfunction-7/14; sensitive disfunction (anesthesia, hypoesthesia)-6/14; migraines-2/14
Comorbidities: lupus nephritis-2/14
Patients with SLE relapses: 4/14
Definitive diagnosis of PML-JC virus identification: cerebrospinal fluid (CSF)-6/14; brain biopsy-5/14; both-1/14; autopsy-2/14
PML management: stop all immunosuppresion-10/14; high dose iv Methylprednisolone-4/14; high dose iv Methylprednisolone+plasmapheresis-1/14; iv CYC-3/14; corticosteroids+AZA-1/14; immunoglobulins-1/14; Mefloquin-2/14; Cidofovir-2/14; Interferon alpha-1/14; Levetiracetam-1/14; Mirtazapine-2/14; Citarabine-1/14; no treatment (advanced age)-2/14
Outcome: recovered with minimal deficits-3/14; recovered with sequelae-3/14; death-6/14; lost from monitoring-2/14

Conclusions: There was correlation found between initial immunosupression with MMF and subsequent stopping and better outcomes, as well as worse outcomes in patients that initially received AZA and those that afterwards received a combination of steroids

and AZA or CYC. There was no correlation found between age and outcome. Although rare, PML must be taken into consideration in SLE patients presenting with neurological symptoms that don't respond to conventional treatment.

PV047 / #805

Poster Topic: *AS05 - CNS Lupus*
Late-Breaking Abstract

SOLUBLE ENDOGLIN LEVELS AS A MARKER OF CEREBROVASCULAR DISORDERS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Cerebrovascular manifestations in patients with systemic lupus erythematosus (SLE) are quite frequent and diverse. Their prevalence ranges from 12% to 95%. Recently, the attention of scientists has been drawn to the biomolecule endoglin (ENG) associated with the pathogenesis of certain neurological and autoimmune diseases. The role of soluble endoglin (sol-endoglin) as an antiangiogenic agent has been studied in various diseases. However, no information has been found on the levels of sol-endoglin in the serum of SLE patients. Our goal is to study the level of sol-endoglin in SLE patients and assess its relationship with lesions of the central and peripheral nervous system, as well as some indicators of mental health.

Methods: 96 SLE patients aged 19 to 55 years were examined, 7 (7.3%) men and 89 (92.7%) women, mean disease duration was 6.2±0.4 years, mean age was 37.5±0.9 years and 20 people in the control group with a mean age of 39.0±1.09. To assess the neurological status, the following were used: Zung Depression Scale, Spielberger Anxiety Scale, Montreal Cognitive Assessment Scale (MCA), visual and auditory memory tests. The content of endoglin in blood serum was determined by ELISA.

Results: In SLE patients, the level of endoglin was significantly higher by 90.4% ($p<0.001$) compared to the control group. Thus, in the control group, the level of endoglin fluctuated in the range of 1.14-2.56 ng/ml (95% CI) with a median of 1.86 ng/ml, and in SLE patients the level of endoglin fluctuated in the range of 1.58-6.53 (95% CI) with a median of 3.28 ng/ml. In order to assess the relationship between endoglin levels and the characteristics of the patient's psychoneurological condition, all SLE patients were divided into 4 subgroups depending on the level of endoglin: the 1st quartile (Q1) included 24 individuals with an endoglin level <2.55 ng/ml; 2nd quartile (Q2) – 25 people with endoglin levels of 2.55-3.28 ng/ml; 3rd quartile (Q3) – 23 people with levels of 3.29 – 4.24 ng/ml; 4th quartile (Q4) – 24 people with levels of >4.24 ng/ml. From the 1st to the 4th quartile, an increase in the proportion of patients with nervous system damage was observed. In group Q4, the proportion of people with CNS damage was significantly higher by 3.28 times ($p<0.05$) than in group Q1. The proportion of patients with peripheral nervous system damage in Q3 and Q4 exceeded 50% and was higher by 2.99-3.38 times ($p<0.05$) than among patients with endoglin levels less than

2.55 ng/ml. Analysis of mental health indicators of SLE patients depending on the quartile distribution of endoglin levels showed that almost all of the studied mental health indicators of patients significantly worsened from the 1st to the 4th quartile. Thus, in the Q4 group, the proportion of patients with verified anxiety, depressive disorders, and cognitive dysfunction was statistically significantly higher by 2.4; 5.52 and 2.74 times ($p<0.05$) than in the Q1 group. A high frequency of memory disorders and sleep disorders was recorded in all quartile groups (without statistically significant intergroup differences).

Conclusions: Thus, serum endoglin levels in SLE patients with SLE are significantly higher than in the control group. Increased serum endoglin levels were associated with worsening mental health indicators in SLE patients, and namely a significant increase in the proportion of individuals with significant anxiety, depressive, and cognitive disorders, as well as insomnia.

PV048 / #473

Poster Topic: *AS05 - CNS Lupus*

CLINICAL FEATURES AND OUTCOMES OF SEIZURE DISORDERS IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHMATOSUS IN CHINA

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Background/Purpose: Patients with Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) experience impaired quality of life, while the underlying causes remain unknown. Seizure, one of the common subtypes of NPSLE, is predictive of poor prognosis for SLE. In this study, we evaluated clinical features and the risk factors with prognostic outcome in a large dataset of NPSLE with seizure in China.

Methods: NPSLE inpatients and outpatients with seizure (after diagnosed of SLE, or before but within 6 months) treated mainly at Peking Union Medical College Hospital and other multiple institutions around China between July 2011 and June 2024 were considered. SLE was diagnosed when the SLE classification criteria recommended by the American College of Rheumatology (ACR) in 1997 or those of the Systemic Lupus International Collaborating Clinics (SLICC) in 2012 and the diagnostic criteria for NPSLE in SLE proposed by the ACR in 1999 were fulfilled. Clinical data and laboratory examination results were retrospectively collected. The SLE disease activity index (SLEDAI) was used to evaluate lupus activity. SLEDAI ≥ 15 points indicates severe SLE activity. SPSS 27.0 software and GraphPad Prism 10.2.0 were used for statistical analyses.

Results: Data were collected from a total of 632 NPSLE patients with seizures; of these, 556 (88.0%) were female, with an average age of 34.1 years (range, 9-73). The median duration of SLE was 3.0 years (range, 0-42), and the median duration of NP was 2 months (range, 0-150). Among all patients, 301 (47.6%) had central nervous system (CNS) involvement aside from seizures, 20 (3.2%) had peripheral nervous system (PNS) involvement, and 13 (2.1%) had both. The most common NP subtypes were acute confusional state (ACS), cognitive impairment, cerebrovascular disease, headache, and psychosis. [Table 1]

Table1. Baseline characteristics of NPSLE patients with seizure.

Characteristics	Value (n = 632)
Female (%)	556 (88.0)
Age (years)	34.1 (9, 73)
SLE duration (years)	5.6 (0, 42)
NP duration (years)	2.8 (0, 12)
Other Subtypes of NPSLE (%)	
Central nervous system involvement	301 (47.6)
Acute confusional state	142 (22.5)
Cerebrovascular disease	86 (13.6)
Headache	85 (13.5)
Psychosis	50 (7.9)
Cognitive impairment	93 (14.7)
Mood disorder	28 (4.4)
Demyelination	7 (1.1)
Dyskinesia	19 (3.0)
Myelitis	5 (0.8)
Aseptic meningitis	15 (2.4)
Anxiety disorder	26 (4.1)
Peripheral nervous system involvement	20 (3.2)
Cranial neuropathy	15 (2.4)
AIDP	1 (0.2)
Single/multiplex mononeuropathy	6 (0.9)
Polyneuropathy	5 (0.8)

NPSLE: neuropsychiatric systemic lupus erythematosus; AIDP: acute inflammatory demyelinating polyradiculoneuropathy.

In the prognostic analysis, 23 patients (3.6%) died, of whom 20 (87.0%) were women, and 17 (73.9%) were older than 25 years. Comparing the deceased and surviving groups, there were significant differences in the prevalence of serositis ($p = 0.003$), respiratory involvement ($p = 0.002$), cardiac involvement ($p = 0.003$), renal involvement ($p = 0.013$), proteinuria ($p = 0.025$), elevated serum creatinine (Scr) ($p < 0.001$), and SLEDAI score ≥ 15 ($p = 0.021$). These findings indicate that these factors are associated with a poor prognosis. [Table 2]

Table 2. Prognostic analysis of clinical characteristics of NPSLE patients with seizure.

Risk factors	Dead group (N = 23), n (%)	Survival group (N = 609), n (%)	χ2	P value
Female	20 (87.0)	536 (88.0)	0.000	1.000
Age older than 25 years	17 (73.9)	449 (73.7))	0.000	0.984
Acute confusional state	6 (26.1)	136 (22.3)	0.179	0.672
Cerebrovascular disease	6 (26.1)	80 (13.1)	2.156	0.142
Psychosis	3 (13.0)	47 (7.7)	0.287	0.592
Rash	14 (60.9)	303 (49.8)	1.095	0.295
Oral ulcer	3 (13.0)	128 (21)	0.441	0.507
Vasculitis	4 (17.4)	46 (7.6)	1.749	0.186
Arthritis	10 (43.5)	236 (38.8)	0.208	0.648
Serositis	15 (65.2)	215 (35.3)	8.567	**0.003**
Respiratory involvement	8 (34.8)	68 (11.2)	9.559	**0.002**
Cardiac involvement	11 (47.8)	120 (19.7)	9.024	**0.003**
Renal involvement	19 (82.6)	344 (56.5)	6.186	**0.013**
Proteinuria	12 (52.2)	184 (30.2)	4.996	**0.025**
Elevated serum creatinine	8 (34.8)	63 (10.3)	10.935	**<0.001**
Hematological involvement	17 (73.9)	456 (74.9)	0.011	0.917
Hypocomplementemia	19 (82.6)	519 (85.2)	0.002	0.962
Anti-dsDNA positive	16 (69.6)	422 (69.3)	0.001	0.978
Anti-Sm positive	13 (56.5)	251 (41.2)	2.135	0.144
Anti-RNP positive	8 (34.8)	210 (34.5)	0.001	0.976
Anti-SSA positive	13 (56.5)	312 (51.2)	0.248	0.618
Anti-SSB positive	5 (21.7)	108 (17.7)	0.046	0.830
Anti-ribosomal positive	1 (4.3)	130 (21.3)	2.932	0.087
Anticardiolipin positive	7 (30.4)	136 (22.3)	0.831	0.362
Anti-β2 glycoprotein 1 positive	3 (13.0)	130 (21.3)	0.488	0.485
Lupus anticoagulant positive	2 (8.7)	133 (21.8)	1.564	0.211
SLEDAI ≥ 15	12 (52.2)	180 (29.6)	5.360	**0.021**
Elevated ESR	10 (43.5)	182 (29.9)	1.936	0.164
Elevated CRP	5 (21.7)	89 (14.6)	0.415	0.519

NPSLE: neuropsychiatric systemic lupus erythematosus; dsDNA: double-stranded deoxyribonucleic acid; RNP: ribonucleoprotein; Sm: Smith; SSA: Sjogren's syndrome antigen A; SSB: Sjogren's syndrome antigen B; SLEDAI: systemic lupus erythematosus disease activity index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein. Significant P values are shown in bold typeface.

Conclusions: NPSLE patients with seizures, combined with serositis, respiratory, cardiac, or renal involvement, proteinuria, elevated serum creatinine, or high disease activity, may have a poorer prognosis.

PV048a / #612

Poster Topic: *AS05 - CNS Lupus*

VOLUME AND DYNAMIC BLOOD FLOW OF THE CHOROID PLEXUS IN NEUROINFLAMMATORY DISEASE

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Background/Purpose: Systemic lupus erythematosus (SLE) and multiple sclerosis (MS) are autoimmune neuroinflammatory diseases that lead to cerebrovascular alterations. Compromise of cerebral microvasculature is a plausible route by which immune actors infiltrate the brain parenchyma, resulting in damage. The blood-brain-barrier (BBB), comprised of the brain capillary endothelial cell layer with tight junctions, is the most studied regulator of blood-parenchyma exchange. We have demonstrated regionally increased permeability of the BBB in SLE compared to healthy controls[1]. A recent murine study of SLE found CSF immune infiltrates in CSF even with the BBB intact, suggesting alternative mechanisms of brain tissue infiltration at interfaces between blood and CSF[2]. The Blood-CSF barriers (BCSFB) are in the choroid plexus (CP) within ventricles and at the meningeal barrier that surrounds the brain. In the CP, fenestrated capillaries exchange with a stromal layer at the basal side of an epithelium thereby regulating exchange with ventricular CSF. Once an infiltrate enters the ventricules, it can exchange with parenchyma through the ependymal layer at the ventricular surface. Imaging studies provide evidence for a BCSFB route to MS pathology by observation of periventricular gradients of tissue abnormalities. Our ongoing study is investigating alteration of the BCSFB at the CP in SLE and MS including changes in volume, blood flow, and periventricular gradients in properties of normal-appearing white matter. We report preliminary findings for volume and dynamic blood flow of the CP in SLE and MS patients vs. healthy controls.

Methods: Preliminary analysis includes 5 SLE (4F, 15.8(2.9)yrs), 5 MS (5F, 18.6(3.2)yrs), and 15 healthy controls (HC, 8F, 21.7(3.1)yrs) who completed MRI to assess CP volume (3D T1-weighted) and perfusion dynamics (pseudocontinuous arterial spin labeling at 15 label+delay times from 900 to 4000ms). The protocol also included diffusion, relaxometry, and quantitative susceptibility imaging to assess periventricular white matter. ASCHOPLEX[3] was used to segment the CP and determine volume on the T1-weighted images. Dynamic perfusion signal was fitted to a model to determine arrival time and blood flow at the CP. Pairwise group comparisons of volume, arrival time, and

blood flow were expressed as effect size (Cohen's d) with statistically significant results reported at $p<0.05$.

Results: Total CP volume was found to be significantly lower for MS compared to either HC ($p=0.012$) or SLE ($p=0.032$) groups (Figure 1). HC and SLE CP volumes were similar (effect size $d < 0.2$). Among all three groups, arrival time was not found to differ pairwise with remarkable effect size ($d < 0.2$). Pairwise blood flow differences did not reach statistical significance at $p<0.05$, but did attain robust effect sizes (Figure 2). CP blood flow was greater in both MS and SLE groups compared to HC with effect sizes of $d=0.84$ and 1.11, respectively. SLE blood flow exceeded MS with a moderate effect size of $d=0.33$.

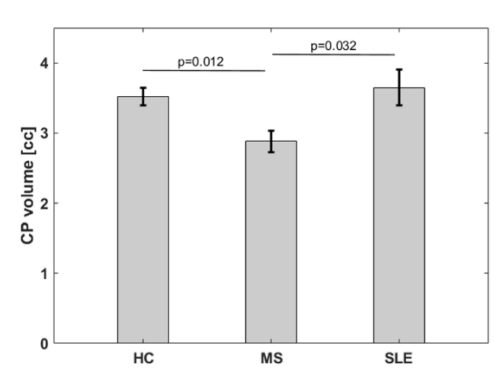

Figure 1: CP volume comparisons. Error bars reflect standard error.

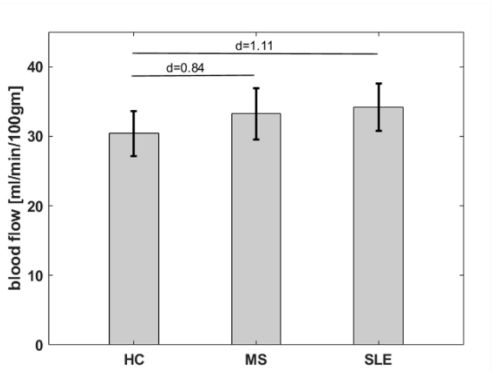

Figure 2: CP blood flow comparisons. Error bars reflect standard error.

Conclusions

Volumetric and blood flow changes in the CP were observed in neuroinflammatory disease compared to controls. Interestingly, reduced CP volume was evident in MS but not SLE, suggesting pathophysiological differences. Increased blood flow to the CP in SLE and MS was unexpected assuming vascular compromise but might be explained as compensatory blood flow increases associated with some inflammatory processes. If evidence for a CP route of brain infiltration is found with collection of more data, it could realign ways to phenotype SLE and MS and develop targeted therapies.

PV049 / #291

Poster Topic: ***AS06 - Comorbidities***

ASSESSMENT OF ATHEROSCLEROSIS RISK IN LUPUS: A COMPARISION OF CLINICAL ALGORITHMS AND CAROTID ULTRASOUND

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Background/Purpose: Systemic Lupus Erythematosus (SLE) patients have twice the incidence of cardiovascular diseases (CVD) than the general population. Traditional factors (obesity, smoking, dyslipidemia) do not fully explain the accelerated rate of atherosclerosis and cardiovascular disease in patients with SLE. Carotid Ultrasound (CU) is a surrogate marker for atherosclerotic CVD.

Methods: We included consecutive SLE patients with 18 years or older. Calculation of several algorithms to assess cardiovascular risk (Fragminham, SCORE, QRISK3, mSCORE and mFragminham) and CU with with measurement of carotid intima media thickening (CIMT) and evaluation of presence of plaques. In addition disease related variables and traditional CV risk factors were reviewed. Statistic was done according to nature of the variables, p values <0.05 were considered statistically significant, after adjusting fr multiple comparisons. Considering plaque seen on ultrasound as a gold standard, sensibility/specificity of each clinical score was calculated.

Results: We included 159 SLE patients [median age 51.1years; 149 (93.7%) women]. Thirty-two (20.1%) patients presented atherosclerotic plaques on CU and altered CIMT was observed in 141 (88%) patients. All of the clinical scores and traditional CV risk factors had statistical significance in patients with plaques (Table 1). Traditional and disease-linked factors were associated with clinical scores positivity (Table 2). When using the presence of plaques as gold standard of atherosclerosis, SCORE and Mscore had the highest sensitivity, however all clinical scores had a poor accuracy, ranging of 17.7-31.2 (Table 3).

Table 1. Statistical significance of Clinical and algorithms variables in patients with established plaques

Variables	
ESC	<0.001
Fragminham	0.001
QRISK3	0.009

Mscore	0;009
Mfragminham	0.001
Age	0.001
Hypertension	0.03
Total Cholesterol	0.009
Stroke	0.03
Myocardial Infarction	0.01

Table 2. Relevant clinical traits associated with each score (p <0,05)

Score	Fragminham	Qrisk3	mScoree	mFragminham
Current Age	Current Age	Current Age	Current Age	Current Age
Hypertension	Hypertension	Hypertension	Hypertension	Hypertension
Dyslipidemia	Dyslipidemia	Dyslipidemia	Dyslipidemia	Dyslipidemia
Stroke		Stroke		
Myocardial Infarction		Myocardial Infarction		
	Diabetes	Diabetes	Diabetes	Diabetes
	HOMA IR	HOMA IR	HOMA IR	HOMA IR
Use of Hydroxicloroquine		Use of Hydroxicloroquine	Use of Hydroxicloroquine	Use of Hydroxicloroquine
	Lupus Nephritis			
	C Reative Protein	C Reative Protein		C Reative Protein
		Disease duration	Disease duration	Disease duration

			Duration of use of Hydroxicloroquine	
		Hemossedimentation Rate		
		Duration of use of Corticoidsteroids		
Cumulative dose of Corticoesteroids		Cumulative dose of Corticoesteroids	Cumulative dose of Corticoesteroids	Cumulative dose of Corticoesteroids
SLICC			SLICC	SLICC

Table 3. Characteristics of each clinical score

Test	Sensitivity	Specificity	Accuracy	LR+	LR-
Score	0.87	0.54	28.4	1.91	0.23
Fragminham	0.53	0.88	17.7	4.49	0.53
Qrisk3	0.68	0.71	22.5	2.42	0.43
*mSCORE	0.96	0.36	31.2	0.33	0.08
mFragminham	0.8	0.36	20.3	1.3	0.52

* Most accurate test

Conclusions: Clinical scores failed to predict the presence of carotid atherosclerotic disease as seen on ultrasound. Mscore is the most accurate clinical score in this study. Longitudinal studies are needed to show the interaction between traditional and disease linked factors.

PV050 / #831

Poster Topic: *AS06 – Comorbidities*
Late-Breaking Abstract

RELATIONSHIP BETWEEN COPING STRATEGIES AND DISEASE ACTIVITY, SEVERITY, AND TOTAL DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Previous studies have reported a higher prevalence of stress, anxiety, and depression in individuals with Systemic Lupus Erythematosus (SLE). However, no literature establishes a relationship between coping strategies and disease activity, severity, and cumulative damage in SLE.

Methods: Adult patients diagnosed with SLE were recruited during routine appointments and completed validated Portuguese translations of the BRIEF-COPE scale (assessing coping strategies for stressful events), the Perceived Stress Scale (PSS-10), the Hospital Anxiety and Depression Scale (HADS), and the Short-form Health Survey (SF-36v2). Clinical and laboratory disease features, as well as prior anxiety or depression diagnoses, were obtained from electronic medical records. Flares were defined according to the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) for the year preceding recruitment. Disease severity was assessed using the Lupus Severity Index (LSI): being 0 no severity and 10 the higher severity possible. Damage accrual was evaluated by the SLICC Damage Index (SDI).

Results: A total of 27 adults diagnosed with SLE were recruited. All participants met the ACR classification criteria, were in active follow up, and had a mean LSI of 6.71 ± 1.69. Five (18.5%) experienced a flare in the previous year, and 10 (37.5%) presented cumulative damage. Analysis of global indicators from the BRIEF-COPE scale revealed that participants scored at the general population average for both problem-focused coping strategies and emotion-focused strategies, and below average for avoidance strategies. Their quality of life was lower than the general population average, both physically and mentally. Most participants with damage accrual exhibited adaptive coping strategies, particularly problem-focused (62.5% ± 16.03) and emotion-focused (63.5% ± 20.04) approaches. Among participants without a flare in the previous year,

35% engaged in avoidance strategies versus 19% of those who experienced a flare. Avoidance coping was inversely related to overall severity of SLE by LSI.

Conclusions: This is the first study using the BRIEF-COPE scale in adults with SLE to examine the relationship between coping strategies, disease activity, overall severity, and cumulative damage. Individuals living with SLE appear to exhibit above-average adaptive coping strategies, particularly those with damage accrual. Furthermore, our findings suggest that higher disease severity is associated with a lower adoption of maladaptive coping strategies.

PV051 / #529

Poster Topic: *AS06 - Comorbidities*

ANALYSIS OF PULMONARY COMPLICATIONS IN SLE PATIENTS WITH AND WITHOUT COVID-19: A NATIONAL INPATIENT STUDY

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Background/Purpose: While respiratory failure in Systemic Lupus Erythematosus (SLE) patients
with Coronavirus Disease 2019 (COVID-19) is well-documented, the spectrum of acute pulmonary complications compared to SLE patients without COVID-19 remains incompletely characterized. We aimed to analyze rates and predictors of acute pulmonary complications between these groups.

Methods: Using the 2021 National Inpatient Sample, we identified adult SLE patients (n=170,085) and stratified by COVID-19 status. Primary outcomes included pulmonary embolism (PE) and mechanical ventilation. We employed survey-weighted logistic regression to calculate adjusted odds ratios (aOR) comparing SLE patients with versus without COVID-19.

Results: Of 170,085 hospitalized SLE patients, 12,710 (7.47%) had COVID-19 and 157,375 (92.53%) did not. PE rates were higher in SLE patients with COVID-19 versus those without (9.52% vs 8.64%, p = 0.0013). After adjustment, COVID-19 remained associated with increased PE risk (aOR 1.12, 95% CI 0.97-1.30, p = 0.126). Mechanical ventilation rates were substantially higher in the COVID-19 group (11.25% vs 2.76%, p < 0.001), with an aOR of 4.87 (95% CI 4.22-5.62, p < 0.001). Within the COVID-19 group, risk factors for PE included African American versus Caucasian race (29.50% vs 48.03%, aOR 1.37, 95% CI 1.24-1.51, p < 0.001), obesity (31.94% vs 22.23%, aOR 1.32, 95% CI 1.09-1.51, p = 0.015), and severe comorbidity burden (41.03% vs 9.87%, aOR 4.20, 95% CI 3.51-5.03, p < 0.001). Among SLE patients with COVID-19 who developed PE, intensive care admission rates were higher (42.8% vs 28.3%, p < 0.001),
and hospital length of stay was longer (11.2 vs 8.1 days, p < 0.001) compared to those without PE.

Conclusions: This analysis demonstrates significantly higher rates of acute pulmonary complications in SLE patients with COVID-19 compared to those without, particularly regarding mechanical ventilation needs. The increased PE risk in COVID-19 patients,

especially in certain demographic groups, suggests the need for enhanced thromboprophylaxis protocols in this population.

PV052 / #534

Poster Topic: *AS06 - Comorbidities*

PREDICTORS OF MECHANICAL VENTILATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH CORONAVIRUS DISEASE 2019: INSIGHTS FROM NATIONAL INPATIENT DATA

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Background/Purpose: Mechanical ventilation represents a critical outcome in Systemic Lupus Erythematosus (SLE) patients with Coronavirus Disease 2019 (COVID-19). We aimed to identify specific risk factors and predictors of mechanical ventilation in
this population using nationally representative data.

Methods: Analyzing the 2021 National Inpatient Sample, we identified adult SLE patients with COVID-19 (ICD-10 code M32). The primary outcome was mechanical ventilation. Using survey-weighted logistic regression, we calculated adjusted odds ratios (aOR) for ventilation risk, controlling for demographics, comorbidities, and clinical
factors.

Results: Among 170,085 SLE patients, 12,710 (7.47%) had COVID-19. The mechanical ventilation rate was significantly higher in COVID-19 patients versus non-COVID-19 (11.25% vs 2.76%, p < 0.001). After adjustment, COVID-19 remained strongly associated with ventilation risk (aOR 4.87, 95% CI 4.22-5.62, p < 0.001). Demographic analysis revealed higher ventilation rates in males versus females (11.76% vs 8.82%, aOR 1.06, 95% CI 0.79-1.12, p = 0.472) and African American versus Caucasian patients (13.3% vs 9.8%, aOR 1.17, 95% CI 1.00-1.37, p = 0.038). Comorbidity burden strongly predicted ventilation need: severe versus mild Elixhauser index (41.03% vs 9.87%, aOR 11.80, 95% CI 8.06-17.29, p < 0.001). Notable comorbidity associations included obesity (31.94% vs 22.23%, aOR 1.21, 95% CI 1.10-1.37, p < 0.001), diabetes (30.02% vs 23.54%, aOR 1.18, 95% CI 1.09-1.28, p < 0.001),
and hypertension (34.70% vs 30.56%, aOR 0.60, 95% CI 0.51-0.70, p < 0.001). Acute complications significantly associated with ventilation included acute kidney injury (29.31% vs 21.38%, aOR 2.47, 95% CI 2.31-2.65, p < 0.001) and cardiac arrest (2.64% vs 0.92%, aOR 2.98, 95% CI 2.28-3.90, p < 0.001).

Conclusions: This analysis identifies key predictors of mechanical ventilation in SLE patients with COVID-19, highlighting the complex interplay between demographics, comorbidities, and acute complications. The nearly five-fold increased risk of ventilation
in COVID-19 patients, along with identified risk factors, can inform clinical decision-making and resource allocation for this high-risk population.

PV053 / #179

Poster Topic: *AS06 - Comorbidities*

DELAYED SLEEP PHASE SYNDROME CHARACTERIZES CIRCADIAN DISORDER IN PATIENTS WITH ACTIVE SLE

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Background/Purpose: Poor sleep quality is a common complaint of patients with SLE. Although chronic sleep disruption is known to drive circadian rhythm disorders, the effects of poor sleep quality have not yet been elucidated in SLE. Actigraphy is a validated approach to objectively assess 21 sleep variables and motor activity using a noninvasive accelerometer. In addition, actigraphy can characterize circadian dysfunction by assessments of activity. We examine the relationship of actigraphy data from patients with SLE with 1) disease activity and 2) subjective patient-reported outcome measures of sleep quality.

Methods: Seventy-six consented subjects from the Washington University Lupus Center with classified SLE were enrolled. Participants wore a wrist-mounted actigraph (Micro Motionlogger, Ambulatory Monitoring Inc, Ardsley, NY) for one week. Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Patient Reported Outcomes Measurement Instrument System (PROMIS)-Sleep Related Impairment (SRI), and PROMIS-Sleep Disturbance (SD) survey instruments were administered to measure subjective sleep quality. SLEDAI-2000 Responder Index-50 (S2K RI-50) assessed disease activity (>4, active SLE). Actigraphy data were analyzed using Action W (Ambulatory Monitoring Inc), and circadian variables were derived using ClockLab (Actimetrics, Wilmette, IL). Unpaired Student *t* tests (two-sided, $\alpha < 0.05$) were used to compare sleep quality and circadian dysfunction in patients with active versus inactive disease. Pearson correlation coefficient was used to assess correlation of actigraphy and circadian variables with subjective sleep quality. Statistical analyses were performed using SPSS Statistics (IBM, Armonk, NY).

Results: No differences in actigraphic measures of sleep quality (e.g., total sleep duration, percent sleep, wake after sleep onset, etc.) were observed in active versus inactive disease. Active SLE was associated with phase-dependent circadian variables including bedtime, acrophase (peak of circadian activity), M start (beginning of most

active hours), and M start – waketime (p=0.01, discrepancy between natural circadian rhythm and actual activity pattern) **(Table 1).**

	Inactive SLE (Mean ± SD)	Active SLE (Mean ± SD)	*p*-value
Bedtime (HH:MM)	22.72 ± 1.86	23.59 ± 1.25	0.0195
Waketime (HH:MM)	7.55 ± 1.54	7.91 ± 1.53	0.3344
Total Sleep Duration (mins)	504.92 ± 72.78	500.97 ± 62.05	0.8077
% Sleep	82.71 ± 11.68	81.34 ± 10.66	0.6107
Sleep Efficiency (%)	88.67 ± 10.07	86.91 ± 9.26	0.4517
Wake after sleep onset (WASO) (mins)	52.80 ± 43.50	61.05 ± 46.37	0.4578
Sleep Fragmentation (#)	3.28 ± 1.96	3.73 ± 1.94	0.3473
Wake Episodes (#)	12.43 ± 5.37	14.00 ± 6.38	0.29
Sleep Episodes (#)	11.71 ± 5.33	13.34 ± 6.30	0.265
Alpha Counts (#)	158149.94 ± 29367.25	159217.30 ± 27384.74	0.8807
Rho Counts (#)	18709.94 ± 9061.08	19910.95 ± 8670.39	0.5904
Total Counts (#)	176859.89 ± 32033.70	179128.25 ± 29326.66	0.7675
Amplitude (unitless)	173.99 ± 43.92	175.94 ± 34.87	0.8411
Acrophase (HH:MM)	15.11 ± 1.48	16.08 ± 1.44	0.0104
Mesor (unitless)	122.78 ± 22.24	124.34 ± 20.37	0.7692
L Start (HH:MM)	24.94 ± 1.36	25.47 ± 1.36	0.1266
M Start (HH:MM)	9.84 ± 2.08	11.34 ± 1.93	0.004
Intradaily Variability (unitless)	0.54 ± 0.16	0.51 ± 0.15	0.4603
Intradaily Stability (unitless)	0.66 ± 0.17	0.66 ± 0.13	0.9489
L Start - Bedtime (HH:MM)	2.21 ± 2.35	1.77 ± 0.90	0.2765
M Start - Waketime (HH:MM)	2.29 ± 1.79	3.40 ± 1.668	0.0131

PROMIS-SRI and PROMIS-SD showed no correlation with actigraphy or circadian measures, while PSQI and ESS correlated moderately with % sleep and rho counts (activity during sleep period), and ESS additionally showed modest correlation with measures such as sleep efficiency, sleep and wake episodes, and MESOR (measure of mean activity level) (**Table 2**).

	PROMIS-SRI	PROMIS-SD	PSQI Global	ESS
Bedtime (HH:MM)	0.12	0.11	-0.13	-0.10
Waketime (HH:MM)	-0.03	0.08	0.01	0.02
Total Sleep Duration (mins)	-0.04	0.08	0.28	-0.15
% Sleep	-0.26	-0.18	**-0.34**	**-0.39**
Sleep Efficiency (%)	-0.21	-0.12	-0.29	**-0.40**
Wake after sleep onset (WASO) (mins)	0.17	0.09	0.28	**0.35**
Sleep Fragmentation (#)	0.23	0.11	0.25	**0.48**
Wake Episodes (#)	0.09	0.00	0.17	**0.31**
Sleep Episodes (#)	0.10	0.01	0.17	**0.32**
Alpha Counts (#)	0.07	0.00	-0.01	0.21
Rho Counts (#)	0.29	0.28	**0.38**	**0.36**
Total Counts (#)	0.14	0.08	0.10	**0.30**
Amplitude (unitless)	-0.04	0.04	0.05	-0.19
Acrophase (HH:MM)	0.17	0.16	0.01	0.21
Mesor (unitless)	0.14	0.08	0.10	**0.30**
L Start (HH:MM)	0.13	0.10	0.10	0.05
M Start (HH:MM)	0.14	0.09	-0.01	0.21
Intradaily Variability (unitless)	-0.11	-0.11	0.02	0.07
Intradaily Stability (unitless)	-0.19	-0.17	-0.13	-0.25
L Start - Bedtime (HH:MM)	0.01	0.01	0.19	0.11
M Start - Waketime (HH:MM)	0.19	0.04	-0.01	0.20

Conclusions: Changes in circadian phase, but not sleep quality, is associated with SLE disease activity, with a phase delay in those with active disease. The ESS was the PRO that most highly associated with several actigraphy-assessed sleep parameters, including sleep efficiency and fragmentation. Circadian dysfunction may be an underlying cause for other widely experienced symptoms of SLE including cognitive dysfunction and fatigue. Future work will focus on examining this relationship.

PV054 / #546

Poster Topic: *AS06 - Comorbidities*

POLYPHARMACY AMONG PEOPLE LIVING WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Polypharmacy is known to be associated with adverse health outcomes in the general population. Recent studies have reported high rates of polypharmacy among people living with systemic lupus erythematosus (SLE). However, the relationship between polypharmacy and health outcomes in SLE remains unknown. This study aimed to 1) Identify demographic and clinical characteristics associated with polypharmacy; and 2) Determine the association between baseline polypharmacy and subsequent risk of mortality among people living with SLE.

Methods: This was a secondary analysis of data from a prospective observational cohort of adults with SLE followed at a single academic medical center between 2000 and 2021. All participants met the 1997 revised American College of Rheumatology (ACR) classification criteria for SLE and were assessed annually for medication use, disease activity (measured using the Systemic Lupus Erythematosus Disease Activity Index 2000 [SLEDAI-2K]), organ damage (measured using the SLICC/ACR Damage Index [SDI]), and other measures. The baseline visit for this analysis was defined as the first study visit for each patient at which data were available for all relevant variables. Polypharmacy was defined as the concurrent exposure to five or more medications at the baseline visit. Mortality was defined as any recorded death within the follow-up period. Chi-square tests and Wilcoxon rank-sum tests were used to assess the difference in baseline characteristics between those with versus without baseline polypharmacy. Cox proportional hazards regression was used to evaluate the association between baseline polypharmacy and subsequent mortality risk during follow-up. The multivariable model was adjusted for potential confounders, including baseline age, baseline SDI score, and baseline corticosteroid use.

Results: The 226 included patients (89.4% female) had a median (IQR) age of 45 (34-54) years and a median (IQR) disease duration of 10.0 (2.3-15.6) years at baseline. Polypharmacy was present in 134 patients (59.3%) at baseline. At baseline, polypharmacy was associated with increased age, higher SDI scores, corticosteroid use, immunosuppressive use, and frailty **(Table 1)**. The Kaplan-Meier curves for mortality risk by baseline polypharmacy status are shown in **(Figure 1)**. There was a significant association between baseline polypharmacy and mortality risk during follow-up in the unadjusted analysis (hazard ratio [HR] 4.16, 95% CI 1.93-8.97). After adjusting

for baseline age, SDI score, and corticosteroid use, the association was no longer statistically significant (HR 2.02, 95% CI 0.87-4.71, p=0.10).

Table 1. Baseline characteristics of SLE patients with versus without baseline polypharmacy.

	No polypharmacy n=92	Polypharmacy n=134	p-value
Age, years, median (IQR)	42 (32-48)	50 (37-57)	< 0.05
Female, n (%)	82 (89.1%)	120 (89.6%)	0.92
White race, n (%)	81 (88.0%)	123 (91.8%)	0.35
Current smoker	19 (20.8%)	35 (26.1%)	0.34
Disease duration, years, median (IQR)	8.0 (1.8-14.9)	11.2 (2.3-15.6)	0.13
Prednisone use, n (%)	10 (10.9%)	55 (41.7%)	< 0.05
Immunosuppressant use, n (%)	24 (26.1%)	76 (56.7%)	< 0.05
Antimalarial use, n (%)	58 (63.0%)	89 (66.4%)	0.60
Renal disease	25 (27.2%)	40 (29.9%)	0.66
SLEDAI-2K, median (IQR)	2 (0-4)	2 (0-4)	0.51
SDI score $\geq$ 1, n (%)	21 (22.8%)	67 (50.0%)	< 0.05
Frail (SLICC-FI > 0.21), n (%)	10 (10.9%)	51 (38.1%)	< 0.05

IQR = interquartile range; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SDI = SLICC/ACR Damage Index; SLICC-FI = SLICC Frailty Index.

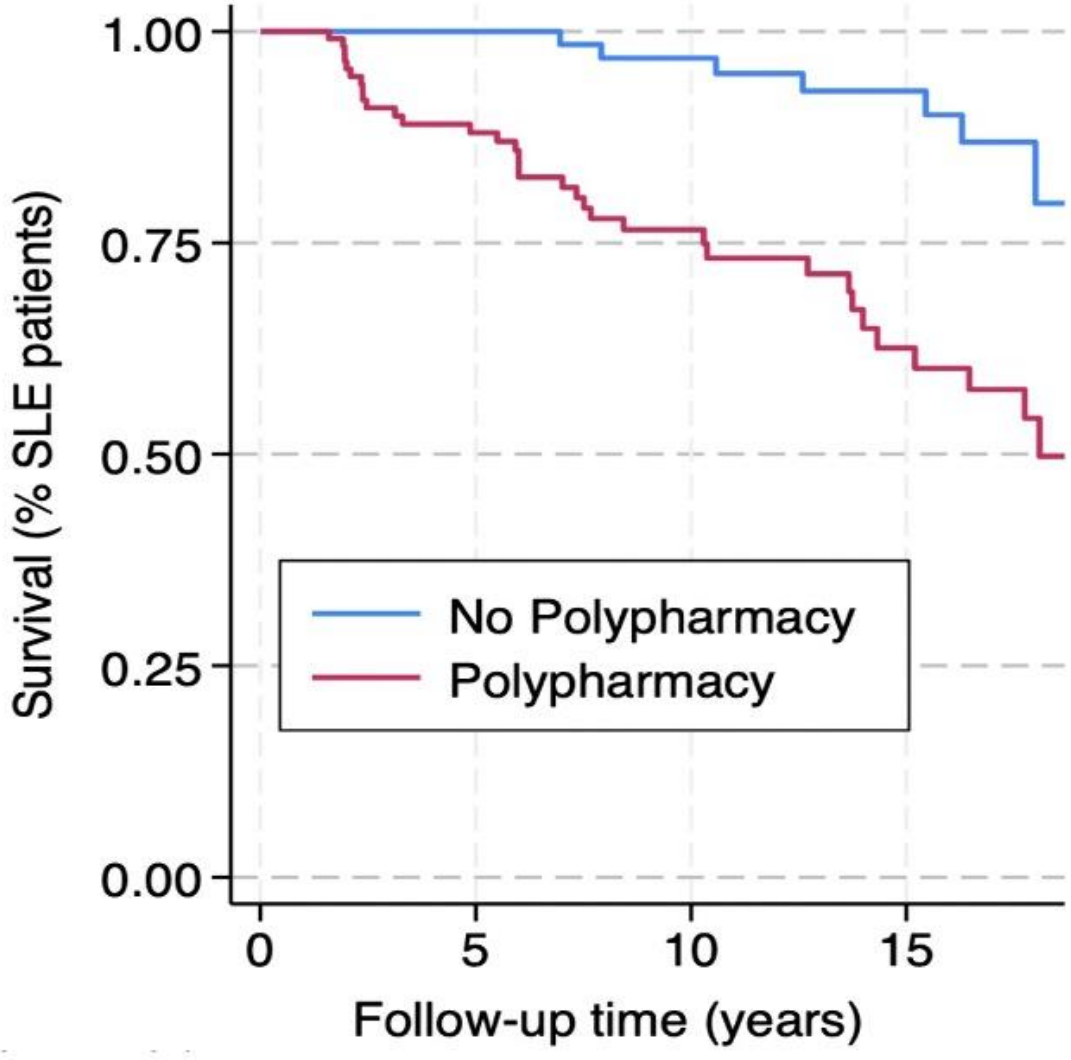

Figure 1. Kaplan-Meier survival curves for mortality risk during follow-up among SLE patients with baseline polypharmacy (in red) versus without baseline polypharmacy (in blue).

Conclusions: Among people living with SLE, baseline polypharmacy was associated with increased risk of mortality during follow-up, but these results were no longer statistically significant after accounting for potential confounders. Future research will aim to understand the the association of polypharmacy with other health outcomes (e.g., organ damage accrual), as well as the trajectories of polypharmacy and high-risk medication use over time in people living with SLE.

PV055 / #458

Poster Topic: ***AS06 - Comorbidities***

PREVALENCE, RISK FACTORS, AND OUTCOMES OF CHRONIC KIDNEY DISEASE IN SLE PATIENTS WITH AND WITHOUT LUPUS NEPHRITIS

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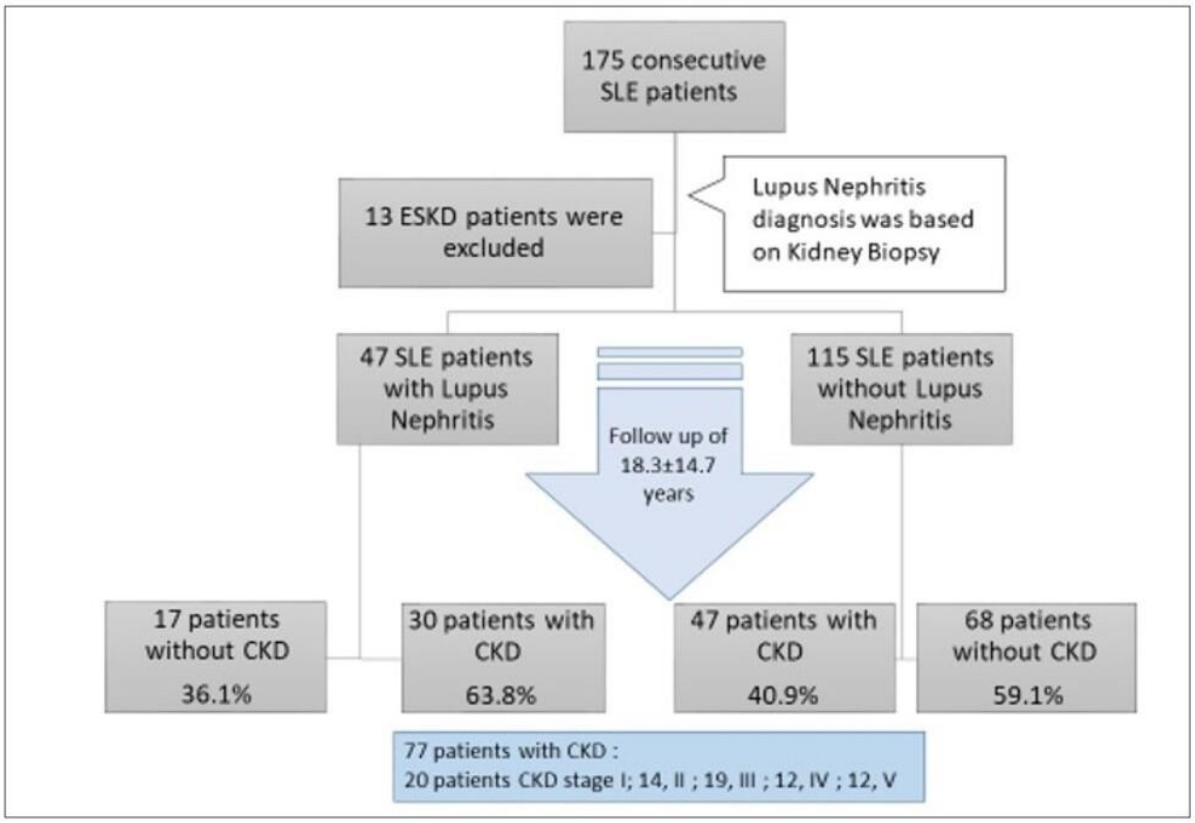
Background/Purpose: Background: Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function persisting for >3 months, detected by decreased estimated glomerular filtration rate (eGFR) or albuminuria. While lupus nephritis (LN) is a well-known cause of CKD in patients with systemic lupus erythematosus (SLE), other risk factors also contribute to the development of CKD in these individuals. Currently, guidelines recommend monitoring urinary protein rather than albumin, which may lead to delayed diagnosis of CKD in SLE patients despite potential benefits of earlier detection. **Aims:** To assess the prevalence, associated factors, and long-term clinical outcomes of CKD among SLE patients, both with and without a history of LN.

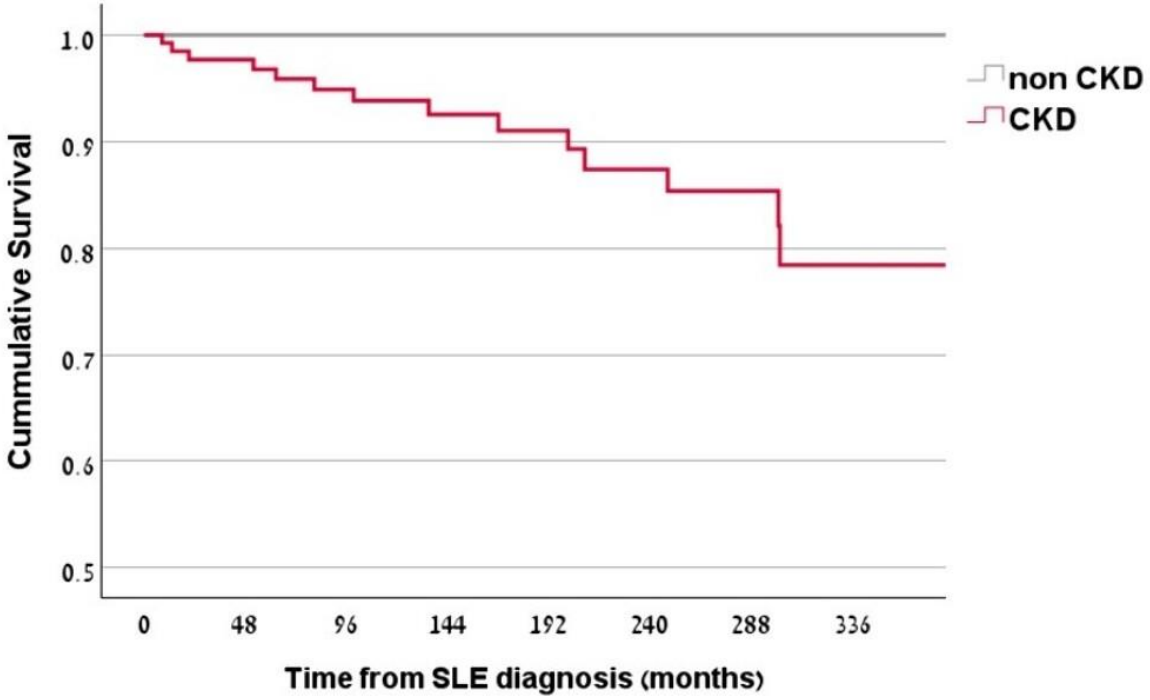
	CKD (n=77)	non-CKD (n=85)	p value
Female, n (%)	53 (68.8%)	85 (100%)	<0.001
Age at diagnosis, years ± SD	35.5 ± 16.1	37 ± 14.4	0.5
Follow-up time, years ± SD	20.3 ± 17.2	16.5 ± 11.7	0.1
Ethnicity, n (%)			0.1
Jews	57 (74.0%)	64 (75.3%)	
Arabs	20 (26.0%)	17 (20.0%)	
Other	0 (0%)	4 (4.7%)	
eGFR at diagnosis, ml/min/m2, mean ± SD	80 ± 38	94 ± 29	0.03
Medications*, n (%)			
Hydroxychloroquine, ever	54 (98.1%)	69 (100.0%)	0.30
Corticosteroids, ever	49 (89.1%)	54 (78.3%)	0.3
Belimumab, ever	12 (21.8%)	17 (24.6%)	0.9
Calcineurin inhibitors, ever	1 (1.8%)	1 (1.4%)	0.1
Azathioprine, ever	21 (38.2%)	15 (21.7%)	0.004
MMF, ever	21 (38.2%)	17 (24.6%)	0.02
Cyclophosphamide, ever	7 (10.1%)	16 (29.1%)	0.001
Antiplatelet, last	26 (47.3%)	26 (37.7%)	0.270
Anticoagulation, last	26 (47.3%)	17 (24.6%)	0.013
Comorbidities, n (%)			
CVA	11 (14.3%)	5 (5.8%)	0.07
IHD	16 (20.8%)	3 (3.5%)	<0.001
APS	31 (40.3%)	23 (27.1%)	0.07
Heart failure	16 (20.8%)	1 (1.2%)	<0.001
Diabetes mellitus	17 (22.1%)	8 (9.4%)	0.03
Hypertension	41 (53.2%)	25 (29.4%)	0.002
Systolic BP, last, mean ± SD	133 ± 22	123 ± 18	<0.001
Diastolic BP, last, mean ± SD	75 ± 13	73 ± 11	0.4
Hospitalization, n (%)			
CVE	17 (22.1%)	11 (13.4%)	0.200
SLE exacerbation	35 (45.5%)	20 (24.4%)	0.005
Severe infection	39 (50.6%)	20 (24.4%)	<0.001
SDI	3.77 ± 3.0	1.45 ± 1.4	<0.001
Mortality, n (%)	18 (23.4%)	0 (0%)	<0.001

*Only 124 patients included in this analysis, 55 in CKD group and 69 in non-CKD group

CKD: Chronic kidney disease; eGFR: estimated glomerular filtration rate; MMF: mycophenolate mofetil; CVA: cerebrovascular accident; IHD: ischemic heart disease; APS: antiphospholipid syndrome; BP: blood pressure; SLE: systemic lupus erythematosus; CVE: cardiovascular event; SDI: Systemic Lupus International Collaborating Clinics /American College of Rheumatology Damage Index



SLE: systemic lupus erythematosus; ESKD: end-stage kidney disease; CKD: chronic kidney disease



CKD: chronic kidney disease; SLE: systemic lupus erythematosus

Methods: Methods: A retrospective single-center study, conducted between 2014–2023 and included adult patients diagnosed with SLE for at least 12 months. Patients were categorized into CKD or non-CKD groups. CKD was defined as having a decreased eGFR <60 ml/min/1.73m2 and/or albuminuria ≥30 mg/24h both in 2 or more consecutive tests spaced at least 3 months apart. eGFR was calculated using MDRD formula. Patients who developed end-stage kidney disease (ESKD) during follow-up were excluded. Study flowchart is shown in Figure 1. Data on sociodemographic and clinical characteristics were collected.

Results: Results: A total of 162 SLE patients were included, of them 77 (47.5%) were diagnosed as having CKD. Among these, 57 (35.2%) had albuminuria, 43 (26.5%) had decreased eGFR, and 22 (13.6%) patients had both albuminuria and decreased eGFR. Notably, 47 (61.1%) of the CKD patients, had never been diagnosed with LN. The odds ratio (OR) for having CKD was 2.55 (95%CI 1.3-5.2, p=0.008) in patients with LN as compared to patients without LN. Strikingly, all male patients were categorized as CKD. CKD was associated with higher rates of antiphospholipid syndrome, diabetes, hypertension, and heart disease (Table 1). Additionally, CKD patients experienced higher rates of severe SLE exacerbations and severe infections requiring hospitalizations and more damage accumulation (Table 1). Despite comparable follow-up time, CKD patients had significantly higher mortality rates compared to non-CKD on univariate analysis (23.4% vs 0, p<0.001). Multivariate COX, age- and sex-adjusted model is shown in Figure 2, p<0.01).

Conclusions: Conclusion: CKD is prevalent among patients with SLE, including those without a diagnosis of LN. CKD in SLE patients is associated with higher rates of comorbidities, severe disease exacerbations, and markedly increased mortality. Given the chronic and progressive nature of CKD, these findings suggest that proactive monitoring in SLE patients should include the measurement of albuminuria in addition to proteinuria. This approach could facilitate the introduction of new treatment options, thereby reducing the substantial morbidity and mortality associated with CKD in SLE.

PV056 / #703

Poster Topic: ***AS06 - Comorbidities***

ARTERIAL STIFFNESS IN DIFFERENT AGE AND CARDIOVASCULAR RISK GROUPS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is associated with increased cardiovascular morbidity and mortality. Arterial stiffness (ArS) is a marker of vascular ageing and atherosclerosis and is a well-recognized predictor of cardiovascular risk in the general population; however, data in SLE is scarce. We compared ArS in SLE versus healthy controls (HC) and assessed potential predictors.

Methods: ArS was assessed in 194 SLE patients versus 1:1 age/sex/mean arterial pressure (MAP)-matched HC using the carotid-femoral pulse wave velocity (PWV) and augmentation index at 75 beats/min (AIx@75). ArS was examined in different age groups (18-37, 38-57, 58-75 years) and cardiovascular risk groups (low-moderate, high-very high) classified by the Systematic Coronary Risk Evaluation (SCORE). Carotid and femoral ultrasounds were performed to detect atherosclerotic plaque presence. Linear regression models were used to examine potential predictors of ArS, including patient demographic characteristics, Systemic Coronary Risk Evaluation (SCORE), the sum of modifiable cardiovascular risk factors (CVRFs) (among hypertension, dyslipidemia, smoking, exercise, and body weight), the achievement of Lupus Low Disease Activity State (LLDAS) and Definition of Remission in SLE (DORIS) clinical remission, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index, cumulative glucocorticoid exposure, consistent hydroxychloroquine use, cardiovascular disease (CVD)-related medications, and antiphospholipid antibody (aPL) positivity at the time of the assessment.

Results: SLE patients had increased AIx@75 versus HC (β = 3.353, 95% CI 1.964-6.526, p = 0.019) (Table 1, model A), but not PWV (β = 0.102, 95% CI -0.117, 0.321, p = 0.361). Patients aged 18-37 had higher PWV (β = 0.409, 95% CI 0.095-0.722, p = 0.011) and AIx@75 (β = 10.115, 95% CI 6.111-14.119, p < 0.001) than HC (Table 1, models B and C). Low-moderate CVD risk patients had higher AIx@75 than HC (β = 3.387, 95% CI 0.735-6.039, p = 0.012) (Table 1, model D). PWV and AIx@75 were independently associated with atherosclerotic plaque presence (carotid or femoral) (β = 0.297, 95% CI 0.005-0.589, p = 0.046 and β = 4.867, 95% CI 1.989-7.746, p = 0.001, respectively). In SLE, PWV and AIx@75 were independently associated with age (β = 0.061, 95% CI 0.040-0.082, p < 0.001 and β = 0.426, 95% CI 0.278-0.574, p < 0.001, respectively), MAP (β =

0.051, 95% CI 0.031-0.070, p < 0.001 and β = 0.328, 95% CI 0.189-0.466, p < 0.001, respectively), and the sum of modifiable CVRFs (β = 0.258, 95% CI 0.055-0.461, p = 0.013 and β = 2.035, 95% CI 0.587-3.483, p = 0.006, respectively) (Table 1, models E and G). PWV was additionally associated with SCORE (β = 0.607, 95% CI 0.414-0.800, p < 0.001) (Table 1, model F). Among disease-related factors, AIx@75 was associated with disease duration (β = 0.274, 95% CI 0.081-0,467, p < 0.001) (Table 1, model H), and PWV correlated with past use of corticosteroids in patients aged 58-75 years (β = 1.660, 95% CI 0.185-3.135, p = 0.029).

Table 1 Multivariate linear regression models of pulse wave velocity and augmentation index in SLE versus HC (models A, B, C, D), and within SLE (models E, F, G, H)

	B Coef.	95% CI	P-value
Model A			
AIx@75 (SLE vs HC)	3.353	0.564-6.142	0.019
Plaque presence (carotid or femoral)	4.867	1.989-7.746	0.001
Model B			
PWV (SLE vs HC)	0.409	0.095-0.722	0.011
Model C			
AIx@75 (SLE vs HC)	10.115	6.111-4.119	<0.001
Model D			
AIx@75 (SLE vs HC)	3.387	0.735-6.039	0.012
BMI	0.634	0.385-0.882	<0.001
Plaque presence (carotid or femoral)	6.868	3.961 9.775	<0.001
Model E			
CVRFs	0.258	0.055-0.461	0.013
Age	0.061	0.040-0.082	<0.001
Model F			
SCORE	0.607	0.414-0.800	<0.001
Model G			
CVRFs	2.035	0.587-3.483	0.006
Age	0.426	0.278-0.574	<0.001
Model H			
BMI	0.377	0.096-0.659	0.009
Disease duration	0.274	0.081-0,467	0.006
Plaque presence (carotid or femoral)	4.763	0.988-8.537	0.014

Only statistically significant values are shown in the table.
PWV: pulse wave velocity; AIx@75: augmentation index at 75/beats/min; HC: healthy controls; SCORE: Systemic Coronary Risk Evaluation prediction of 10-year fatal cardiovascular disease corresponding to the 2016 European Society of Cardiology (ESC) guidelines in low-risk countries; CKD: chronic kidney disease; sum of CVRFs: sum of cardiovascular risk factors (among hypertension, dyslipidemia, smoking status, physical activity, and body weight [BMI and waist circumference]); SLICC/SDI: Systemic Lupus International Collaborating Clinics Damage Index.
Model A: AIx@75 in SLE vs HC (entire cohort); also adjusted for SCORE, BMI, use of antiplatelet drugs and CKD stage
Model B: PWV in SLE vs HC (age group 18-37 years old) adjusted also for sum of CVRFs, age and carotid/femoral plaque presence
Model C: AIx@75 in SLE vs HC (age group 18-37 years old) adjusted also for cardiovascular risk class stratified by SCORE, BMI, carotid/ femoral plaque presence
Model D: AIx@75 in SLE vs HC classified in low-moderate risk class according to SCORE
Model E: PWV in SLE adjusted also for disease duration, carotid/femoral plaque presence, CKD stage and SLICC/SDI
Model F: PWV in SLE adjusted also for BMI, carotid/femoral plaque presence, stage of chronic renal disease, SLICC/SDI
Model G: AIx@75 in SLE adjusted also for gender, disease duration, carotid/femoral plaque presence.
Model H: AIx@75 in SLE adjusted also for carotid/femoral plaque presence, disease duration, CKD stage and SLICC/SDI

Conclusions: Increased ArS in SLE compared to HC is associated with traditional CVRF burden, emphasizing the need for early CVRF evaluation and treatment in SLE, particularly in young low CVD risk patients. ArS screening may help detect high CVD risk in low-moderate risk patients with SLE.

PV057 / #707

Poster Topic: *AS06 - Comorbidities*

NON-ALCOHOLIC FATTY LIVER DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS: ASSOCIATIONS WITH CARDIOVASCULAR RISK FACTOR GOAL ACHIEVEMENT AND ATHEROSCLEROTIC PLAQUE PROGRESSION OVER THE PAST 10 YEARS

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Background/Purpose: Non-alcoholic fatty liver disease (NAFLD) is a broad term including different stages of liver steatosis and fibrosis, and is the most common liver disease worldwide. It has been identified as an independent predictor of cardiovascular disease in the general population,[1.] and has been associated with multiple cardiovascular risk factors (CVRFs) and atherosclerosis. However, evidence on the prevalence and predictors of NAFLD in Systemic Lupus Erythematosus (SLE) is limited. We compared the prevalence of NAFLD in patients with SLE versus healthy controls (HCs) and examined associations with sustained CVRF goal achievement, progression of atherosclerotic plaques over the past 10 years, and potential disease-related CVRFs.

Methods: Patients with SLE and age and sex-matched HCs who had a 10-year carotid and femoral ultrasound follow-up examination in our department were contacted to participate in the study. Liver transient elastography was performed to assess liver steatosis and fibrosis presence in 77 patients with SLE and 45 age- and sex-matched HCs. Liver steatosis was graded based on Control Attenuation Parameter (CAP) values, as follows: S0 (absent): 100–238 decibels/meter (dB/m), S1 (mild): 238–260 dB/m, S2 (moderate): 260–290 dB/m, and S3 (severe): > 290dB/m. Liver steatosis presence was defined as grade ≥ S1. Liver stiffness was graded as F0–F1: 2–7 kilopascals (kPa), F2: 7–10 kPa, F3: 10–14 kPa, and F4: > 14 kPa. Liver fibrosis was defined as grade ≥ F2. Logistic regression analysis assessed potential predictors of NAFLD in patients with SLE, including alcohol consumption defined as drinks per week, Mediterranean Diet score (tool for the assessment of mediterranean diet adherence), CVRFs (blood pressure, total cholesterol, Low-Density Lipoprotein, High-Density Lipoprotein, triglycerides, smoking status, physical activity, BMI, waist circumference, family history of coronary artery disease), Systemic Coronary Risk Evaluation (SCORE) prediction score, sustained CVRF target attainment for blood pressure, lipids, smoking, physical activity, and body weight, as defined by the 2016 European Society of Cardiology guidelines, and

atherosclerotic carotid and femoral plaque progression. Among disease-related potential predictors, we examined the persistent achievement of Lupus Low Disease Activity State (LLDAS) and Definition of Remission in SLE (DORIS) clinical remission, and persistent antiphospholipid antibody positivity during the 10-year follow up period. Cardiovascular disease-related (antihypertensives, lipid-lowering agents and antiplatelets) and SLE-related medications (cumulative glucocorticoid exposure, consistent hydroxychloroquine use during the 10-year follow-up, immunosuppressives) were also assessed.

Results: Liver steatosis presence did not differ significantly between SLE and HC individuals (40,25% versus 44,44% respectively, p = 0.651). No liver fibrosis was detected in either group. In the SLE group, multivariate analysis showed that atherosclerotic femoral plaque progression over the past 10 years was associated with a 3.6-fold higher risk for NAFLD (Odds Ratio [OR]: 3.62, 95% CI 1.018-12.93, p = 0.021). NAFLD was also independently associated with persistent positivity of IgG anti-beta2 glycoprotein I antibodies (OR: 6.58, 95% CI 1.33-32.566, p = 0.021) during the 10-year follow up. Each cardiovascular risk factor (including blood pressure, lipids, smoking, physical activity, and body weight) persistently on target during the 10-year follow-up period reduced NAFLD risk by 55% (OR: 0.45, 95% CI 0.231-0.889, p = 0.021).

Conclusions: Atherosclerotic femoral plaque progression and persistent IgG anti-beta2 glycoprotein I antibodies positivity were independent predictors of liver steatosis in patients with SLE, which can be drastically mitigated by sustained CVRF goal achievement. Reference [1.] Stahl EP J Am Coll Cardiol 2019;73:948-63.

PV058 / #431

Poster Topic: ***AS06 - Comorbidities***

THE ROLE OF ANTIPHOSPHOLIPID ANTIBODIES IN RETINAL MICROVASCULATURE CHANGES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: AN ANALYSIS OF TWO INTERNATIONAL REFERRAL CENTERS.

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Background/Purpose: Retinopathy is a common ocular manifestation in SLE, and it is often caused by microangiopathy resulting from immune complex deposition, leading to vasculitis and thrombosis in the retinal microcirculation. Antiphospholipid antibodies (aPL) are present in around 30% of SLE patients, with 10% developing antiphospholipid syndrome (APS). Retinal involvement in APS can manifest as arterial and venous thrombosis. While macrovascular involvement manifests with prominent symptoms such as amaurosis fugax or transient diplopia, microvascular involvement may remain asymptomatic and manifest at the retinal level with microhaemorrhages, microaneurysms, and cotton-wool spots. This study aimed to evaluate the association between aPL positivity and preclinical retinal vascular changes in SLE patients.

Methods: This cross-sectional, two-center study included 112 SLE patients and 134 healthy controls recruited from Hospital Clinic de Barcelona and Policlinico Tor Vergata in Rome. Patients underwent ophthalmological evaluations, including visual acuity measurement, slit-lamp biomicroscopy, intraocular pressure measurement, and fundus examination. Retinal structural changes, such as macular thickness (MT) and retinal nerve fiber layer (RNFL) thickness, were assessed using spectral-domain optical coherence tomography (SD-OCT). Retinal vascular changes, including vessel density (VD), vascular perfusion (VP), and foveal avascular zone (FAZ), were evaluated using OCT angiography (OCTA). Statistical analysis was performed to compare differences between SLE subgroups stratified based on aPL positivity or the presence of APS.This cross-sectional, two-center study included 112 SLE patients and 134 healthy controls recruited from Hospital Clinic de Barcelona and Policlinico Tor Vergata in Rome. Patients underwent ophthalmological evaluations, including visual acuity measurement, slit-lamp biomicroscopy, intraocular pressure measurement, and fundus examination. Retinal structural changes, such as macular thickness (MT) and

retinal nerve fiber layer (RNFL) thickness, were assessed using spectral-domain optical coherence tomography (SD-OCT). Retinal vascular changes, including vessel density (VD), vascular perfusion (VP), and foveal avascular zone (FAZ), were evaluated using OCT angiography (OCTA). Statistical analysis was performed to compare differences between SLE subgroups stratified based on aPL positivity or the presence of APS.

Results: OCTA analysis revealed decreased vascular parameters in SLE patients compared to controls in both cohorts. Specifically, the Barcelona cohort showed significant reductions in VD and VP (Table 1), while the Rome cohort showed significant reductions in parafoveal superficial VD. No clear association was found between aPL positivity and alterations in OCTA vascular parameters in SLE patients. However, a possible correlation between aPL positivity and variations in RNFL thickness was observed in both cohorts (Table 2 and Table 3).

Table 1. Spectral-domain Optical Coherence Tomography (SD-OCT) and Angiography by Optical Coherence Tomography (OCTA) parameters at Barcelona cohort, right eye*.

	Control N= 67	SLE group N= 58	P value
SD-OCT			
Macular thickness (μ)	260.6 (255.4-265.7)	259.8 (254-265.6)	0.279
RNFL thickness (μ)			
Average	95.4 (93.1 97.7)	95.7 (93.1 98.2)	0.851
Superior	113.6 (107.8 119.4)	112.7 (107 118.4)	0.230
Temporal	68.3 (65.6-71.1)	68.6 (65.4-71.8)	0.457
Inferior	123 (119-127.1)	123 (117.7-128.1)	0.820
Nasal	72.7 (69.4-76)	76.8 (72.2-81.5)	0.259
OCTA			
VD (mm/mm²)	17.8 (17.4 18.3)	17.2 (16.7 17.6)	0.002
VP (%)	0.43 (0.43-0.44)	0.41 (0.39-0.43)	0.012
FAZ			
Area (mm²)	0.22 (0.20-0.25)	0.25 (0.22-0.28)	0.678
Perimeter (mm)	1.9 (1.8-2)	2 (2.1-2)	0.374

* All parameters are expressed as mean (95% IC)
Abbreviations: RNFL: retinal nerve fiber layer; VD: vascular density; VP: vascular perfusion; FAZ: foveal avascular zone.

Table 2. Spectral-domain Optical Coherence Tomography (SD-OCT) and Angiography by Optical Coherence Tomography (OCTA) parameters at Barcelona cohort, by antiphospholipid antibodies, right eye*.

	SLE group N= 64	LA N= 19	aCL N= 21	ß2GP1 N= 20	Triple positivity N= 14	Any positivity N= 27	P value
SD-OCT parameters							
Macular thickness (µ)	260 (25.2)	260.3 (34.1)	260.7 (26.3)	262.7 (32.9)	266.9 (24.2)	258.7 (29.6)	0.911
RNFL thickness (µ)							
Average	95.7 (9.3)	93 (9.4)	93.2 (9.5)	94.7 (9.4)	93.4 (10.6)	93.7 (9)	0.158
Superior	112.5 (21.1)	107.3 (30.2)	111 (16.9)	112.2 (17.7)	113.1 (19.3)	106.7 (25.6)	0.250
Temporal	68.7 (12.1)	68.3 (13.4)	70 (13.1)	68.9 (14.2)	67.3 (14.7)	69.3 (13)	0.753
Inferior	122.1 (20)	**113.4 (20.6)**	**114.1 (20.2)**	**113.6 (23.3)**	**112.1 (22.4)**	**114.2 (21.5)**	**0.052**
Nasal	77.8 (17)	75 (20.6)	76.2 (19.1)	82.6 (25)	78.5 (23)	79.1 (22.8)	0.426
OCTA parameters							
VD (mm/mm²)	16.8 (2.5)	17.1 (1.6)	16.3 (3.4)	17.3 (1.6)	17.6 (1.6)	17 (2.1)	0.738
VP (%)	0.41 (0.09)	0.42 (0.13)	0.40 (0.15)	0.43 (0.09)	0.44 (0.16)	0.42 (0.12)	0.612
FAZ							
Area (mm²)	0.25 (0.12)	0.27 (0.14)	0.25 (0.13)	0.27 (0.14)	0.28 (0.14)	0.25 (0.13)	0.429
Perimeter (mm)	2.05 (0.55)	2.09 (0.61)	2.02 (0.58)	2.14 (0.56)	2.16 (0.60)	2.04 (0.54)	0.734

* All parameters are expressed as mean (SD).

Abbreviations. RNFL: retinal nerve fiber layer; VD: vascular density; VP: vascular perfusion; FAZ: foveal avascular zone.

Table 3. Spectral-domain Optical Coherence Tomography (SD-OCT) and Angiography by Optical Coherence Tomography (OCTA) parameters at Rome cohort, by antiphospholipid antibodies, right eye*.

	SLE group N= 46	LA N= 9	aCL N= 12	ß2GP1 N= 8	Triple positivity N= 4	Any positivity N= 15	P value
SD-OCT parameters							
Macular thickness (µ)							
Foveal thickness	253.9 (22.1)	257.7 (23.1)	262.3 (22)	262.9 (21.3)	269 (17.2)	256.2 (23.4)	0.574
Parafoveal thickness	314.4 (28.7)	323.4 (14.7)	310 (46.3)	321.9 (14.9)	321.8 (13.6)	311.2 (41.4)	0.294
Retinal thickness (µ)							
Average	276.2 (26)	275.7 (31.3)	303.7 (27.9)	284.8 (28.5)	293.7 (19.6)	284.3 (36.6)	0.959
Outer superior	299.1 (11.9)	303 (17.9)	307 (19.9)	303.3 (19.8)	293.3 (12.7)	301.6 (15.8)	0.346
Outer temporal	279.4 (12.7)	281.3 (16.7)	282.5 (17.9)	282.5 (17.9)	278.3 (23.4)	280.9 (14.6)	0.662
Outer inferior	286.7 (15.6)	291.9 (24.4)	283.5 (28.8)	288.2 (27.2)	276 (23.4)	287 (23.4)	0.339
Outer nasal	314.1 (16.1)	318.7 (24.4)	317.5 (27.2)	317.3 (27.2)	305.7 (23.1)	317.3 (21.5)	0.399
Inner superior	342.8 (17.4)	345.4 (23.7)	351.5 (21.7)	348.8 (23.5)	343.3 (13.7)	345 (20.6)	0.662
Inner temporal	325.5 (21.1)	331.4 (19.5)	337.8 (18.7)	332.3 (20.9)	332 (19.4)	332 (17.8)	0.419
Inner inferior	337.7 (18.8)	343.4 (20.5)	337.7 (26.7)	340.7 (25.1)	338 (18.5)	337.9 (21.6)	0.379
Inner nasal	342.4 (18.8)	347.3 (24.4)	351.2 (23)	349.5 (25)	348.3 (19)	344.9 (21.8)	0.454
RNFL thickness (µ)							
Average	13.4 (4.2)	13.3 (2)	17.8 (8)	14 (1.7)	14.3 (0.6)	15.7 (7.1)	0.921
Outer superior	40.5 (6.4)	40.1 (9.7)	42.3 (8.9)	40.7 (8.6)	35 (4)	41.7 (8.9)	0.888
Outer temporal	21.2 (6.8)	20.1 (2.2)	21.5 (3.7)	19.8 (2.1)	19 (2)	21.2 (3.2)	0.651
Outer inferior	43.3 (6.7)	44.6 (8.3)	44.3 (10.5)	41.5 (6.7)	36.7 (2.9)	46.1 (9.1)*	0.329
Outer nasal	54.2 (11.1)	56.6 (7.5)	61 (17.5)	53.5 (7.1)	52 (5.3)	60 (14.5)	0.535
Inner superior	27 (4.6)	25.9 (4.6)	30.8 (8.1)	27.2 (4.6)	25 (1.7)	28.4 (7.5)	0.507
Inner temporal	19 (5.1)	18.7 (2.2)	23.2 (11.7)	18 (1.3)	18 (1)	21.9 (9.6)*	0.872
Inner inferior	26.9 (4.4)	26.7 (1.7)	30 (9)	26.2 (1.7)	27 (1.7)	28.8 (7.4)	0.909
Inner nasal	23.1 (5.8)	23.6 (2.4)	29.3 (12.2)	23.5 (2.6)	24.7 (2.1)	27 (10.3)*	0.830
OCTA parameters							
VD (%)							
Superficial foveal VD	22.1 (8.5)	22.4 (5.4)	24.7 (7.9)	24.7 (4.9)	21.7 (3.6)	24 (8.1)	0.976
Deep foveal VD	39.4 (8.6)	39.4 (6.7)	43.1 (8.8)	43.3 (4.3)	41.1 (5.2)	41.4 (9.1)	0.997
Superficial parafoveal VD	53.1 (5.5)	53.1 (6)	53.7 (5.4)	55.4 (2.8)	53.9 (2.2)	52.8 (6.2)	0.969
Deep parafoveal VD	58.4 (5.6)	58.3 (4.5)	59.9 (3.3)	60.3 (4.1)	57.8 (3.8)	59.7 (4.1)	0.982
FAZ							
Area (mm²)	0.25 (0.11)	0.25 (0.09)	0.24 (0.13)	0.22 (0.06)	0.20 (0.10)	0.25 (0.12)	0.983
Perimeter (mm)	1.90 (0.42)	1.93 (0.32)	1.84 (0.46)	1.79 (0.25)	1.74 (0.40)	1.90 (0.42)	0.805

* All parameters are expressed as mean (SD). * p <0.05

Abbreviations: RNFL: retinal nerve fiber layer; VD: vascular density; VP: vascular perfusion; FAZ: foveal avascular zone.

Conclusions: While SLE patients exhibited significant alterations in vascular OCTA parameters compared to healthy controls, the study did not find a definitive association between aPL positivity and changes in OCTA parameters in SLE patients. However, the study suggests a potential correlation between aPL positivity and variations in RNFL thickness in both cohorts. Further studies are needed to confirm these results and understand their biological significance.

PV060 / #81

Poster Topic: *AS07 - Cutaneous Lupus*

PAIN IN CUTANEOUS LUPUS ERYTHEMATOSUS CATEGORIES & SUBTYPES

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Background/Purpose: Cutaneous lupus erythematosus (CLE) is a chronic inflammatory autoimmune disease encompassing a broad range of dermatologic manifestations. CLE findings may be divided into LE-specific and LE-nonspecific skin disease, whereby LE-specific lesions show histopathologically distinct findings. Based on clinical characteristics, CLE can be categorized into three major categories of LE-specific skin disease and further into subtypes within each category (Table 1). Pain in CLE is an area that is understudied, with only one previous study showing that patients with both specific and non-specific CLE lesions had higher pain levels than those with only one lesion type. [1] There have been no studies examining differences in pain across the categories and subtypes of CLE. In this study, we set out to delineate differences in pain across the various categories and subtypes of CLE as well as to examine how pain changes over time in order to better guide clinicians in evaluating for pain, which may negatively impact patient quality of life.

Methods: Subjects were selected from a longitudinal database of CLE patients seen at the outpatient autoimmune skin disease clinic of the Hospital of the University of Pennsylvania (HUP). Those included were patients with a diagnosis of CLE with moderate to severe disease as measured with the CLE Disease Area and Severity Index (CLASI), a validated clinical tool used to quantify disease activity and damage in CLE. Patients were classified by category into acute CLE (ACLE), subacute CLE (SCLE), and chronic CLE (CCLE). Within each category, patients were further subtyped (Table 1). Pain was quantified using a 10-cm visual acuity scale (VAS) for pain, with 0-cm as none and 10-cm as most severe. The Kruskal-Wallis test was used to compare median pain across all CLE categories and subtypes at their initial clinic visit. To examine change in pain over time, we used a linear mixed model (LMM) approach to look at pain across all visits within year one of initial presentation while controlling for disease duration. For the LMM analysis, only patients with a VAS pain score greater than 3 at their initial visit were included in order to capture patients who were experiencing at least mild pain.

Results: A total of 528 patients were included in the study. Across patients, 31% has a VAS pain score above 4, signaling moderate to severe pain. Generalized ACLE (ACLE-G) and chilblain had the highest median pain scores at visit one, though this was not statistically significant ($p>.05$) (Table 1). Across all categories and subtypes, significant change in pain over time was only seen in ACLE (23 patients), and CCLE (121 patients) ($p<.05$) (Figure 1) with pain scores increasing in the year following visit one.

Table 1. Comparison of Pain Scores Across CLE Categories/Subtypes			
		Median Pain (± IQR)	*Pain p-value*
CLE Category (% of patient population)	ACLE (11%)	2 ± 4	0.72
	SCLE (24%)	1 ± 5	
	CCLE (66%)	2 ± 5	
CLE Subtype (% of patient population)	ACLE-G (4%)	4 ± 3	0.421
	ACLE-L (5%)	2 ± 5	
	DLE (55%)	2 ± 5	
	Chilblain (1%)	4 ± 3	
	Panniculitis (2%)	0 ± 4	
	LET (7%)	3 ± 5	
DLE Subtype (% of patient population)	DLE-G (20%)	3 ± 5	0.449
	DLE-L (33%)	1 ± 4	
	Hypertrophic (1%)	1 ± 4	

Key: CLE = cutaneous lupus erythematous, ACLE = acute cutaneous lupus erythematous, SCLE = subacute cutaneous lupus erythematous, CCLE = chronic cutaneous lupus erythematous, ACLE-G = generalized acute cutaneous lupus erythematous, ACLE-L = localized acute cutaneous lupus erythematous, DLE = discoid lupus erythematous, LET = tumid lupus erythematous, DLE-G = generalized discoid lupus erythematous, DLE-L = localized discoid lupus erythematous. IQR = interquartile range. Values for median pain correlate to scores for visual analog scale pain. P-values represent differences in pain, and itch across CLE categories, CLE subtypes, and DLE subtypes calculated using the Kruskal-Wallis test.

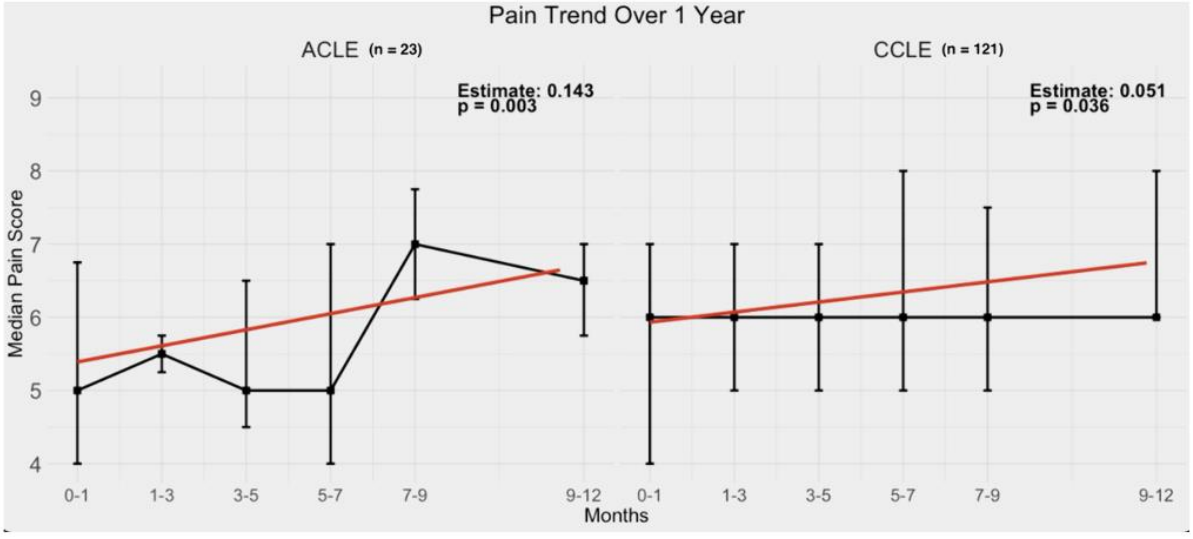

Figure 1: Linear mixed model analysis of change in pain over time across CLE categories and subtypes. ACLE = acute cutaneous lupus erythematous. CCLE = chronic cutaneous lupus erythematous. Median pain score represents pain visual analog scale (VAS) score across all visits.

Conclusions: Results from our study show that pain was not significantly different between CLE categories and subtypes at their initial visit. Significant change in pain across year one was observed in ACLE and CCLE with pain scores increasing. At initial presentation, almost one-third of patients had moderate to severe pain with a VAS pain score greater than 4. As pain may have a negative impact on quality of life, it should be carefully considered during not only initial clinical evaluation but subsequent visits.
References: 1. Méndez-Flores S, Orozco-Topete R, Bermúdez-Bermejo P, Hernández-Molina G. Pain and pruritus in cutaneous lupus: their association with dermatologic quality of life and disease activity. Clin Exp Rheumatol. 2013;31(6):940-2.

PV061 / #136

Poster Topic: *AS07 - Cutaneous Lupus*

CALCINOSIS CUTIS IN LUPUS ERYTHEMATOSUS PANNICULITIS SHOW PREDILECTION FOR TRUNCAL LOCATION

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Background/Purpose: Lupus erythematosus panniculitis (LEP) is a rare form of chronic cutaneous lupus erythematosus characterized by indurated nodules or plaques resulting in pronounced skin atrophy. Calcinosis cutis (CC) is a disease sequela associated with LEP, leading to the significant impact on patients' quality of life due to pain and limited treatment options. The frequency of development and risk factors associated with CC in LEP remain unclear. This study aims to assess the rate of CC in LEP patients and identify factors that may increase development of CC, thereby providing insights into monitoring and management strategies for LEP patients.

Methods: This retrospective cohort study reviewed data from 26 patients diagnosed with LEP and treated at the outpatient dermatology clinics of the University of Texas Southwestern Medical Center and Parkland Health between April 2009 and August 2024. The primary outcome measure was the presence of CC, confirmed through clinical evaluation by a dermatologist, biopsy, or imaging. Patient data included demographic details, smoking history, disease duration, lesion location, medications, and ANA positivity. Frequency counts and medians were calculated for categorical and continuous variables, respectively. We analyzed predictor variables for presence of CC using Mann-Whitney U and Fisher's exact tests to examine associations.

Results: Of the 26 LEP patients, 10 (38%) were diagnosed with CC (**Table 1**). For these ten patients, the median duration after diagnosis of LEP to diagnosis of CC was 3.98 years. LEP Patients that were diagnosed with calcinosis cutis had greater LEP involvement of their trunk, with 9/10 (90%) patients with LEP truncal involvement having CC, compared to only 5/16 (31%) in the group that did not have CC (p=0.01) (**Table 2**). The CC lesions on the 10 patients that developed this sequela were found predominantly on the trunk (6) and arms (5). No significant associations were found between CC development and other variables, including demographic factors, ANA positivity, smoking history, medications, and follow-up duration (**Table 1**).

Table 1: Univariate analysis of demographics and clinical risk factors of lupus erythematosus panniculitis (LEP) patients with and without calcinosis cutis (CC)

	All LEP Patients (N=26)	LEP w/ CC (N=10)	LEP w/o CC (N=16)	
Gender (N,%)				p = 0.67
Male	7 (26.9%)	2 (20%)	5 (31.3%)	
Female	19 (73.1%)	8 (80%)	11 (68.7%)	
Race/Ethnicity (N,%)				p > 0.99
Black, Non-Hispanic	17 (65.4%)	7 (70%)	10 (62.5%)	
Other	9 (34.6%)	3 (30%)	6 (37.5%)	
Smoking History (ever) (N,%)	10 (38.5%)	5 (50%)	5 (31.3%)	p = 0.43
Age At LEP Diagnosis (years) (median, IQR)	34.3 (26.3-42.8)	34 (25.8-42.3)	34 (28.75-42.25)	p = 0.89
Disease Duration (years) (median, IQR) [a]	N/A	3.98 (0.32-6.99)	N/A	
Follow Up Duration (years) (median, IQR) [b]	3.86 (1.68-9.22)	6.02 (3.19-11.02)	2.60 (1.41-7.97)	p = 0.36
Symptom onset to LEP Dx (months) (median, IQR) [c]	8.31 (4.0-22.9)	17.9 (2.46-30.5)	6.90 (4.93-17.4)	p = 0.79
Medication History (N,%)				p = 0.42
Topicals + Antimalarials	14 (53.8%)	4 (40%)	10 (62.5%)	
Topicals + Antimalarials + Other immunosuppressants [d]	12 (46.2%)	6 (60%)	6 (37.5%)	
Concurrent Diagnoses (N,%)				
DLE	16 (61.5%)	7 (70%)	9 (56.3%)	p = 0.68
SLE	12 (46.2%)	6 (60%)	6 (37.5%)	p = 0.12

[a] LEP diagnosis date to CC diagnosis date

[b] LEP diagnosis date to last follow-up visit

[c] Patient reported symptoms to LEP diagnosis were available in 8 LEP patients with CC and 15 LEP patients without CC

[d] Immunosuppressants ever taken in the LEP with CC group included mycophenolate mofetil (N=5), methotrexate (N=4), azathioprine (N=3), thalidomide (N=1). Immunosuppressants ever taken in the LEP without CC group included mycophenolate mofetil (N=5), belimumab (N=2), methotrexate (N=1), azathioprine (N=1), rituximab (N=1), leflunomide (N=1), and IV immunoglobulin (N=1).

Abbreviations: CC: calcinosis cutis, DLE: discoid lupus erythematosus, LEP: lupus erythematous panniculitis, SLE: systemic lupus erythematosus

Table 2: Body site involvement of lupus erythematosus panniculitis (LEP) lesions in LEP patients with and without calcinosis cutis (CC)

Body Site [a]	LEP w/ CC (N=10) [b]	LEP w/o CC (N=16)	
Head & Neck (N,%)	**5 (50%)**	**12 (75%)**	**p = 0.23**
Scalp	3 (30%)	4 (25%)	
Nose	0	3 (18.8%)	
Face	3 (30%)	11 (68.8%)	
V Area of Neck	1 (10%)	0	
Trunk (N,%)	**9 (90%)**	**5 (31.2%)**	**p = 0.01**
Chest	4 (40%)	1 (6.3%)	
Abdomen	2 (20%)	0	
Buttocks	5 (50%)	3 (18.8%)	
Back	3 (30%)	4 (25%)	
Upper Extremities (N,%)	**5 (50%)**	**6 (37.5%)**	**p = 0.69**
Lower Extremities (N,%)	**5 (50%)**	**4 (25%)**	**p = 0.23**

[a] Indicates the number of patients with one or more lesions in individual body site
[b] CC was found on the trunk of 6 patients (3 chest, 1 abdomen, 4 buttocks, 1 back), on the arms of 5 patients, on the legs of 2 patients, and on the face of 1 patient.
Abbreviations: CC: calcinosis cutis, LEP: lupus erythematous panniculitis

Conclusions: In one of the larger cohorts of LEP patients studied to date, over one-third had CC, and truncal lesions, such as those in the chest and buttocks, were significantly correlated with this complication. The median disease duration from LEP diagnosis to CC diagnosis was about 4 years. The substantial occurrence of CC in LEP highlights the need for vigilant clinical monitoring of CC in LEP. This study is limited by its single-center, retrospective design, and small sample size. Further prospective studies with larger sample sizes are necessary to confirm these results and clarify the timing and mechanisms behind CC development in LEP patients.

PV062 / #535

Poster Topic: *AS07 - Cutaneous Lupus*

ANALYSING THE RECURRENCE PATTERNS IN CUTANEOUS LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS OF SCLE AND DLE FLARES

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Background/Purpose: Although morphologically distinct, subacute cutaneous lupus erythematosus (SCLE) and discoid lupus erythematosus (DLE) can leave patients with damage and remnants of previous inflammation including dyspigmentation, scarring, atrophy and alopecia. Tissue resident memory T (Trm) cells have been implicated in the recurrence of SCLE and DLE.[1,2] However, the flare patterns in SCLE and DLE - whether in healed, scarred, dyspigmented, or uninvolved skin - remain underexplored. To address this gap, we conducted a retrospective study of SCLE and DLE patients, examining Cutaneous LE Disease Area and Severity Index-Activity (CLASI-A) scores and photographic documentation of inflammation recurrence.

Methods: Subjects were selected from a database of CLE patients seen at the autoimmune skin disease clinic of the Hospital of the University of Pennsylvania that has been ongoing since January 2007. A significant flare of skin disease was determined as an increase in the CLASI-A score of 7 or above in sequential clinic visits as previously described.[3] Two reviewers independently screened images before and after a flare and documented whether a flare occurred in previously inflamed skin, never involved skin, or both. The anatomical location of each flare observed in photographs was cross-verified with location-specific CLASI-A scores. Additional data collected included patient age, sex, smoking status, concomitant SLE, absolute change in CLASI-A score, and CLASI-Damage scores at the time of flare.

Results: Six-hundred and twenty-eight patients were screened, with 77 patients having a flare. We identified 27 patients (11 SCLE and 16 DLE) with photo-documentation of their skin flare. DLE patients were significantly more likely to experience flares confined to previously inflamed sites (83%) compared to SCLE patients (36%) (relative risk [RR] 2.29; $p<0.01$) (Figure 1a-c). In contrast, SCLE patients more frequently developed flares involving both previously affected and new locations (RR 3.8; $p<0.01$) (Figure 1d and e). Involvement of the neck, face and scalp were common locations newly affected by a

flare in SCLE patients. There was no statistically significant association detected from the additional data gathered (as can be seen in Table 1).

Figure 1.

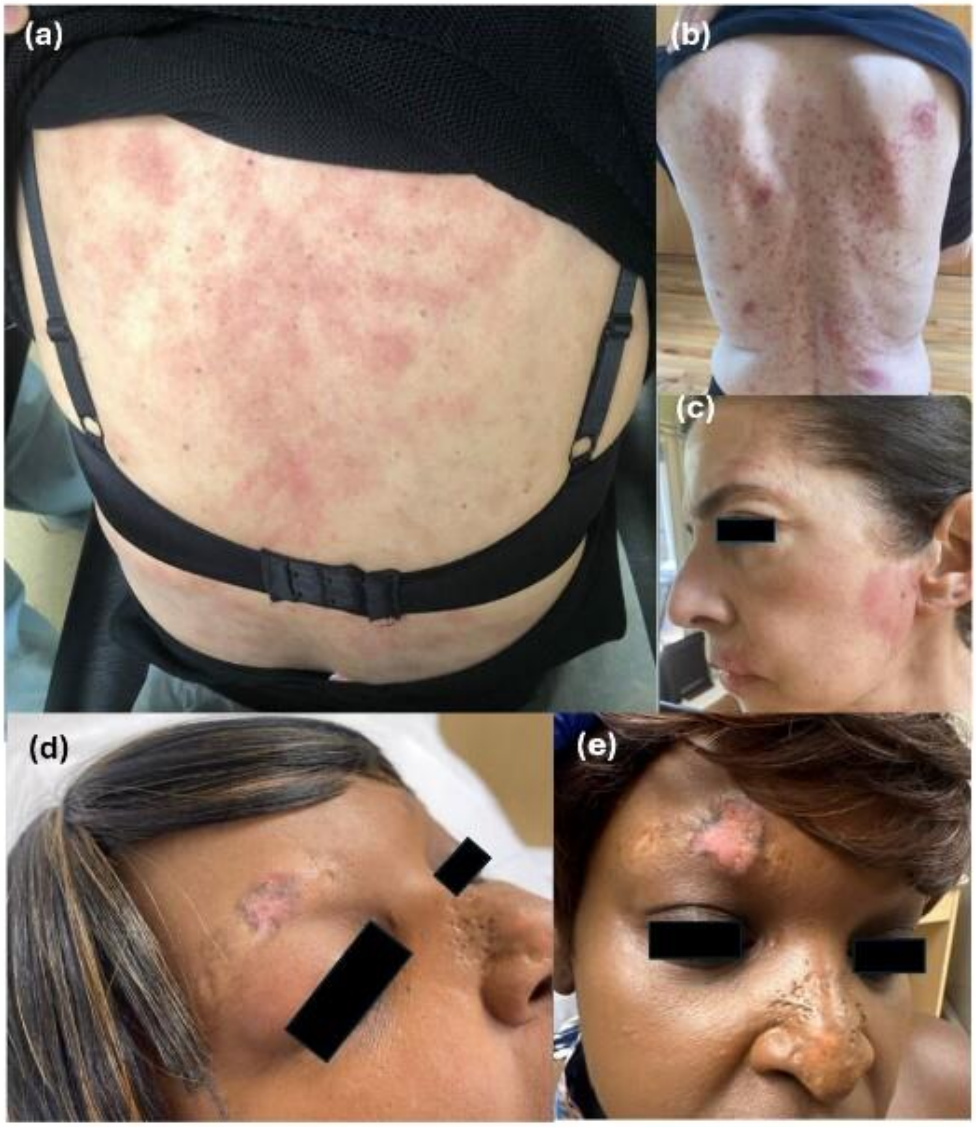

Figure 1. A patient with SCLE (a-c). (a) prior to a flare, showing mild disease confined to the back. (b) and (c) following a flare of skin disease, SCLE lesions not only recur in the same anatomical location, but the patient also developed new lesions to the neck, cheeks, forehead, cutaneous lips and scalp. A patient with DLE (d and e). (d) prior to a flare, showing mild activity to the right medial brow and scarring to the nasal bridge. (e) Flare of DLE to the right medial brow, worsening at the same anatomical location as before.

Table 1

Table 1. Patient Demographics		
	Old Location + New Location	Old Location
Median Age (± IQR)	61 ± 14.5	45 ± 21.5
Sex (%)		
M (n=3)	33	67
F (n= 24)	33	67
Ethnicity (%)		
White (n=19)	42	58
Black (n=7)	14	86
Asian (n=1)	0	100
Smoking Status (%)		
Smoker (n=10)	20	80
Non-Smoker (n=17)	41	59
Diagnosis (%)		
DLE (n=18) **	17	83
SCLE (n=11) **	64	36
Concomitant SLE (n=20)	35	65
		** $p < 0.01$
CLASI-A Score Δ (± IQR)	10 ± 5	11 ± 7
CLASI-D Score at time of flare (± IQR)	8 ± 8	13 ± 13.5

Conclusions: Our findings reveal distinct recurrence patterns in DLE and SCLE, with implications for understanding the mechanisms driving flares in these subtypes of CLE. A high proportion of DLE flares recurred in areas of previous inflammation including areas of scarring, atrophy and dyspigmentation. Previous studies have showed a higher number of Trm cells in DLE lesions compared to SCLE, suggesting a robust accumulation and later activation of Trm cells in healed DLE skin, supporting our observations and underscoring of the role of these cells in flares.[1,2] In contrast, SCLE flares were more likely to involve both previously inflamed sites and new areas, notably on the neck, face, and scalp. This broader distribution of SCLE flares may indicate that, in addition to Trm cell activation, external triggers such as UV exposure or medication-related photosensitivity may play a more significant role in driving disease recurrence. The distinct flare patterns observed in SCLE highlight a complex interplay between resident immune cells and environmental factors, which may contribute to the spread of inflammation to new skin regions even after initial sites have healed. A deeper understanding and further studies focusing on the interactions between Trm cells, the skin microenvironment, and external triggers for CLE flares may enable the development of targeted interventions, ultimately improving quality of life and clinical outcomes for patients with CLE.

PV063 / #180

Poster Topic: *AS07 - Cutaneous Lupus*

NOVEL 3-BASE OLIGONUCLEOTIDE THERAPEUTIC SOF-SKN™ ANTAGONISES TLR7/8 IN AUTOIMMUNE SKIN DISEASE

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Background/Purpose: Toll-like receptors (TLRs) 7 and 8 are innate immune sensors that trigger inflammatory cytokine and Type I interferon (IFN) production in response to short RNA fragments. Several recent studies have established that aberrant TLR7 activation is definitively linked to human lupus. We have discovered that synthetic, RNA-like 3-base oligonucleotides can be designed to bind to TLR7 and TLR8 with low nanomolar potency to effectively block their activation by RNA and synthetic agonists.

Methods: Based on this discovery, we undertook medicinal chemistry studies on select 3-base 2'-OMe oligonucleotides to generate therapeutics that harness TLR7 and TLR8 antagonism, leading to the development of an oligonucleotide drug candidate with dual antagonistic activities on human TLR7 and TLR8 (named SOF-16).

Results: We have previously reported that topical pre-treatment with our most potent murine TLR7 inhibitory oligonucleotide greatly ameliorated skin inflammation and reduced pro-inflammatory gene expression in the skin of mice treated with Aldara™ cream (containing the TLR7 agonist imiquimod). Using a multi-step formulation development process beginning with excipient screening and followed by extensive characterisation, including stability, *in vitro* permeation and release testing, and biological activity assays, we have now developed a proprietary topical formulation that uses Pharmacopoeia-compliant excipients to provide sustained and durable delivery of SOF-16 directly to TLR7/8-expressing immune cells in the dermis. SOF-16 formulated as SOF-SKN™ was able to blunt an inflammatory gene signature associated with Aldara™-driven TLR7 activation in mice. We have also generated crucial pre-clinical data around the pharmacokinetics, toxicity profile, and safety pharmacology of SOF-SKN™.

Conclusions: Our results establish that select 3-base oligonucleotides can be rationally designed to effectively antagonise TLR7/8 and dampen skin autoimmunity. SOF-16 formulated as SOF-SKN™ is currently in pre-clinical development as a first-line topical treatment for cutaneous lupus erythematosus (CLE), with a Phase I clinical trial

– HERACLES (Harnessing Endogenous Regulators Against CLE Study) – slated to begin in Australia in 2025.

PV064 / #310

Poster Topic: ***AS07 - Cutaneous Lupus***

TIME OF ONSET OF DISCOID LUPUS ERYTHEMATOSUS IMPACTS DISEASE OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: A LARGE-SCALE, PROPENSITY-MATCHED RETROSPECTIVE COHORT STUDY

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Background/Purpose: Discoid lupus erythematosus (DLE) is the most common form of chronic cutaneous lupus erythematosus, and up to twenty-five percent of patients with systemic lupus erythematosus (SLE) develop DLE lesions during their disease course. Prior research has suggested that the presence of DLE may modify the risk of disease complications, such as lupus nephritis and serositis, in patients with SLE, however, no studies have assessed the impact of time of onset of DLE on SLE outcomes. To address this gap, we investigated the impact of DLE incidence across three different time points on long-term disease complications in patients with SLE.

Methods: We conducted a retrospective cohort study using TriNetX, a Global Collaborative Network that provides access to the deidentified medical records of more than 130 million patients across 95 healthcare organizations worldwide. TriNetX data is derived from ICD10 codes in patient records; L93.0 was used for DLE and M32.1, M32.8, or M32.9 for SLE. Four cohorts were constructed: early-onset DLE (>1 year prior to SLE), concurrent DLE (within 1 year prior to or following SLE), late-onset DLE (>1 year following SLE), and SLE patients who were never diagnosed with DLE. Within each cohort, we included adults who were diagnosed with SLE within the past 10 years and excluded patients with other systemic connective tissue disorders (M30-M31 and M33-M36). Cohorts were propensity-matched at a 1:1 ratio based on demographics, metabolic syndrome, and other chronic conditions, using greedy nearest neighbor matching. The index event was defined as the date of SLE diagnosis and the risk of five-year incident outcomes following SLE diagnosis was compared between late-onset DLE and either early-onset DLE, concurrent DLE, or SLE without DLE using relative risk (RR) and 95% CI. All statistical analyses were conducted using the R studio package, version 3.2.3, incorporated within TriNetX.

Results: Following propensity-score matching, 4,595 patients were included in the analyses. Across all three analyses, patients with late-onset DLE had increased risk of malignant neoplasms (RR 1.42 [1.06,1.90] compared to early-onset DLE, RR 1.48 [1.09,2.01] compared to concurrent DLE, and RR 2.43 [1.69,3.49] compared to SLE without DLE). In the analysis comparing early-onset to late-onset DLE, the largest number of significant differences in 5-year incident outcomes was observed. SLE

patients with late-onset DLE patients had a higher RR of chronic kidney disease (RR 1.49 [1.02,2.18]), major adverse cardiovascular events (RR 1.61 [1.16,2.21]), bacterial and viral infections (RR 1.60 [1.19,2.16]), and hospitalizations (RR 1.30 [1.03,1.63]). Compared to SLE patients without DLE, patients with late-onset DLE had increased risk of UTI (RR 1.53 [1.08,2.17]) and arthritis (RR 1.39 [1.16,1.66]). In the analysis comparing SLE patients with concurrent DLE to SLE patients with late-onset DLE, the latter had increased risk of hematuria, but patients with concurrent DLE diagnosis had increased risk of mortality (RR 1.98 [1.32,2.97]) and hospitalization (RR 1.24 [1.04,1.48]).

Conclusions: Our findings suggest that the timing of DLE onset relative to SLE diagnosis has a substantial impact on long-term disease outcomes following SLE diagnosis. Late-onset DLE was associated with a notably higher risk of serious complications, particularly when compared to early-onset DLE. This risk stratification based on DLE onset timing highlights the importance of monitoring SLE patients for DLE development, particularly in the later stages of disease, and distinct DLE endotypes to enable earlier intervention and potentially mitigate adverse outcomes.

PV065 / #555

Poster Topic: *AS07 - Cutaneous Lupus*

BLOCKING IL-7 SIGNALING PREVENTS THE DEVELOPMENT OF LUPUS-LIKE AUTOIMMUNITY IN MICE BY RESTRICTING T CELL EXPANSION, ACTIVATION, AND COMMUNICATION WITH STROMAL CELLS

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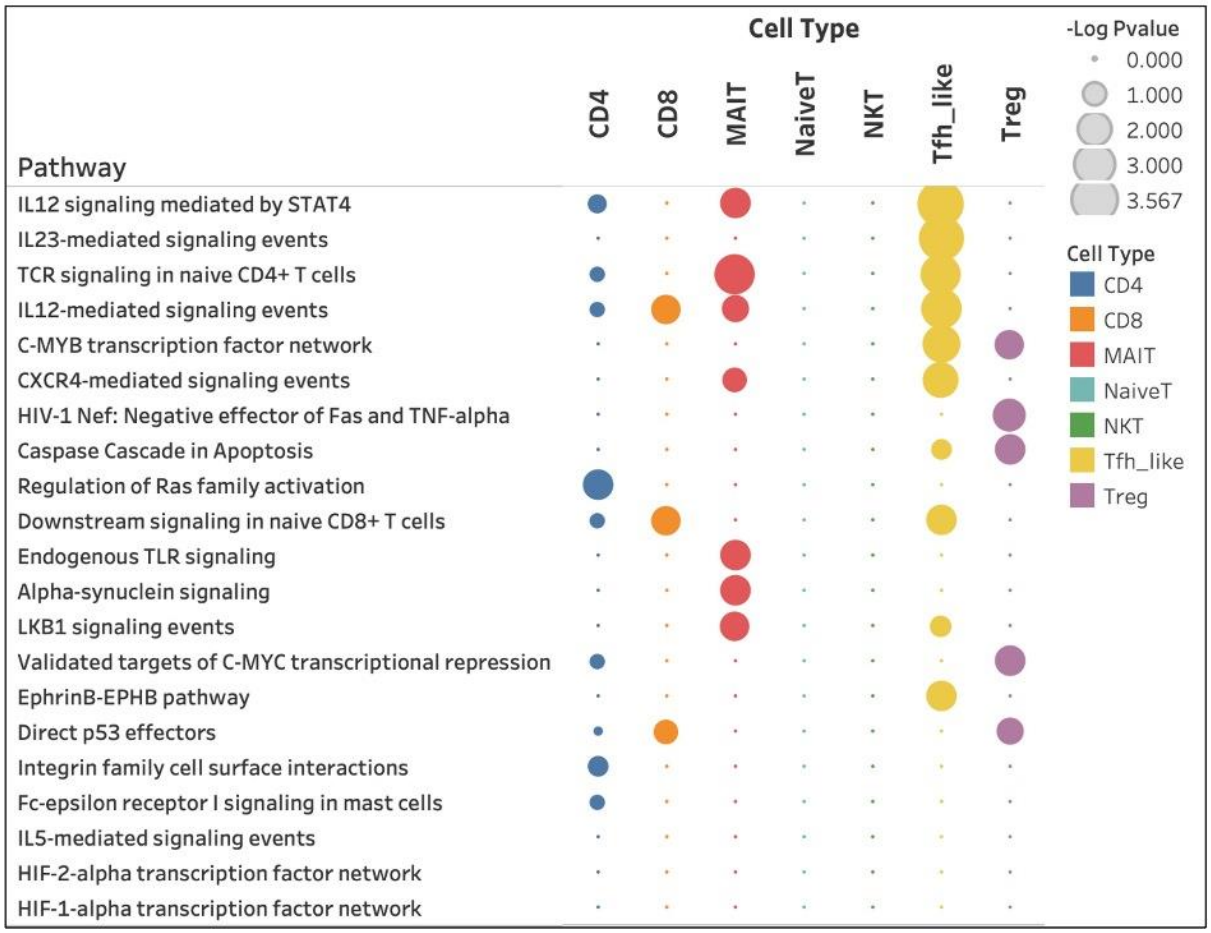
Background/Purpose: Our lab previously discovered that VGLL3, a female biased pro-inflammatory transcription factor, can drive lupus-like systemic inflammation when overexpressed under the *K5* promoter in mouse epidermis [1]. IL-7 signaling is more active in the skin of lupus patients vs. healthy donors and in our *K5-Vgll3* mice vs. *WT* controls. Deletion of peripheral *Il7r* in *K5-Vgll3* mice prevents the development of disease phenotype, with amelioration of dermatitis, splenomegaly, lymphadenopathy, and kidney damage.

Methods: Single-cell RNA sequencing with in-depth analyses was performed to assess cell-specific transcriptomic changes, cell-cell interactions, and molecular pathways shifted by the *Il7r* deletion in skin of *K5-Vgll3* mice (n=3 mice per genotype).

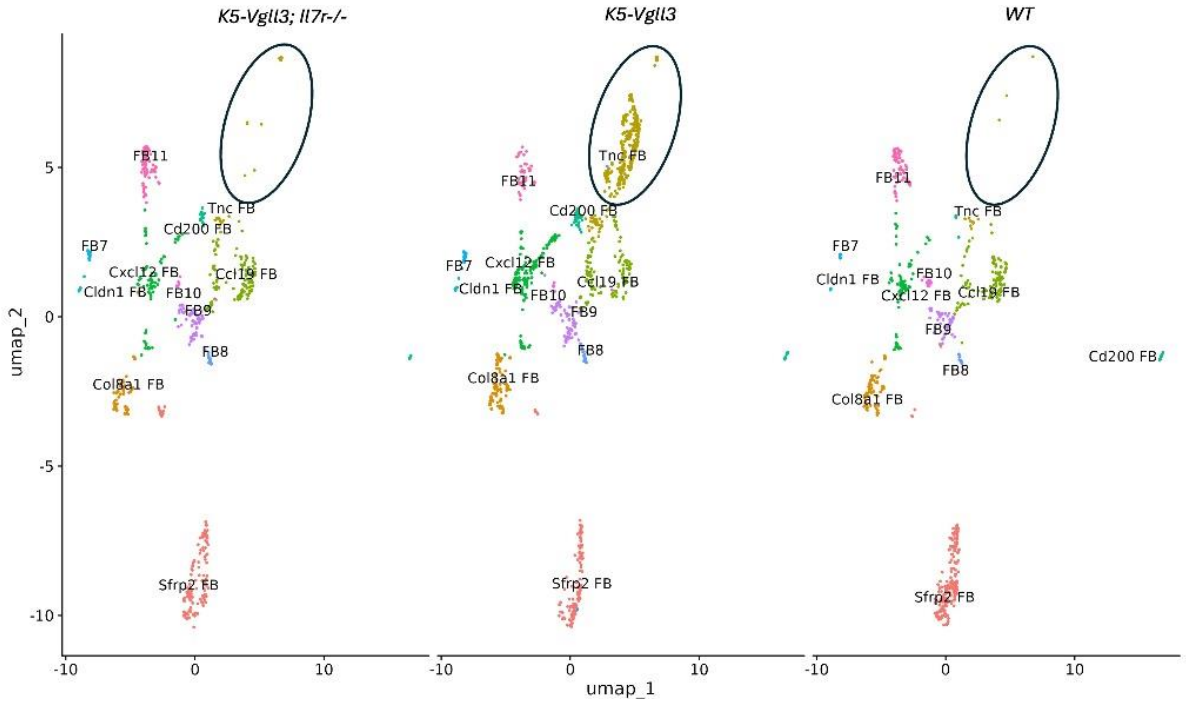
Results: *K5-Vgll3* mice exhibited a striking expansion of T cells in skin compared to *WT*, and *Il7r* deletion drastically reduced CD8, Tfh-like, and MAIT cells. Expression of *Cd69* and *Il2ra* activation markers were reduced across T cell sub-populations. Marked expansion of pro-fibrotic Tnc+ fibroblasts in *K5-Vgll3* mice was entirely eliminated by *Il7r* deletion (Fig. 1). *Il7r* deletion also restored the proportion of differentiated and keratinized keratinocytes to *WT* levels. Ligand-receptor analyses determined that deleting *Il7r* significantly reduced lupus-associated cell-cell interactions, with the highest reduction being in the communication between Cxcl12 fibroblasts and Tfh-like T cells. Pathway analysis identified Beta1 integrin and Syndecan-1 signaling in fibroblasts and Il-12, Il-23, and TCR signaling in T cells (Fig. 2) as the most affected by *Il7r* deletion.

Reference: [1] Billi AC. JCI Insight 2019;Apr18;4(8):e127291.

Pathways affected in T cells by *Il7r* deletion in *K5-Vgll3* mice



Expansion of Tnc fibroblasts in *K5-Vgll3* mice is eliminated by by *Il7r* deletion



Conclusions: VGLL3-driven lupus-like autoimmunity is dependent on IL-7 signaling and involves expansion and activation of several T cell sub-types and changes in stromal composition, most notably an increase in Tnn fibroblasts. Restricting IL-7 signaling by deleting *Il7r* successfully shifts transcriptomic changes and cell-cell interactions towards a healthy state, which underscores the potential of its targetability for therapeutic intervention in lupus patients.

PV066 / #446

Poster Topic: *AS07 - Cutaneous Lupus*

ACCELERATED DERMAL FIBROBLAST AGEING IN CUTANEOUS LUPUS ERYTHEMATOSUS LESIONS

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Background/Purpose: The pathogenesis of cutaneous lupus erythematosus (CLE) is not fully understood. Whilst much attention has been given to the inflammatory cell infiltrate, much less is known about changes to stromal and other structural cells. Aged (or senescent) cells can secrete pro-inflammatory chemokines and cytokines and may contribute to the inflammatory milieu. We aimed to identify whether non-immune cells expressed gene signatures of premature cellular aging in skin samples from patients with SLE.

Methods: Lesional and non-lesional skin biopsies were obtained from patients with SLE and healthy controls (HC). Samples were enzymatically digested and 3' scRNA-seq performed using the Chromium 10x Genomics platform. Six aged gene signatures (senCID) from Tao et. al. [1] were validated in the GSE130973 dataset of young and old HC skin. Each SID is typically enriched in genes of specific function (SID1: cell proliferation, SID2: lipid and nucleotide synthesis, SID3: mitochondria/redox reactions, SID4: unfolded protein response, SID5: protein ubiquitination, SID6: vesicle loading).

Results: Of the 6 gene signatures, SID1-5 scores were increased in the fibroblast (FB) and endothelial cell populations in older HC skin compared to younger skin. We then applied these signatures to 6 samples from 3 patients with SLE (3 lesional and 3 non-lesional) and 3 HC. Overall, the gene scores of each SID demonstrated a bimodal pattern in SLE. For most SIDs, the lower gene scores were in T lymphocytes. As FBs may drive persistence of inflammation in other conditions such as rheumatoid arthritis, we focussed our analysis on aged FB in CLE skin. Whilst there was no difference in the SID1 score in FBs between groups, SID2 and SID3 were increased in lesional FBs compared to both non-lesional or HC FBs. SID4-6 demonstrated a stepwise increase from HC, to non-lesional and lesional FBs. The expression of SID2-6 also varied between fibroblast subsets. Mechano-sensing FBs (expressing *CDH19*) showed little difference in SID2-6 scores between sample types. In contrast, both immunofibroblast subsets (*TNFSF13B+/CCL19+ and TNFSF13B+/CCL19-)* appeared to demonstrate the greatest

difference in SID2-6 scores between sample types. Expression of SID4 and SID6 was also markedly increased in lesional CXCL1+ and pro-fibrotic (DPP4+) FB subsets.

Conclusions: The SID gene modules 1-5 are increased in healthy aged FBs. Distinct FB subsets from cutaneous lesions in SLE show signs of increased cellular ageing. These cells express pro-inflammatory genes and may offer novel therapeutic targets to reduce the persistence of cutaneous inflammation. [1] Tao et. al. Cell Metabolism. 2024;36:1126-1143

PV067 / #449

Poster Topic: *AS07 - Cutaneous Lupus*

CONSTRUCT VALIDITY OF THE EQ-5D-5L IN CUTANEOUS LUPUS ERYTHEMATOSUS: A SECONDARY DATA ANALYSIS

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Background/Purpose: Cutaneous lupus erythematosus (CLE) significantly impacts health-related quality of life (HRQoL). Although the EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) is a widely used HRQoL measure, its psychometric properties in CLE have not been previously investigated. Given the important role of the EQ-5D-5L in health technology assessments (HTA), establishing the validity of this instrument is crucial for accurately reflecting health status and treatment effects in CLE, thereby guiding clinical and HTA decision making and improving patient care. Therefore, this study aimed to investigate the construct validity of the EQ-5D-5L in people with CLE.

Methods: This was a secondary analysis of data from a prospective, cross-sectional, multicenter, multinational study assessing pruritis in participants with CLE [1]. Outcome measures included the EQ-5D-5L, Dermatology Life Quality Index (DLQI), Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity Scale (CLASI-A), Worst Itch Numeric Rating Scale (NRS), Worst Pain NRS, and the 12-item Pruritus Severity Scale (12-PSS). Descriptive analyses were performed on all demographic and disease characteristic variables. Convergent validity was assessed by examining correlations between the EQ-5D-5L domains and derived EQ-5D-5L index value with other disease-specific measures. Known-groups validity was evaluated by analyzing whether the EQ-5D-5L captured expected differences among participant groups with different CLASI-A severity levels: mild (score 0–9), moderate (10–20), and severe (21–70).

Results: A total of 149 people with CLE were included in the study; 75% were female and 79% were Caucasian/White, with a mean (SD) age of 49.6 (15.5) years. Mean (SD) CLASI-A score was 7.35 (7.77; n = 134) and EQ-5D-5L index value was 0.81 (0.21; n = 137). The EQ-5D-5L index value showed statistically significant low moderate (with CLASI-A and Worst Itch NRS) to high moderate (with DLQI, 12-PSS, and Worst Pain NRS)

correlations with select reference variables. The known-groups hypothesis was confirmed with a medium effect size of $\eta^2 = 0.11$. Only the Pain/Discomfort and Anxiety/Depression domains demonstrated statistically significant low moderate to high moderate correlations with at least two reference variables. The known-groups hypothesis was confirmed for the Self-Care, Pain/Discomfort, and Anxiety/Depression domains with small to medium η^2 effect sizes ($0.05 \leq \eta^2 \leq 0.08$). Sensitivity analyses, excluding five outliers, resulted in the disappearance of all high moderate correlations of the EQ-5D-5L domains and derived EQ-5D-5L index value. Only the known-groups hypothesis of the EQ-5D-5L index value and the Self-Care domain remained confirmed, but with a diminished small ($\eta^2 = 0.06$) and medium ($\eta^2 = 0.10$) effect size.

Conclusions: This study is the first to investigate the construct validity of the EQ-5D-5L in CLE, indicating moderate convergent and known-groups validity. However, sensitivity analysis results were notably weaker, compromising the robustness of the findings and suggesting potential limitations in the ability of the EQ-5D-5L measure to fully capture all health status dimensions relevant to CLE. Further psychometric studies are warranted to determine the overall appropriateness of the EQ-5D-5L in CLE. [1.] Samotij D. Lupus 2021;30:1385–93. The healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945) funded the study and editorial support by Bioscript Group.

PV068 / #344

Poster Topic: ***AS07 - Cutaneous Lupus***

ALL SUBCOMPONENTS OF THE CUTANEOUS LUPUS ERYTHEMATOSUS DISEASE AREA AND SEVERITY INDEX–ACTIVITY (CLASI-A) ARE RELEVANT TO IDENTIFY AND DETECT CHANGES IN SKIN ACTIVITY

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Background/Purpose: Part B of the Phase 2 LILAC study (NCT02847598) demonstrated the efficacy of litifilimab versus placebo, with a significant decrease in percent change from baseline in CLASI-A score at Week 16 in participants with active cutaneous lupus erythematosus (CLE) with or without systemic manifestations. [1.] CLASI-A measures disease activity in CLE across several anatomical locations, based on five clinical subcomponents: erythema, scale/hypertrophy, mucous membrane lesions, recent hair loss (preceding 30 days), and non-scarring alopecia. [2.] This exploratory analysis examined the contribution of all five CLASI-A subcomponents or anatomical locations in the total scoring change and explored the association between sunlight-exposed body areas and severity of the symptom.

Methods: The study design and participants' baseline characteristics for LILAC Part B have been reported previously. [1.] The distribution of the CLASI-A clinical subcomponents for the pooled Part B population (all litifilimab doses and placebo; N = 132) was analyzed by anatomical location at baseline and at Week 16. Change in CLASI-A scores by clinical subcomponent for the pooled study population at Week 16 was evaluated using point improvement/worsening from baseline at each anatomical location. Reported changes in CLASI-A subcomponent point scores could fall into the following ranges: erythema (from −3 to +3), scale/hypertrophy (from −2 to +2), mucous membrane lesions and recent hair loss (from −1 to +1), and non-scarring alopecia (from −3 to +3). Data are reported as observed; no imputation of missing data was conducted.

Results: At baseline, a higher proportion of participants reported 'red' (score 2) and 'dark red' (score 3) erythema in the more sunlight-exposed areas of the frontal V-neck area, ears, arms, nose (including malar area), and rest of the face (ranges across these anatomical areas: 25.0%–34.1% ['red'], 2.3%–18.9% ['dark red']) than in the less-exposed areas of the feet, legs, and abdomen (ranges: 4.5%–6.1% ['red'], 0.8%–3.8% ['dark red']) (**Table 1**). At Week 16, changes in CLASI-A scores by subcomponents were observed at all anatomical locations and were consistent with the distribution of scores

at baseline, with the greatest improvements observed in the more highly exposed areas (**Table 2**). Both 1-point and 2-point improvements in the erythema subcomponent score were reported at all anatomical locations, in up to 33.3% and 12.4% of participants per location, respectively. A 3-point improvement in erythema was observed at almost all locations, in up to 2.9% of participants per location. Similar findings were observed for scale/hypertrophy.

Table 1: Distribution of CLASI-A subcomponent scores for each anatomical location at baseline

Anatomical location, n (%)	Erythema (score)				Scale/hypertrophy (score)		
	Absent (0)	Pink (1)	Red (2)	Dark red (3)	Absent (0)	Scale (1)	Verrucous/ hypertrophic (2)
Rest of the face	33 (25.0)	32 (24.2)	42 (31.8)	25 (18.9)	64 (48.5)	54 (40.9)	14 (10.6)
Nose (including malar area)	48 (36.4)	27 (20.5)	45 (34.1)	12 (9.1)	85 (64.4)	37 (28.0)	10 (7.6)
Arms	53 (40.2)	29 (22.0)	35 (26.5)	15 (11.4)	79 (59.8)	42 (31.8)	11 (8.3)
Ears	54 (40.9)	35 (26.5)	33 (25.0)	10 (7.6)	73 (55.3)	51 (38.6)	8 (6.1)
Front V-neck area	67 (50.8)	29 (22.0)	33 (25.0)	3 (2.3)	101 (76.5)	30 (22.7)	1 (0.8)
Hands	80 (60.6)	24 (18.2)	22 (16.7)	6 (4.5)	101 (76.5)	24 (18.2)	7 (5.3)
Posterior neck and/or shoulders	81 (61.4)	18 (13.6)	24 (18.2)	9 (6.8)	98 (74.2)	32 (24.2)	2 (1.5)
Back, buttocks	85 (64.4)	15 (11.4)	19 (14.4)	13 (9.8)	99 (75.0)	27 (20.5)	6 (4.5)
Chest	86 (65.2)	16 (12.1)	24 (18.2)	6 (4.5)	110 (83.3)	21 (15.9)	1 (0.8)
Legs	108 (81.8)	11 (8.3)	8 (6.1)	5 (3.8)	113 (85.6)	16 (12.1)	3 (2.3)
Abdomen	118 (89.4)	5 (3.8)	8 (6.1)	1 (0.8)	121 (91.7)	11 (8.3)	0
Feet	119 (90.2)	5 (3.8)	6 (4.5)	2 (1.5)	122 (92.4)	9 (6.8)	1 (0.8)

	Mucous membrane lesions (score)		Recent hair loss (score)		Alopecia (score)			
	Absent (0)	Lesion/ ulceration (1)	No (0)	Yes (1)	Absent (0)	Diffuse (1)	Focal or patchy in one quadrant (2)	Focal or patchy in more than one quadrant (3)
n (%)	105 (79.5)	27 (20.5)	62 (47.0)	70 (53.0)	46 (34.8)	26 (19.7)	9 (6.8)	51 (38.6)

Participants from all treatment arms in LILAC Part B are included (N = 132). Results are based on observed data; no imputation for missing data was conducted for this analysis.

Table 2: Distribution of change from baseline in CLASI-A subcomponent scores for each anatomical location at Week 16

Anatomical location, n (%)	Erythema (score)							Scale/hypertrophy (score)				
	−3	−2	−1	0	+1	+2	+3	−2	−1	0	+1	+2
Rest of the face	2 (1.9)	13 (12.4)	35 (33.3)	50 (47.6)	3 (2.9)	1 (1.0)	1 (1.0)	3 (2.9)	26 (24.8)	69 (65.7)	7 (6.7)	0
Nose (including malar area)	1 (1.0)	12 (11.4)	35 (33.3)	52 (49.5)	5 (4.8)	0	0	3 (2.9)	23 (21.9)	77 (73.3)	2 (1.9)	0
Arms	3 (2.9)	11 (10.5)	30 (28.6)	55 (52.4)	4 (3.8)	2 (1.9)	0	1 (1.0)	17 (16.2)	84 (80.0)	3 (2.9)	0
Ears	1 (1.0)	12 (11.4)	29 (27.6)	58 (55.2)	5 (4.8)	0	0	1 (1.0)	26 (24.8)	73 (69.5)	5 (4.8)	0
Front V-neck area	0	10 (9.5)	20 (19.0)	71 (67.6)	3 (2.9)	1 (1.0)	0	1 (1.0)	18 (17.1)	84 (80.0)	2 (1.9)	0
Hands	1 (1.0)	5 (4.8)	20 (19.0)	75 (71.4)	3 (2.9)	1 (1.0)	0	2 (1.9)	10 (9.5)	89 (84.8)	4 (3.8)	0
Posterior neck and/or shoulders	1 (1.0)	10 (9.5)	16 (15.2)	71 (67.6)	5 (4.8)	2 (1.9)	0	2 (1.9)	14 (13.3)	82 (78.1)	7 (6.7)	0
Back, buttocks	3 (2.9)	10 (9.5)	14 (13.3)	76 (72.4)	2 (1.9)	0	0	3 (2.9)	10 (9.5)	89 (84.8)	3 (2.9)	0
Chest	2 (1.9)	12 (11.4)	11 (10.5)	76 (72.4)	4 (3.8)	0	0	0	13 (12.4)	90 (85.7)	2 (1.9)	0
Legs	3 (2.9)	3 (2.9)	7 (6.7)	92 (87.6)	0	0	0	0	9 (8.6)	96 (91.4)	0	0
Abdomen	0	4 (3.8)	5 (4.8)	93 (88.6)	3 (2.9)	0	0	0	3 (2.9)	102 (97.1)	0	0
Feet	0	3 (2.9)	4 (3.8)	97 (92.4)	1 (1.0)	0	0	0	5 (4.8)	100 (95.2)	0	0

	Mucous membrane lesions (score)			Recent hair loss (score)			Alopecia (score)						
	−1	0	+1	−1	0	+1	−3	−2	−1	0	+1	+2	+3
n (%)	18 (17.1)	85 (81.0)	2 (1.9)	33 (31.4)	66 (62.9)	6 (5.7)	6 (5.7)	2 (1.9)	11 (10.5)	82 (78.1)	4 (3.8)	0	0

Participants from all treatment arms in LILAC Part B are included (N = 132). Results are based on observed data; no imputation for missing data was conducted for this analysis.

Conclusions: No single subcomponent of the measure drives the CLASI-A score or the CLASI-A score changes. CLASI-A is able to identify skin activity in terms of both the overall severity and changes in the visible and uncovered areas that are most vulnerable to photosensitivity and that are important to patients. This further supports the relevance of all five subcomponents of CLASI-A in describing disease activity in CLE. **References:**

[1.] Werth V. N Engl J Med 2022;387:321-31.
[2.] Albrecht J. J Invest Dermatol 2005;125:889-94. This study was funded by Biogen (Cambridge, MA, USA). Writing and editorial support were provided by Selene Medical Communications (Macclesfield, UK), funded by Biogen.

PV069 / #444

Poster Topic: ***AS08 - Cytokines and Cell Trafficking***

INCREASE OF IL10 AND INFA2 ARE ASSOCIATED TO CLINICAL ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS

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Background/Purpose: Systemic lupus erythematous (SLE) is an autoimmune disease characterized by deregulation of cytokine production. Interferon (IFN) is a proinflamatory cytokine considered as a key molecule in the SLE etiopathogenesis, being responsible of the differentiation of dendritic cells from monocytes, and indirectly of IL10 upregulation. Moreover, B lymphocyte stimulator factor (BLyS) is an important factor in the SLE pathology; elevated serum levels of soluble BlyS are at increased risk of flare. We aimed to analyze the association between inflammatory cytokine levels (BLyS, IFNa2, IFNb, IFNg and IL10) and SLE clinical activity in SLE patients.

Methods: A longitudinal, observational prospective study with evaluations at baseline and follow-up visits every 3 months (for 1 year) in SLE patients (SLICC 2012 criteria) was performed. In all cases complete laboratory test, clinical evaluation and SLEDAI score was carried out. We analyzed inflammatory cytokines serum levels by colorimetric methods.

Results: 45 SLE patients (86.7% female) participated in the study, with a mean age at diagnosis of 32.8 (16.2) years and a mean time of disease evolution of 17.9 (11.4) years. The 28.9% of patients showed SLEDAI>6 at the basal visit. 30 patients were under glucocorticoid treatment, 30 under antimalarials and 11 patients initiate belimumab treatment at the basal visit. SLEDAI and inflammatory cytoquine levels during follow-up is shown in table.

	V0 Mean (DS)	V3 Mean (DS)	V6 Mean (DS)	V9 Mean (DS)	V12 Mean (DS)
SLEDAI score	6.1 (5.4)	3.5 (3.4)	5.1 (4.1)	3.7 (2.9)	3.6 (2.6)
IFNa2 (pg/mL)	202.6 (608.1)	115.2 (219.3)	170.6 (634.4)	103.2 (194.4)	157.2 (523.1)
IFNb (pg/mL)	74.6 (91.2)	72.6 (114.6)	76.2 (101.4)	77.2 (114.2)	74.6 (97.5)

IFNg (pg/mL)	257.2 (413.7)	293.6 (395.7)	334.3 (485.6)	289.2 (354.7)	370.5 (794.9)
IL-10 (pg/mL)	14.35 (21.07)	15.48 (16.92)	11.79 (15.23)	11.02 (11.14)	11.86 (11.76)
BLyS (pg/mL)	3073.4 (2198.6)	6232.4 (4838.8)	4111.6 (3593.7)	4812.9 (3786.8)	5432.3 (4747.8)

Statistical analysis showed significant association between high SLEDAI score and increased IL-10 (P=0.014) and IFNa2 levels (0.009), as well as a tendency with IFN-beta (P=0.057), independently of the time of follow-up. High anti-dsDNA levels were significantly associated to elevated IFN-beta (P=0.005) and IFN-gamma (P=0.038), and low levels of C3 with an IL-10 increment (P=0.006). No influence of age at diagnosis, time of evolution, vitamin D levels, corticoids and tobacco use in cytoquine levels was observed. At basal visit, patients under antimalarials treatment exhibit low levels of IL-10 (P=0.007) and IFNb (P=0.024); IL-10 behavior is maintained during follow-up (P=0.012) and there is a tendency for IFNb (P=0.07). Patients under belimumab treatment show high levels of BLyS (P<0.001) and a tendency of a decrease of IL10 levels during follow-up (P=0.06).

Conclusions: High levels of IL-10, IFN-alpha2, IFN-beta and IFN-gamma were associated to clinical activity, independently of the time of follow-up. Antimalarial treatment influence IL-10 and IFNb levels, and Belimumab treatment modify BLyS and IL-10 levels.

PV072 / #309

Poster Topic: ***AS08 - Cytokines and Cell Trafficking***

DIFFERENCES IN CYTOKINE PROFILE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DEPENDING ON DISEASE ACTIVITY

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Background/Purpose: To assess the cytokine profile in patients with SLE depending on the disease activity

Methods: Peripheral blood of 87 patients (81 women (93.1%) and 6 men (6.9%)) with a SLE (SLICC 2012), Me(IQR) age 34 (26-41) years, disease duration 3.0 (0.3-12.0) years; SLEDAI-2K 7 (4-11); 61 patients had a high disease activity (SLEDAI-2K≥6), 26 patients had low disease activity (SLEDAI-2K<6) were assessed for cytokine profile. The level of G-CSF, GM-CSF, IFN-γ, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12(p70), IL-13, IL-17, MCP-1, MIP-1β, TNF-α, IL-1ra, IL-9, IL-15, Eotaxin, FGF basic, MIP-1a, PDGF bb, RANTES, VEGF, CTACK (CCL27), GROa (CXCL 1), HGF, IFNα2, IL-1a, IL-2Ra, IL-3, IL-12(p40), IL-16, IL-18, IP-10, LIF, MCP-3 (CCL 7), M-CSF, MIF, MIG, β-NGF, SCF, SCGF-β, SDF-1a (CXCL 12), TNF-β, TRAIL was tested by multiplex technology xMAP.

Results: Among patients with high disease activity compared with patients with low activity a higher level of IFNγ (1.07 (0.14-3.44) vs 0.44 (0.01-1.0)), IL-7 (0.14 (0.01-6.05) vs 0.01 (0.01-0.23)), IL-2Ra (14.31 (8.95-20.12) vs 9.005 (6.16-11.43)), IL12(p40) (2.33 (0.01-10.55) vs 0.01 (0.01-1.44)), IL-18 (12.91 (9.18-19.72) vs 10.01 (8.03-12.17)), SCGF-β (7954.68 (5835.7-9368.4) vs 6191.1 (5285.1-8117.4)) and a lower concentration of MIP-1β (100 (88.84-111.34) vs116.64 (102.8-123.05)), IL-9 (157.32 (141.3-168.14) vs 171.62 (155.9-179.9)), LIF (11.89 (9.52-14.98) vs 4.26 (11.24-17.69)), CXCL-12 (416.7 (163.1-559.0) vs 542.4 (394.1-724.4)), TNF-β (299.86 (272.3-343.25) vs 354.7 (316.6-400.9)), NGF-β (0.74 (0.1-1.82) vs 1.665 (0.89-3.72)) was detected, $p<0.05$. A positive correlation was found between SLEDAI-2K and levels of G-CSF (r=0.3), IFN-γ (r=0.33), IL-5 (r=0.29), IL-6 (r=0.25), IL-7 (r=0.29), IL-8 (r=0.26),IL-10 (r=0.33), IL-12(p70) (r=0.23), MIP-1a (r=0.26), VEGF (r=0.22), IL-2Ra (r=0.35), IL-12(p40) (r=0.27), IL-16 (r=0.22), IL-18 (r=0.31), M-CSF (r=0.44); negative correlation between SLEDAI-2K and levels of MIP-1β (r =- 0.33), RANTES (r=-0.36).

Conclusions: IFNγ, IL12(p40), IL-18, SCGF-β can be considered as potential markers of systemic lupus erythematosus activity.

PV070 / #88

Poster Topic: ***AS09 - Emerging Approaches in SLE Management***

RESULTS OF THE MOVES STUDY: A FEASIBILITY STUDY OF THE MOTIVATING INDIVIDUALS WITH LUPUS TO EXERCISE PROGRAM

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Background/Purpose: Physical activity is an evidence-based modifiable lifestyle behavior that can manage symptoms of systemic lupus erythematosus (SLE). However, rates of physical activity are low among persons with SLE. This study investigated the feasibility of an exercise intervention grounded in social cognitive theory and motivational interviewing for improving patient-reported outcomes and physical function in SLE.

Methods: Participants were randomized into the MOVES program or a waitlist control. All participants met criteria: >=18 years, self-reported diagnosis of SLE and <150 minutes of moderate-to-vigorous physical activity (MVPA) per week, severe fatigue via fatigue severity scale. The MOVES intervention was a four-month home-based exercise program that included a manual, Fitbit Inspire 2, and resistance bands. Participants completed an orientation session via Zoom and received support from a motivational interviewing coach via six coaching calls (weeks 3, 5, 7, 10, 13, 16). PROMIS® measures of fatigue, physical function, sleep disturbance, pain interference, anxiety, and depression were measured at baseline, post-intervention, and follow-up (two months post-intervention). Accelerometers were worn for seven days during waking hours to measure daily MVPA minutes (2020+counts) at baseline and post-intervention, with valid monitoring defined as a minimum of 3 days of 10+ hours of wear time. Weekly MVPA minutes were calculated as mean daily MVPA minutes times seven. Descriptive statistics were calculated, and data were analyzed using linear mixed models.

Results: Twenty-eight participants, mean(SD) age was 46(9.5); 100% identified as female, 50% self-identifying as Black/African American, 46.4% White, 3.6% Asian; 85.7% having some college education, completed baseline, post, and follow-up testing (16 intervention, 12 control; no significant differences at baseline). Linear mixed model analyses showed that the intervention group had significantly larger improvements in fatigue and physical function than the control group, both clinically and statistically, at both the post-intervention (p=0.01 for both) and follow-up (fatigue p=0.01, physical function p=0.02) While no statistically significant differences were observed for pain interference, anxiety, depression, sleep disturbance, or MVPA at post-intervention or

follow-up, clinically meaningful changes were evident in the intervention group at post-intervention. Clinically meaningful changes, as indicated by Cohen's d, were observed for fatigue (d=-1.7), physical function (d=0.56), pain interference (d=-0.99), anxiety (d=-0.98), and depression (d=-1.16) between baseline and post-intervention. These clinically meaningful changes were observed for fatigue (d=-1.7), physical function (d=0.52), anxiety (d=-0.62), and depression (d=-1.09) between baseline and follow-up.

Table 1. Outcomes by Timepoint and Group

Timepoint	Group	Fatigue	Pain Interference	Anxiety	Depression	Sleep Disturbance	Physical Function	Average Weekly MVPA
Baseline	Control	65.00 (4.65)	64.30 (7.90)	58.00 (7.75)	58.90 (13.40)	55.60 (10.95)	37.60 (8.45)	35 (49.50)
	Intervention	65.80 (6.70)	63.40 (10.68)	62.95 (7.00)	60.50 (10.83)	56.10 (11.75)	37.05 (12.60)	28 (37)
Post	Control	65.95 (6.45)	65.45 (7.05)	60.50 (15.03)	57.50 (17.50)	56.45 (9.18)	37.50 (6.45)	24 (94.50)
	Intervention	51.75 (14.13)	56.85 (12.33)	53.15 (14.40)	53.30 (10.28)	52.95 (17.76)	44.00 (10.58)	35 (34)
Follow-up	Control	65.90 (5.88)	61.55 (10.13)	57.65 (18.13)	51.95 (20.45)	55.05 (5.40)	37.00 (8.80)	--
	Intervention	55.40 (9.15)	60.25 (12.25)	56.85 (13.40)	53.85 (4.60)	54.60 (13.58)	46.50 (16.75)	--

Note: Data presented as Median(IQR); MVPA=moderate-to-vigorous physical activity

Conclusions: The MOVES intervention led to significant and maintained improvements in fatigue and physical function, with clinically meaningful reductions observed in fatigue, pain interference, anxiety, and depression and improvements in physical function. Findings highlight the potential of the MOVES program to address key patient-reported outcomes among persons with SLE.

PV071 / #233

Poster Topic: ***AS09 - Emerging Approaches in SLE Management***

PLACENTA ABNORMALITIES IN SYSTEMIC LUPUS ERYTHEMATOSUS: NOVEL MARKER OF ADVERSE PREGNANCY OUTCOMES

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Background/Purpose: Placenta-mediated adverse pregnancy outcomes (APO) are a huge concern in SLE. Recent efforts to understand APO include the establishment of the 2016 Amsterdam classification criteria, developed to standardize placental pathology evaluation. No study to date evaluated the Amsterdam criteria in SLE. Using the prospective "Lupus prEGnAnCY (LEGACY)" biobank, we assessed the relationship between placental abnormalities, lupus anticoagulant (LAC), and APO, applying the Amsterdam criteria.

Methods: LEGACY is a prospective cohort enrolling SLE pregnancies (before the 17th gestational week). Relevant information is collected at each trimester and/or end-of-pregnancy visits. We evaluated pregnancies delivered beyond 17 weeks at the Montreal site. Placenta pathology was defined as abnormal if fulfilling at least one of the 4 main Amsterdam classification subtypes: 1) maternal vascular malperfusion, 2) fetal vascular malperfusion, 3) acute chorioamnionitis, and/or 4) villitis of unknown etiology. Pregnancies with and without abnormal pathology were further characterized based on presence of LAC and APO (i.e. stillbirth, placental insufficiency, gestational hypertension, preeclampsia, small-for-gestational age neonate <5%).

Results: Of 44 LEGACY pregnancies delivered (beyond 17 weeks), 32 (73%) had placenta pathology available. Among these 32, 15 (47%) had abnormal pathology. Of those with abnormal pathology, 6/15 (40%) had maternal vascular malperfusion, 5/15 (33%) acute chorioamnionitis, 4/15 (27%) villitis of unknown etiology, and 1/15 (7%) fetal vascular malperfusion. Mean gestational age at delivery was substantially lower in pregnancies with abnormal pathology [mean 33.7 weeks, standard deviation (SD) 6.8] versus those with normal pathology (mean 37.8 weeks, SD 1.7), with a difference in mean gestational age of -4.1 weeks (95% CI -0.6, -7.6). LAC was more frequent in pregnancies with abnormal pathology (4/15; 27%) as opposed to pregnancies with normal pathology (2/17; 12%). APO occurred in 8/15 (53%) pregnancies with abnormal pathology (including 3 with early preterm preeclampsia <34 weeks) as opposed to 7/17 (41%) pregnancies with normal pathology (none with early preterm preeclampsia). Maternal vascular malperfusion was strongly associated with APO (odds ratio 8.1; 95% CI 0.8, 83.7), although the CI included the null.

Conclusions: In this cross-sectional analysis, SLE pregnancies with abnormal placental pathology, particularly maternal vascular malperfusion, experienced shorter gestation and more severe placenta-mediated APO, including early preterm preeclampsia. Future studies will aim to expand the sample, and investigate if placental abnormalities in one pregnancy helps predict APO in subsequent pregnancies.

PV073 / #286

Poster Topic: ***AS09 - Emerging Approaches in SLE Management***

SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS IN HEALTHY VOLUNTEERS OF VENT-03, A NOVEL CGAS INHIBITOR FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: The detection of foreign DNA by the innate immune system is a vital component of the host response to pathogens. In mammalian cells, this task is performed in large part by cyclic GMP AMP synthase (cGAS). Although the indiscriminate detection of DNA by cGAS ensures the detection of almost all pathogens, it can also trigger autoinflammation in response to the aberrant accumulation of self-DNA, central to the immunopathology of multiple diseases such as systemic lupus erythematosus (SLE), systemic sclerosis, dermatomyositis, and several forms of cardiomyopathies. cGAS is therefore a drug target with a broad therapeutic potential across autoimmune disorders. VENT-03 is a potent, selective and orally available cGAS inhibitor discovered by Ventus Therapeutics using a proprietary platform for identifying novel small molecule therapeutics (ReSOLVE™). VENT-03 is the first cGAS inhibitor to be tested in humans and herein we describe its safety, tolerability, pharmacokinetics and pharmacodynamics in healthy volunteers.

Methods: 72 healthy male and female volunteers received single ascending oral doses (SAD) of VENT-03 or placebo up to 2000 mg, or multiple ascending doses (MAD) up to 900 mg administered once daily (QD) for 10 days. Each SAD and MAD cohort included 8 participants, of which 6 received VENT-03 and 2 received placebo in a double-blind manner. Volunteers were monitored for adverse events, clinical laboratory parameters, ECG and vital signs. Serial blood samples were taken to characterize the pharmacokinetics of VENT-03, and pharmacodynamics was assessed using a novel proprietary whole blood assay.

Results: There were no deaths or serious adverse effects during the trial. VENT-03 was safe and well-tolerated across all tested SAD and MAD dose levels. There were no significant changes in clinical laboratory parameters, ECG or vital signs. There were no dose-related adverse effects, and the observed adverse effects were mild, transient and easily managed. Absorption of VENT-03 in a fasted state was rapid with peak plasma concentrations appearing 4-6 hours post dose. Exposure increased with ascending

doses, and the pharmacokinetic profile of VENT-03 supports a QD dosing regimen. Pharmacokinetic steady state is reached in approximately 7 days with significant accumulation in plasma. Administration of VENT-03 with food delayed the time of peak plasma levels but did not significantly affect the overall exposure. VENT-03 demonstrated robust target engagement, and plasma levels exceed what is required to fully inhibit the activity of cGAS in patients.

Conclusions: VENT-03 was safe and well-tolerated in healthy volunteers, demonstrating a favorable pharmacokinetic profile and robust target engagement. The efficacy of VENT-03 in SLE patients with active cutaneous manifestations will be evaluated in an upcoming Phase 2a study.

PV074 / #830

Poster Topic: *AS10 - Environment and SLE*
Late-Breaking Abstract

EXPLORING PHYSICAL ACTIVITY ENGAGEMENT AND SUPPORT IN INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE IMPACT OF SOCIAL SUPPORT, HEALTHCARE PROVIDER RELATIONSHIPS, AND BUILT ENVIRONMENTS

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Background/Purpose: Physical activity is recognized as a valuable form of treatment for managing lupus, but a significant number of individuals with lupus do not meet the recommended guidelines. Moreover, examining social determinants of health in the context of lupus research is vital for a comprehensive understanding of how external factors impact the experiences and health outcomes of people with lupus. Lupus is not only influenced by biological factors but is also intricately connected to social, economic, and environmental conditions. This study aims to explore the experiences of individuals with systemic lupus erythematosus (SLE) regarding physical activity access and support, focusing on the roles of social supports, healthcare provider relationships, and built environments.

Methods: We used a qualitative, interpretive description approach involving semi-structured interviews with adults with SLE. The interview guide included questions on how current physical function, social supports, healthcare provider relationships and conversations, and built environments impact physical activity engagement. We analyzed the de-identified transcripts using deductive, thematic analysis with input from representatives of the study population. Our theme development focused on how the intersection of SLE and social determinants influence physical activity engagement and support.

Results: This study included 31 interviews (100% female, age range = 24-65 years). Our analysis resulted in three main themes: 1) The paradox of social support: Encouraging and prohibiting physical activity; 2) Underutilized position of power: Healthcare provider influence on physical activity engagement; and 3) SLE amplifies the challenges of navigating the built environment.

Conclusions: This study highlights the role of social and built environments in shaping physical activity engagement among individuals with SLE. By acknowledging the

complex interplay between physical activity and SLE management, our findings can guide healthcare providers in personalizing their advice and interventions to accommodate each patient's distinct social and environmental circumstances. Further, this study emphasizes the importance of collaboration between healthcare systems and community planners to develop supportive environments and infrastructure to mitigate physical activity barriers.

PV075 / #90

Poster Topic: ***AS10 - Environment and SLE***

FINE PARTICULATE MATTER AIR POLLUTION AND ANTI-NUCLEAR ANTIBODY POSITIVITY: THE ONTARIO HEALTH STUDY

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Background/Purpose: Air pollution has been increasingly linked to systemic autoimmune rheumatic diseases (SARDs), but studies of fine particulate matter (PM2.5) and SARD-related serologic biomarkers are limited. In this study, we aimed to assess exposure to ambient PM2.5 and anti-nuclear antibodies (ANA) in the general population.

Methods: We used data and sera from the Ontario Health Study (OHS), which has enrolled 225,000 general population residents of the province of Ontario in Canada. Serum samples from 3548 subjects (collected at enrolment between 2010-2013) were randomly selected from the OHS database/biorepository. Indirect immunofluorescence assay on Hep-2 cells assessed ANA titres (>1:160, >1:320, >1:640, and >1:1280). Annual mean ambient PM2.5 levels for the five-year period before sera collection were assigned based on subjects' 6-digit residential postal codes. Our multivariable logistic regression models computed adjusted odds ratios (ORs) for ANA positivity, comparing the highest (fourth) quartile to the lowest (first) quartile in terms of ambient PM2.5. We adjusted for sex, age, race/ethnicity, smoking, and the Rurality Index of Ontario (to characterize subjects' urban/rural status).

Results: Of the 3548 subjects, 2215 (62.4%) were female and 3131 (88.2%) were white. Mean age at serum collection was 54.7 (standard deviation 9.5) years. Multivariate analyses showed females were more likely to be ANA positive than males. Comparing the highest versus lowest quartile PM2.5 exposure, the adjusted OR for ANA positivity related to a titre of ≥1:160 was 1.04 (95% CI 0.75-1.44), while for a titre of ≥1:320 the aOR was 1.14 (95% CI 0.77-1.68), for a titre of ≥1:640 the aOR was 1.67 (95% CI 0.99-2.82) and for a titre of ≥1:1280 the aOR was 2.33 (95% CI 1.11-4.91).

Table 1. Antinuclear positivity in Ontario Health Study general population subjects*

Covariate	Subgroup	Negative	Titre			
			≥1:160	≥1:320	≥1:640)	≥1:1280
Sex	Female	1393	301	232	146	143
	Male	925	169	126	71	42
Age	<35	70	18	5	8	7
	35-44	323	45	45	22	18
	45-54	654	125	84	60	49
	55-64	917	200	166	87	81
	≥65	337	82	58	40	30
Race/ethnicity	White	2040	433	309	187	162
	Asian	134	20	23	15	12
	Black	26	10	7	3	4
	Hispanic	19	2	1	3	0
	Others or missing	83	21	18	9	7
Smoking	Never	1297	241	206	114	100
	Ever	1010	221	151	101	85
	Missing	11	8	1	2	0
Rurality Index of Ontario*	Urban: ≤40	2228	444	339	210	178
	Rural: >40	83	22	18	7	7
	Missing	6	4	1	0	0

* A continuous variable for urban/rural status, ranging from 0 (most urban areas) to 100 (most rural areas).

Table 2. Adjusted odds, OR (95% confidence interval, CI) for ANA* positivity for ambient fine particulate matter ($PM_{2.5}$, comparing highest to lowest quartile) adjusting for sex, age, race/ethnicity, smoking, and the Rurality Index of Ontario, RIO

Variable	Adjusted OR (95% CI)
Ambient $PM_{2.5}$	2.33 (1.11-4.91)
Age	1.00 (0.98-1.03)
Male Sex	0.42 (0.23-0.72)
White race/ethnicity	1.70 (1.20-2.42)
Smoking (ever)	0.76 (0.47-1.23)
RIO	1.02 (1.00-1.04)

*Antinuclear antibody titre ≥1:1280

Conclusions: Our analyses suggested relationships between PM2.5 exposure and ANA positivity which were most prominent at highest titres. This strengthens the argument for systemic immune system effects of air pollution, which could in turn lead to autoimmune disease.

PV076 / #248

Poster Topic: ***AS10 - Environment and SLE***

IS PHYSICAL ACTIVITY (PA) BEHAVIOR ANOTHER CASUALTY OF DEPRIVED NEIGHBORHOODS IN PERSONS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)?

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Background/Purpose: SLE, a chronic inflammatory, autoimmune disease with pervasive self-reported fatigue, negatively impacts most individuals with SLE. Because of its recognized benefits in improving oxygen capacity and endurance, physical activity (PA) is one modifiable lifestyle behavior to help reduce fatigue in patients with SLE who are typically not physically active and afraid to exercise. Recent research suggests a role for Social Determinants of Health (SDOH) in identifying environmental impact on medical care and conditions. The Area Deprivation Index (ADI), a composite score which ranks geographical areas of the US based on environmental living conditions, measures neighborhood resources and can estimate SDOH. Lupus Intervention Fatigue Trial (LIFT) is a 12-month phase II randomized, parallel group, single blind 2-arm investigator-initiated trial, comparing effectiveness of a motivational interviewing program intervention combining diet and physical activity strategies versus an educational program control arm to reduce fatigue in persons with lupus (NCT02653287). This ancillary analysis assessed the correlation between objectively measured PA behavior and ADI disadvantage of the participant's home at the LIFT baseline visit.

Methods: All LIFT participants met criteria: ≥18 years of age, BMI: 18-40 kg/m2, ambulate household distances (50ft), classification criteria for SLE per American College of Rheumatology (ACR) or Systemic Lupus International Collaborating Clinics (SLICC). Accelerometers were worn for seven consecutive days during waking hours to measure daily PA minutes and were categorized as sedentary minutes (<100 counts), light PA (LPA) minutes (100-2019 counts), and moderate-vigorous PA (MVPA) minutes

(2020+ counts). Valid PA monitoring was defined as at least 4 days of 10+ hours of accelerometer wear. Weekly MVPA minutes were calculated as mean daily MVPA minutes times seven. The ADI uses nine-digit zip codes to calculate a national ranking score on a scale from 0-100 (low to high deprivation rank). Descriptive statistics were calculated, and the associations between ADI and PA minutes (all categories) were estimated using Spearman correlation.

Results: Among 160 LIFT participants, mean (SD) age was 43.3 (13) years; 92% identify as female with 52% participants self-identifying as White, 33% Black/African American, 8% Asian, 1% Hawaiian/Pacific Islander, and 5% unknown/not reported; 95% having some college education. The mean (SD) for the following were BMI 27 (5), [disease activity measure] SLEDAI 2.9 (3.1), SLICC/Damage 1.2 (1.6), and ADI 34.7 (21.4), respectively. The total PA daily mean (SD) minutes were 262.3 (83.4); mean (SD) daily minutes category were sedentary 582.8 (92.8), LPA 242.2 (75.5), and MVPA 20.1 (19.6). Thirty-two percent met PA guidelines (≥150 minutes/week of MVPA). Mean daily MVPA minutes correlated with ADI rank, r= -0.20, p= 0.01 (Table 1).

Table 1. Spearman Correlations Between PA Measures and ADI in Baseline LIFT Participants (n=160)

ADI and PA daily minutes	Mean (SD)	Correlation coefficient between ADI and PA	p-value
ADI	34.7 (21.4)	1	N/A
Sedentary	582.8 (92,8)	0.09	0.252
LPA	242.2 (75.5)	-0.08	0.299
MVPA	**20.1 (19.6)**	**-0.20**	**0.010**
Total PA	262.3 (83.4)	-0.13	0.113

Conclusions: This analysis documents that only 32% of LIFT participants met weekly PA guidelines of ≥ 150 minutes of MVPA at baseline. Mean MVPA minutes were negatively correlated with ADI rank suggesting those participants living in higher ADI deprivation areas had lower MVPA minutes. Future analyses are planned to assess changes in PA between baseline & 6-month visit in the intervention and control groups in LIFT by ADI rank or if other interventions are necessary.

PV077 / #669

Poster Topic: ***AS10 - Environment and SLE***

EXPOSURE TO PER- AND POLYFLUOROALKYL SUBSTANCES (PFAS) AND SYSTEMIC LUPUS ERYTHEMATOSUS: A PILOT STUDY IN THE MICHIGAN LUPUS EPIDEMIOLOGY & SURVEILLANCE (MILES) PROGRAM

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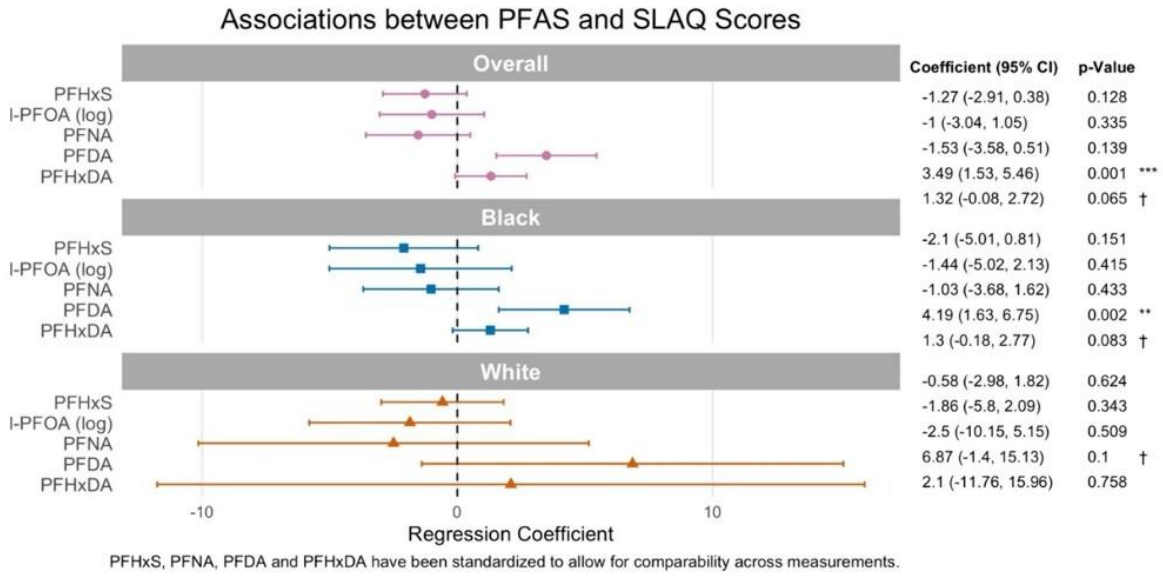
Background/Purpose: Per- and polyfluoroalkyl substances (PFAS), often called “forever chemicals”, are a large class of chemicals found in consumer products and as contaminants in food and drinking water. PFAS are known to be immunotoxic. Evidence supports a link between PFAS and some autoimmune conditions, but their relationship with systemic lupus erythematosus (SLE) risk and disease severity has not been well characterized. This pilot study in women with SLE explored the relationship between serum PFAS levels and disease activity. We hypothesized that higher PFAS levels would be linked to increased disease activity in Black and White women.

Methods: In serum specimens from 70 female participants with SLE (self-reported race: Black n=35, White n=35) in the Michigan Lupus Epidemiology and Surveillance (MILES) Cohort, we quantified 48 PFAS analytes using isotope dilution and solid-phase extraction followed by liquid chromatography mass-spectrometry. Disease activity was measured by the Systemic Lupus Activity Questionnaire (SLAQ), a validated patient-reported outcome measure. For PFAS analytes that were detected in ≥40% of participants, we first modeled the relationship between each PFAS concentration and SLAQ score, adjusting for age, race, and BMI. Combining Least Absolute Shrinkage and Selection Operator (LASSO) and expertise knowledge, we selected the most important PFAS features for a multivariable regression, adjusted for covariates, to model PFAS mixtures in all women and stratified by race.

Results: Among the 48 PFAS measured, 28 were detected in at least 1 serum specimen, and 16 were “commonly detected” in ≥40% of samples. Five PFAS had significantly higher rates of detection (%) or median levels in Black compared to White women. Adjusting for other confounders, two of the 16 commonly detected PFAS exhibited statistically significant associations with SLAQ score (p-value <0.05). Perfluorodecanoic acid (PFDA) was positively associated [1.69 unit increase SLAQ per 1-unit increase in standardized PFDA (95% CI 0, 3.37)], and perfluorohexanesulfonic acid (PFHxS) was inversely associated [-1.62 (95% CI -3.23, -0.01)] with SLAQ. We applied LASSO to identify the most important PFAS features relevant to SLAQ and prevent overfitting. Five

PFAS, selected by LASSO, were modeled simultaneously with SLAQ. PFDA and perfluoro-n-hexadecanoic acid (PFHxDA) had consistent positive associations in all women and when stratified by race, whereas no significant inverse associations were detected in the mixture analysis.



Conclusions: This pilot study is the first to examine relationships between environmental exposures to immunotoxic PFAS and SLE activity. We observed associations between higher serum concentrations of two PFAS – PFDA and PFHxDA – with increased disease activity, measured by SLAQ score. Data suggest that immunotoxicity of PFAS may extend to SLE, a prototypic autoimmune disease.

PV077a / #777

Poster Topic: *AS11 - Epidemiology and Public Health*
Late-Breaking Abstract

ECONOMIC BURDEN OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN INDIA: A SYSTEMATIC LITERATURE REVIEW

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Background/Purpose: While the clinical burden of SLE (systematic lupus erythematosus) is well-recognized, its economic impact in India remains poorly understood. This scoping review aims to assess the current evidence on the economic burden of SLE in India and identify gaps in the existing literature.

Methods: A systematic literature review was conducted to identify relevant studies reporting on the economic burden of SLE in India, adhering to PRISMA guidelines. PubMed was searched in August 2024 for all studies reporting economic outcomes, healthcare resource utilization (HCRU), or cost-related data in SLE patients among Indian females, without time restrictions. Data on study characteristics, patient demographics, economic analyses, cost outcomes, and HCRU were extracted. Risk of bias was assessed using the Newcastle-Ottawa Scale.

Results: Out of 701 initial records screened, four observational studies met the inclusion criteria (one prospective, three retrospective), with sample sizes ranging from 17 to 1,354 patients (total N=1,628). The female population represented 92.7% (n=1,509) of the total sample. All studies utilized hospital-based data sources from North India (2 studies) and South India (2 studies). No study performed a model-based comprehensive economic evaluation. One retrospective study reported direct costs, noting a 6-month per-patient expenditure of INR 630 (USD 8.85) for IV cyclophosphamide and INR 50 (USD 0.70) for oral therapy. HCRU data indicated higher hospitalization rates and longer hospital stays in SLE patients with infections compared to those without, but the HCRU data were not translated to economic metrics. The risk of bias was rated “good” in one study and “fair” in the remaining three.

Conclusions: There is an acute paucity of studies evaluating the economic burden of SLE in India. Existing data are limited to direct costs and basic HCRU metrics, with no comprehensive economic evaluations or assessments of indirect costs. This significant gap emphasizes the urgent need for prospective, large-scale health economic studies

to inform policy decisions and optimize resource allocation for SLE management in India.

PV078 / #557

Poster Topic: ***AS11 - Epidemiology and Public Health***

ACUTE CARE UTILIZATION IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME AND/OR SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Little is known about acute care utilization in patients with antiphospholipid antibodies (aPL) or antiphospholipid syndrome (APS) and systemic lupus erythematosus (SLE). This study focuses on hospitalizations, intensive care unit (ICU) admissions and emergency department (ED) visits, in patients with APS and/or SLE, both 1 year prior to and after diagnosis with SLE or identification of positive aPLs, compared to a control population in Alberta, Canada.

Methods: Patients from our observational aPL/APS and SLE registries were included. Patients had persistently positive aPL (medium positive [40-80 GPU] or high positive [80-160 GPU] anticardiolipin or anti-beta-2 glycoprotein 1 or a positive lupus anticoagulant test, measured at least 12 weeks apart) and/or fulfilled ACR or SLICC SLE classification criteria. Patients diagnosed with APS met revised Sapporo Criteria. The index date was defined as the date that persistently positive aPL were first identified or that SLE classification criteria were met, whichever came first. If the index date was prior to 2002, the date of registry enrollment was used instead, as administrative data was not available. Acute care utilization one year prior to and after the index date (between April 1st 2007 and March 31st 2024) was determined. Data were sourced from several Albertan health-related databases, including the Discharge Abstract Database, National Ambulatory Care Reporting System, and Alberta Provincial Registry, linking participants via their Alberta Personal Health Number. Acute care utilization was compared to age- and sex-matched controls, matched to cases 5:1, excluding any individuals with results for aPLs, ANA, ENA or anti dsDNA or those with any practitioner claim codes or inpatient/outpatient ICD codes for SLE or APS. Controls were assigned the index date of their matched case.

Results: 466 patients participated, aPL positive only (n=7), APS only (n=19), SLE only (n=339), SLE and aPL positive (n=55), and SLE and APS (n=46) (Table 1). A total of 1,857,127 potential control candidates were identified, from which 2,330 controls were randomly selected. One year prior to the index date, the proportion of participants with inpatient hospitalizations were as follows: APS only (5.56%), SLE only (10.07%), SLE and aPL positive (4.17%), SLE and APS (14.63%), and control (3.79%), with no hospitalizations recorded among the aPL positive only group. Patients who had SLE and

APS experienced the highest ED visit rate (36.59%). The lowest ED visit rate was observed in the control group (11.84%) (Table 2). One year after the index date, the highest hospitalization rates were observed in patients with SLE and APS (44.44%) and APS (42.11%) groups, while the control group had the lowest rate (3.81%). SLE and APS participants had the longest average hospital length of stay (18.45 days). ICU admissions were rare, peaking at 5.26% in the APS group. ED visits were most frequent in SLE and APS (66.67%) and APS (52.63%) groups, compared to 12.25% in controls (Table
2).

Table 1: Baseline characteristics at index date*

	aPL positive	APS only	SLE only	SLE and aPL positive	SLE and APS	Control
N	7	19	339	55	46	7
Mean age at index date (years, SD)	44.57 (18.56)	44.74 (14.15)	42.13 (16.91)	41.25 (17.37)	36.65 (17.82)	41.65 (17.00)
Female, N (%)	6 (85.71%)	15 (78.95%)	315 (92.92%)	45 (81.82%)	36 (78.26%)	2085 (89.48%)
Urban region of residence, N (%)	7 (100.00%)	17 (89.47%)	311 (91.74%)	51 (92.73%)	39 (84.78%)	2259 (96.95%)

*Index date is defined as the date that aPL were first identified or SLE diagnosed, whichever came first.

Table 2 Acute care utilization one year prior to, and one year after index date*

		aPL positive	APS only	SLE only	SLE and aPL positive	SLE and APS	Control
	N	7	19	339	55	46	2330
	Availability of data						
Prior to index date	N (%)	7 (100%)	18 (94.74%)	298 (87.91%)	48 (87.27%)	41 (89.13%)	2060 (88.41%)
After index date	N (%)	7 (100%)	19 (100%)	309 (91.15%)	51 (92.73%)	45 (97.83%)	2155 (92.49%)
	Hospitalizations						
Prior to index date	N (%)	0 (0%)	1 (5.56%)	30 (10.07%)	2 (4.17%)	6 (14.63%)	78 (3.79%)
	Mean (Std)	-	2 (-)	1.40 (0.72)	1.00 (0.00)	1.33 (0.52)	1.36 (0.77)
After index date	N (%)	2 (28.57%)	8 (42.11%)	77 (24.92%)	6 (11.76%)	20 (44.44%)	82 (3.81%)
	Mean (Std)	1.00 (0.00)	1.63 (1.41)	1.71 (1.36)	2.17 (2.04)	1.80 (1.58)	1.15 (0.39)
	Hospitalizations - total length of stay, days						
Prior to index date	Mean (Std)	-	90.00 (-)	8.80 (14.55)	1.00 (0.00)	16.83 (34.41)	7.92 (13.38)
After index date	Mean (Std)	3.50 (3.54)	10.25 (14.45)	11.81 (13.57)	7.17 (5.78)	18.45 (28.17)	9.40 (21.20)
	ICU admissions						
Prior to index date	N (%)	0 (0%)	1 (5.56%)	0 (0%)	0 (0%)	1 (2.44%)	3 (0.15%)
	Mean (Std)	-	1 (-)	-	-	1 (-)	1.33 (0.58)
After index date	N (%)	0 (0%)	1 (5.26%)	3 (0.97%)	0 (0%)	1 (2.22%)	2 (0.09%)
	Mean (Std)	-	1 (-)	1.00 (0.00)	-	2 (-)	1.00 (0.00)
	ED Visits						
Prior to index date	N (%)	1 (14.29%)	3 (16.67%)	85 (28.52%)	16 (33.33%)	15 (36.59%)	244 (11.84%)
	Mean (Std)	1(-)	2.33 (1.53)	1.85 (1.19)	2.00 (2.13)	2.20 (1.90)	1.58 (1.17)
After index date	N (%)	5 (71.43%)	10 (52.63%)	140 (45.31%)	20 (39.22%)	30 (66.67%)	264 (12.25%)
	Mean (Std)	1.80 (1.30)	4.00 (6.09)	2.23 (1.60)	1.70 (1.03)	2.53 (1.94)	1.57 (1.10)

*Index date is defined as the date that aPL were first identified or SLE diagnosed, whichever came first.

Conclusions: Patients with APS and/or SLE have a high number of hospitalizations and ED presentations compared to a control population, both 1 year prior to and after the first identification of positive aPLs or diagnosis of SLE.

PV079 / #745

Poster Topic: ***AS11 - Epidemiology and Public Health***
Late-Breaking Abstract

CORRELATES OF COVID VACCINATION UPTAKE AMONG ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: EMERGING FINDINGS FROM THE 2024-25 RESPIRATORY VIRUS SEASON

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Background/Purpose: People with systemic lupus erythematosus (SLE) are considered more susceptible to COVID; those who become infected may also experience greater severity and disease consequences. COVID vaccination among people with autoimmune diseases is a public health priority. The current study identifies correlates of uptake of the 2024-25 COVID vaccine formulation among people with SLE.

Methods: Participants were adults 18 years of age and older diagnosed with SLE who live, work, or seek care in Alabama, Louisiana, and Mississippi recruited between August 23, 2024, and January26, 2025 as part of an ongoing study (n=122). Multivariable logistic regression was used to examine 2024-25 COVID vaccination assessed through self-report.

Results: Approximately 18% of participants (n=22) reported receiving the most recent COVID vaccine. Satterthwaite t-tests revealed that those reporting more barriers to accessing healthcare—lack of transportation, greater distance, competing demands (work, family), cost, and inadequate insurance—were less likely to report receiving the most recent COVID vaccine ($t=3.3$, 53.4 df, $p<0.01$). Similarly, reporting barriers within medical contexts—dislike of their hospital, wait times, confusion with the healthcare system, distrust of their doctor, not feeling listened by their doctor, not believing in the efficacy of treatment, and worry about what would happen at the appointment—was associated with lower self-reported vaccination ($t=2.1$, 59.6 df, $p<0.05$). Older age was associated with greater reports of vaccination ($t=-2.9$, 27.2 df, $p<0.01$). Multivariable logistic regression models were specified, including barriers to access, medical care barriers, demographic (age, race, relationship status), socioeconomic (income,

education, work status), and health characteristics (years since SLE diagnosis, organ damage), as well the time of assessment. In this model, barriers to access (OR 0.4, 95% CI 0.2-1.0, p=0.06) and age (OR 1.1, 95% CI 1.0, 1.1, p=0.5) were associated with COVID vaccination at the trend level. Timing of participant assessment was significant at the p=0.07 level (chi-square 7.1, 3 df). As expected, compared to those assessed in October and earlier, those who participated in subsequent months had greater odds of reporting vaccination, but in a non-linear fashion (November: OR 4.1; December: OR 37.1; January: OR 17.4). Self-reported vaccination was lower in January compared to December, suggesting that vaccination may taper during this time period.

Conclusions: This study presents recent findings on uptake of the 2024-25 COVID vaccine among adults with SLE. Results suggest that lessening healthcare barriers, particularly those associated with access such as structural challenges, concerns about cost, and multiple role responsibilities, may facilitate COVID vaccination in this population. Efforts to promote COVID vaccination in the time preceding the release of updated formulations may enhance uptake in earlier months, where we saw the lowest reports of vaccination. We found that self-reported vaccination was lower in January compared to December in our sample, suggesting that continued campaigning in later months of the respiratory virus season may be warranted.

PV080 / #137

Poster Topic: ***AS11 - Epidemiology and Public Health***

MENTAL HEALTH DIAGNOSES AND ACUTE CARE USE AMONG INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE ALL OF US RESEARCH PROGRAM

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Background/Purpose: Mental health disorders, including depression, anxiety, and post-traumatic stress disorder, are prevalent among people living with SLE. We hypothesized that these mental health conditions may increase recurrent acute care use (emergency department [ED] visits, hospitalizations) among patients with SLE.

Methods: We used data from the nationwide All of Us Research Program (version 7), an NIH cohort of >287,000 U.S. adults who enrolled and consented for linkage to their electronic health records. We identified those with ≥ 2 ICD-10 or SNOMED codes for SLE in the ≤ 2 years pre-enrollment. We assessed the exposure of concomitant mental health diagnoses during that time, identified by ≥ 2 ICD-10 or SNOMED codes for major depression, anxiety, or PTSD (mental health diagnoses) in the ≤ 2 years pre-enrollment. The outcome was number of emergency department visits (only) and hospitalizations (including those from emergency department) after *All of Us* enrollment date. We used multivariable negative binomial regression models to examine associations between having a mental health diagnosis and acute care use. Models were adjusted for age, sex, race, ethnicity, calendar year of enrollment, other baseline period sociodemographic factors and comorbidities.

Results: We identified 1,683 with SLE, among whom 1,029 (61.1%) had depression, anxiety, and/or PTSD. Mean age overall was 49.45 (14.26) and 89.4% were female. (**Table 1**) Those with diagnoses of ≥ 1 mental health condition were more likely to be less educated, in a low-income group, to have ever smoked, and to have more baseline comorbidities. Patients were followed for a mean of 29.9 months (SD 15.3) after enrollment. In adjusted analyses (**Table 2**), we found associations between having mental health diagnoses and higher rates of acute care use, both emergency department visits (adjusted IRR 1.84, 95%CI 1.52-2.22) and hospitalizations (IRR 1.40, 95%CI 1.11-1.78). This was true both for all emergency visits and hospitalizations for SLE (IRR 1.61, 95% CI 1.32-1.97) and for all diagnoses (IRR 1.45, 95% CI 1.19, 1.78).

Table 1. Characteristics of the Patients with SLE in the All of Us Research Program (version 7) by presence of Concomitant Mental Health Diagnoses			
	Without Mental Health Diagnoses (n=654)	With Mental Health Diagnoses (n=1,029)	p
Age, mean years (SD)	49.82 (15.40)	49.22 (13.50)	0.40
Female at birth, N (%)	570 (87.2)	935 (90.9)	**0.03**
Self-reported Race and Ethnicity, N (%)			**<0.01**
Asian	29 (4.4)	16 (1.6)	
Black	192 (29.4)	306 (29.7)	
Hispanic	174 (26.6)	251 (24.4)	
>1 Race	-	-	
White	223 (34.1)	382 (37.1)	
Other/Missing	27 (4.1)	54 (5.2)	
≤ High school education, N (%)	173 (26.5)	312 (30.3)	**0.01**
Annual household income <$35,000, N (%)	232 (35.5)	463 (45.0)	**<0.001**
U.S. region of residence, N (%)			0.80
Northeast	192 (29.4)	325 (31.6)	
South	136 (20.8)	203 (19.7)	
Midwest	122 (18.7)	185 (18.0)	
West	204 (31.2)	316 (30.7)	
Self-reported ever smoking, N (%)	181 (27.4)	352 (34.2)	**0.01**
Obesity[a], N (%)	246 (37.6)	506 (49.2)	**<0.001**
Charlson comorbidity index, mean (SD)[b], N (%)	1.66 (2.19)	2.59 (2.76)	**<0.001**
Mental health diagnoses[c], N (%)			
Depression	-	809 (78.6)	
Anxiety	-	758 (73.7)	
PTSD	-	81 (7.9)	
>1 one mental health diagnosis	-	559 (54.3)	
Follow-up, months (mean, SD)	28.11 (15.93)	31.02 (14.81)	**<0.001**

[a]Obesity: Body Mass Index (BMI) ≥30 kg/m^2 from enrollment physical measurement data
[b]Charlson comorbidity index calculated using 16 comorbidities, excluding connective tissue disease
[c]Not mutually exclusive, >1 mental health diagnosis in 559 (54%)
Missing data: education level in 47 subjects, income in 412 subjects, smoking for 57 subjects, obesity in 88. Missing indicator in models.
- Cell sizes < 20 suppressed per All of Us reporting requirements

Table 2. Incidence Rate Ratios for Acute Care Use for Patients with Mental Health Conditions compared to those without among Patients with Systemic Lupus Erythematosus in the All of Us Research Program, v.7 (14,680 person-years)		
	Incidence Rate Ratios	95% CI
All Emergency Department Visits		
Model 1	2.37	(1.96, 2.86)
Model 2	1.84	(1.52, 2.22)
Emergency Department Visits with SLE diagnosis codes		
Model 1	2.49	(2.04, 3.04)
Model 2	2.12	(1.73, 2.60)
All Hospitalizations		
Model 1	1.73	(1.37, 2.18)
Model 2	1.40	(1.11, 1.78)
Hospitalizations with SLE diagnosis codes		
Model 1	1.81	(1.47, 2.24)
Model 2	1.45	(1.16, 1.80)
All Emergency Department Visits and Hospitalizations		
Model 1	1.84	(151, 2.25)
Model 2	1.45	(1.19, 1.78)
Emergency Department Visits and Hospitalizations with SLE diagnosis codes		
Model 1	2.01	(1.66, 2.45)
Model 2	1.61	(1.32, 1.97)

Model 1 adjusted for age, sex, race, ethnicity, and calendar year of enrollment
Model 2 additionally adjusted for annual household income, education level, smoking, obesity, and Charlson comorbidity index (calculated with 16 comorbidities, excluding connective tissue disease)

Conclusions: In this large, diverse US-wide population of patients with SLE, we found that those with mental health diagnoses had higher rates of recurrent acute care use compared to those without these diagnoses. Mental health conditions may complicate the treatment and severity of SLE, leading to increased recurrent acute care use. As patients with frequent acute care use are less likely to receive standard-of-care long-term medications and preventive care, contributing to inequities, further research is needed to develop interventions to decrease this recurrent acute care use for patients with SLE and mental health disorders.

PV081 / #18

Poster Topic: ***AS11 - Epidemiology and Public Health***

TREATMENT ADHERENCE AND ASSOCIATED FACTORS IN PATIENTS WITH CUTANEOUS LUPUS, A PROSPECTIVE MULTICENTER STUDY

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Background/Purpose: Cutaneous lupus erythematosus (CLE) is an autoimmune disease with a significant impact on quality of life. Many patients with CLE do not improve with conventional treatments. While poor adherence to treatment is well-documented in systemic lupus, data on adherence in CLE is lacking. The aim of this study was to evaluate therapeutic adherence in CLE, and to identify factors associated with poor adherence.

Methods: This is a prospective, cross-sectional, multicenter study. Patients with CLE completed validated adherence assessment questionnaires (MASRI and MMAS4) at a follow-up visit. According to the MASRI, adherence was defined by a visual analog scale (VAS) greater than or equal to 80%. According to the MMAS4, adherence was defined by a maximum score of 4 out of 4 . The CLASI score, which evaluates disease activity (CLASI-A) and damage (CLASI-D), was used to assess the severity of CLE. Quality of life (DLQI), anxiety and depression (HAD), opinion of medication (BMQ), feeling of illness (EVA), and quality of the doctor-patient relationship (CARE and CollaboRATE) were also assessed. Factors associated with adherence (according to MASRI and MMAS4) were assessed by multivariate analysis using logistic regression. Relationships between the different variables were examined using a correlation matrix.

Results: We included 108 patients with CLE from three university hospitals in France. Treatment adherence was 88% according to MASRI and 44.8% according to MMAS4. Younger age ($p = 0.0233$), presence of discoid lupus ($p = 0.0004$), disease severity ($p = 0.0004$) and number of therapy lines ($p = 0.0209$) were significantly associated with poorer adherence according to MMAS4. A higher number of physicians consulted ($r_s = 0.23$) and the presence of anxiety and depressive symptoms ($r_s = 0.21$) were correlated with lower adherence. Severity of cutaneous lupus was correlated with higher anxiety and depressive symptoms ($r_s = 0.24$) and greater impairment of quality of life ($r_s = 0.28$). Physician empathy ($r_s = 0.26$) and shared decision-making ($r_s = 0.22$) were correlated with lower anxiety and depressive symptoms.

Conclusions: Adherence appears to be significantly impaired in patients CLE. The difference between the two adherence scores may be explained by the greater sensitivity of the MMAS4. In our study, there was a significant correlation between the two scores (Figure 1). Lower adherence is associated with more severe CLE, both in terms of activity and scarring. It would be interesting to improve the empathic dimension of the doctor-patient relationship and shared decision-making, and to assess adherence during follow-up.

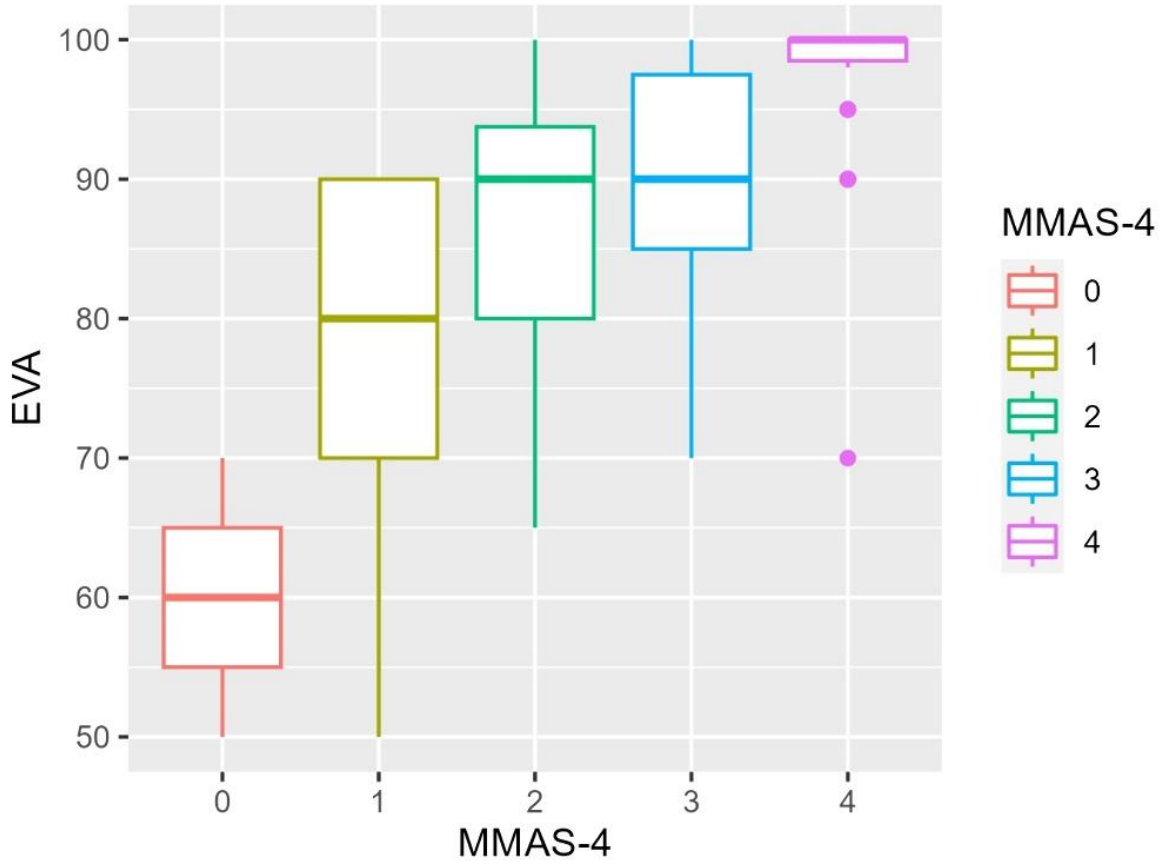

Figure 1 : Distribution of adherence according to the MASRI EVA and the MMAS4

PV082 / #381

Poster Topic: ***AS11 - Epidemiology and Public Health***

BRIDGING THE GAP: IDENTIFYING AND ADDRESSING BARRIERS TO CARE FOR PATIENTS WITH LUPUS AND LUPUS NEPHRITIS

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Background/Purpose: Systemic Lupus Erythematosus (SLE) and Lupus Nephritis (LN) present significant healthcare challenges, particularly in terms of access to care and patient education. This project aims to identify and mitigate these barriers through a needs assessment and provision of supportive services to disadvantaged/underserved patients. The work presented here describes the electronic health record (EHR)-documented healthcare barriers identified among patients with lupus at a large academic healthcare system.

Methods: Patients with lupus were identified through the Carolina Data Warehouse for Health (CDW-H), an EHR data repository for patients who have been admitted to the University of North Carolina (UNC) healthcare system. Inclusion Criteria: Eligible patients were adults aged 18 or older, fluent in English, diagnosed with lupus nephritis, and receiving care at UNC Rheumatology and/or Nephrology clinics.

Results: A total of 1,673 unique patients with various SLE diagnoses were identified, resulting in 11,890 clinical encounters between July 1, 2020, and July 1, 2024. The majority of encounters were in rheumatology (64%) compared to nephrology (36%). Insurance coverage varied, with 52% of patients having other commercial or state health plans, 39% on Medicare, 27% on Medicaid, and 12% with no recorded insurance [**Table 1**]. A total of 803 (48%) patients had recorded responses to Social Determinants of Health (SDOH) questionnaires available in the EHR. Of these patients, 8.2% experienced transportation barriers, 16.3% reported indicators of food insecurity, and 15.4% reported financial instability [**Table 2**].

Conclusions: A number of barriers and priorities to address in assistance programs were identified, including a relatively high number of patients from low socioeconomic status (39% of patients reporting Medicaid or no insurance), and more than 15% of patients reporting financial difficulty meeting their basic needs. This ongoing work aims to bridge the gap in healthcare access and education for patients with SLE and LN, leveraging community resources and targeted interventions to improve patient outcomes. Our goal is to enhance support services and education for patients with lupus by: 1) Improving access to healthcare transportation through rideshare vouchers; 2) Providing pharmacist counseling on medication adherence, adverse effects, and

assistance programs; and 3) Distributing educational materials to increase patient knowledge and perception of lupus and access to care.

Table 1. Patient Insurance Status Recorded in the Electronic Health Record (n=1673 patients with lupus)

Insurance Reported	**% Patients (n=1673)**
Other Commercial/ Agency/State Health Plan	52%
Medicare	39%
Medicaid	27%
Tricare	5%
None Reported	12%

Table 2. Social Determinants of Health (SDOH) Measures Recorded in the Electronic Health Record (n=803, 46% of patients with lupus)

SDOH Measures	**#**	**%**
In the past 12 months, has lack of transportation kept you from medical appointments or from getting medications?		
Yes	66	8.2%
Within the past 12 months, you worried that your food would run out before you got the money to buy more.		
Often / Sometimes true	131	16.3%
How hard is it for you to pay for the very basics like food, housing, medical care, and heating?		
Somewhat hard	124	15.4%

PV083 / #390

Poster Topic: ***AS11 - Epidemiology and Public Health***

ADVANCING EQUITY IN LUPUS CLINICAL TRIALS THROUGH COMMUNITY ENGAGEMENT: PERSPECTIVES FROM QUALITATIVE COMMUNITY FEEDBACK SESSIONS WITH CLINICAL TRIAL INVESTIGATORS AND RESEARCH STAFF

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Background/Purpose: Lupus disproportionately affects racial and ethnic minoritized populations, yet there is a significant disparity between those affected and those enrolled in clinical trials. The aim of the present work is to characterize the perspectives, preferences, and unmet needs of key community members to enhance the participation of underrepresented groups in lupus clinical trials.

Methods: Three Community Feedback Sessions (CFSs) were held over Zoom with experienced investigators and research staff from prominent academic lupus clinical trial centers in North America in January 2024. CFSs were led by trained facilitators utilizing discussion guides developed to gather actionable feedback on: challenges and facilitators for recruiting and enrolling racial and ethnic minority patients into lupus clinical trials; effective communication with diverse patients about clinical trials; and strategies and solutions to promote participation of underrepresented patients in lupus clinical trials. The sessions were recorded, and feedback was summarized to explore key takeaways and recommendations to advance equity in lupus clinical trials.

Results: Nine investigators and seven research staff participated in the feedback sessions, representing 14 centers across North America. Key barriers discussed included socioeconomic factors and inadequate consideration of patient's time and resource constraints within clinical trial designs [**Figure 1**]. Illustrative quotes were selected to portray emergent perspectives, outlined in **Figure 2**. Building relationships with patients and involving trusted community partners (e.g., primary care providers, community health workers, patient advocates) was frequently emphasized as a productive approach to addressing historical and current mistrust in research and medicine. Respondents identified collaborative approaches to enhance continual education and patient engagement to improve communication about clinical trials within and between clinical professionals, patients, and communities. Investigator discussions focused on mentorship and innovative communication methods, while research staff emphasized specific training programs and resources for better understanding lupus and addressing community concerns. All discussions highlighted the necessity of incorporating culturally and linguistically appropriate language and diction when discussing clinical trials, particularly for participants who reported serving large Spanish-speaking patient populations.

Conclusions: Addressing the underrepresentation of diverse populations in lupus clinical trials requires a multifaceted approach. While investigators and research staff shared common concerns and suggestions for advancing equity in lupus clinical trials, each group contributed unique insights and identified unmet needs based on their roles and prior experiences. Engaging and incorporating perspectives from the entire clinical trial research team can help identify comprehensive and actionable strategies to promote equity in lupus clinical trials. **Figure 1**. Perspectives from Investigators (n=9) and Research Staff (n=7) on Barriers and Facilitators to Advance Diversity and Representation in Lupus Clinical Trials

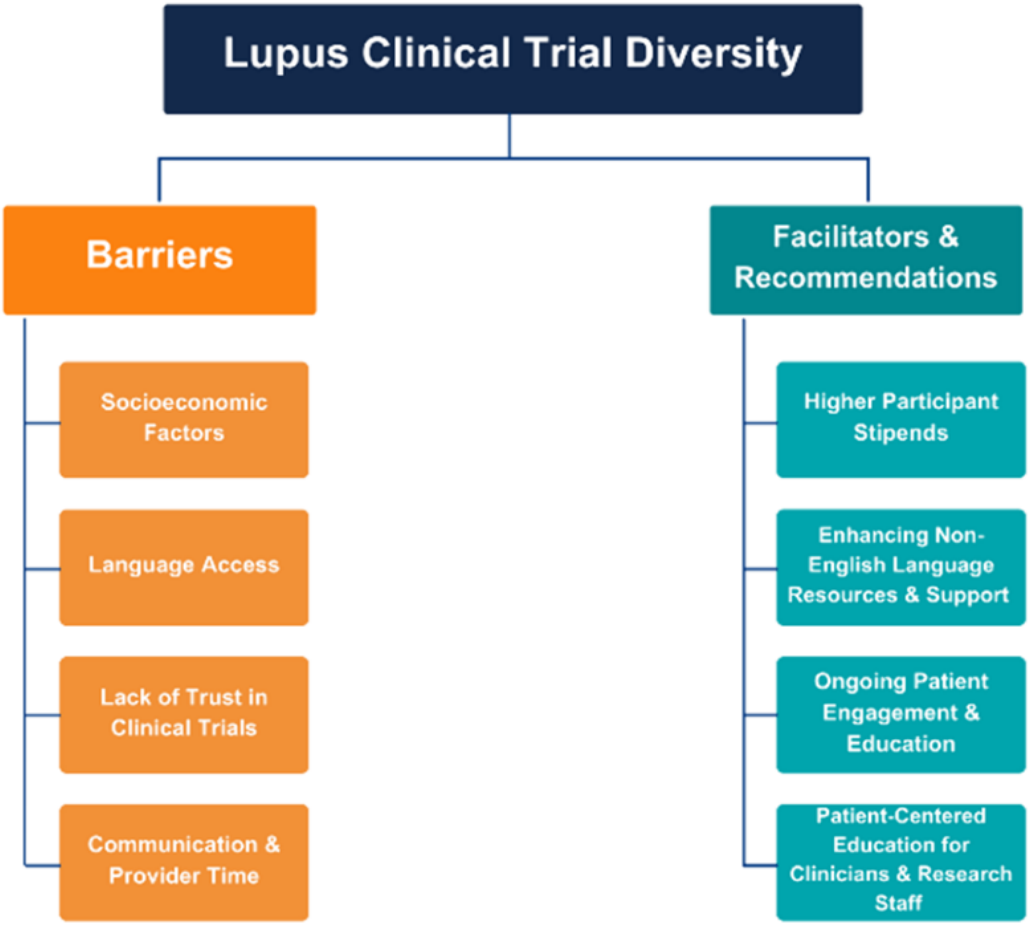

Figure 2. Illustrative Quotes from Investigators and Research Staff Perspectives Advancing Diversity and Representation in Lupus Clinical Trials

Investigator and Research Staff Perspectives

PV084 / #684

Poster Topic: ***AS11 - Epidemiology and Public Health***

PREVALENCE AND INCIDENCE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN CATALONIA (SPAIN). A POPULATION-BASED STUDY

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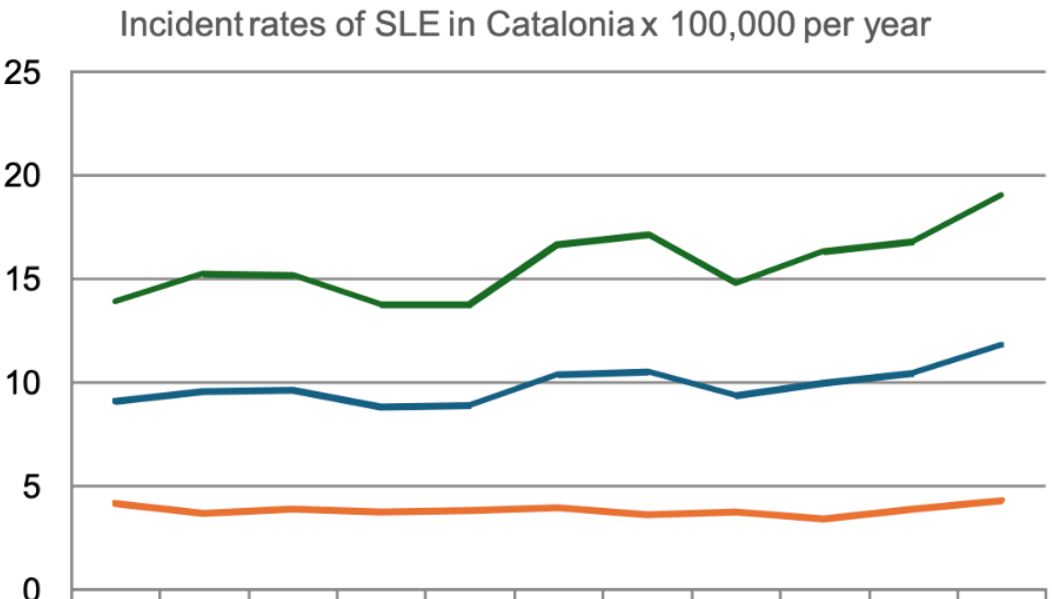
Background/Purpose: According to recent epidemiological studies using administrative data, the prevalence of systemic lupus erythematosus (SLE) in Northern European countries ranges around 45-75/100.000 inhabitants (1-3). The information on epidemiological studies in the European Mediterranean region comes from cohorts of academic centers, but population-based data is limited. Our objective was to determine the prevalence and incidence rates of SLE in Catalonia (Spain) during the period from January 1, 2011, and December 31, 2021.

Methods: We conducted a population-based cohort study of all existing Catalonian cases who received SLE diagnosis from 2006 to 2021 by using ICD-10-CM codes from the Information System for the Development of Primary Care Research (SIDIAP). A database of primary care electronic health records that includes data from 328 primary care practices covering 5.8 million people, 75% of the Catalan population (4). Prevalence rate was defined as the number of affected persons in the population at a specified time divided by the number of persons at that time. The numerator of prevalence rate was the number of persons, within 5-year age-sex groups, who met the definition of SLE between January 1, 2006, and December 31, 2021, and alive and registered with the SIDIAP on Dec 31, 2021. Incidence rates by age and sex were obtained for the 1-year period between January 1, 2011, and December 31, 2021. Persons diagnosed with SLE during the 5-year run-in period from Jan 1, 2006, until December 31, 2010 were not be eligible to become incident cases.

Results: We identified 10.609 prevalent cases of SLE, with a mean age of 47.5 years (SD 16.3). Of these patients, 8,851 (83.4%) were female, and 6,885 (64.9%) had Spanish Nationality. Other places of origin included Latin American countries in 524 (4.9%), 279 (2.6% %) from other European countries, and 158 from Africa (1.4%). We found an overall prevalence rate of 13.84 per 100,000 (Female 22.7, Men 4.6). By age groups, prevalent cases were 1,568 (14.7%) in the 18-29 yrs group, 2,335 (22.0%) in the 30-39 group, 2,390 (22.5%) in 40-49 group, 2,595 (24.9%) in 50-64 in group and 1,721 (16.2%)

in group older than 64 years. Overall incident cases during the study period were 6.166. Overall incident rate was 9.87, per 100,000, 15.69 per 100,000 for females, and 3.85 per 100,000 for males. Sex-specific and overall incidence rates by year are depicted in **Figure 1** and by age groups in **Figure 2**. Detailed information of incident cases from our study period according to age groups and sex is presented in **Table 1**.

Figure 1. Sex-specific and overall incidence rates by year



	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Overall	9,1	9,56	9,64	8,85	8,89	10,41	10,52	9,35	9,98	10,45	11,81
Men	4,16	3,69	3,9	3,73	3,82	3,99	3,65	3,73	3,44	3,9	4,33
Women	13,88	15,23	15,19	13,79	13,79	16,63	17,16	14,78	16,3	16,79	19,05

Figure 2. Incidence rates by age-groups

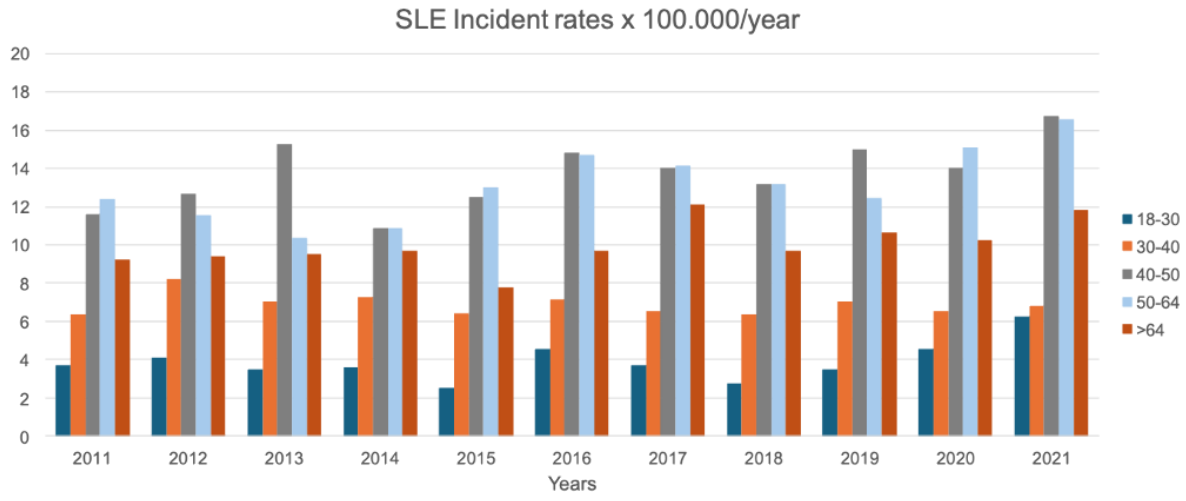


Table 1. Incidence of SLE from 2011-2021

	2011 N = 436	2012 N = 458	2013 N = 462	2014 N = 424	2015 N = 426	2016 N = 499	2017 N = 504	2018 N = 448	2019 N = 478	2020 N = 501	2021 N = 566	Overall N = 6,166
Mean Age (SD)	51.1 (16.4)	49.6 (16.2)	50.1 (16.2)	50.9 (17.0)	50.5 (15.2)	50.6 (16.0)	52.0 (16.0)	51.5 (15.4)	51.3 (16.2)	50.9 (16.0)	50.8 (16.3)	51.2 (16.2)
Sex Women (%)	338 (77.5)	371 (81.0)	370 (80.0)	336 (79.2)	336 (78.8)	405 (81.1)	418 (82.9)	360 (80.3)	397 (83.0)	409 (81.6)	464 (81.9)	4,985 (80.8)
Age groups												
18-29 (%)	42 (9.6)	45 (9.8)	46 (9.9)	40 (9.4)	32 (7.5)	47 (9.4)	39 (7.7)	30 (6.7)	36 (7.5)	48 (9.5)	62 (10.9)	551 (8.9)
30-39 (%)	80 (18.3)	103 (22.4)	96 (20.7)	93 (21.9)	83 (19.4)	91 (18.2)	86 (17.0)	81 (18.0)	95 (19.8)	84 (16.7)	86 (15.1)	1,104 (17.9)
40-49 (%)	100 (22.9)	102 (22.2)	122 (26.4)	86 (20.2)	106 (24.8)	120 (24.0)	118 (23.4)	110 (24.5)	117 (24.4)	118 (23.5)	137 (24.2)	1,448 (23.4)
50-64 (%)	124 (28.4)	114 (24.8)	109 (23.5)	114 (26.8)	130 (30.5)	143 (28.6)	139 (27.5)	129 (28.7)	125 (26.1)	153 (30.5)	172 (30.3)	1,756 (28.4)
> 64 (%)	90 (20.6)	94 (20.5)	89 (19.2)	91 (21.4)	75 (17.6)	98 (19.6)	122 (24.2)	98 (21.8)	105 (21.9)	98 (19.5)	109 (19.2)	1,307 (21.2)

Conclusions: Conclusions: This is the first study assessing the prevalence and incidence of SLE in Catalonia at the population level. We found that more than a quarter of SLE individuals are not from Spanish origin. These may have implications for assessment of the diseases burden, and resource allocations. We found a lower prevalence of SLE in Catalonia than in Northern European countries (1-3). Incidence rates were stable in both genders in our study period, with women showing 4-5 fold higher incidence rates than men. Incidence rates were higher among 40-50 and 50-64 age groups. **References** 1. Rees F et al. Ann Rheum Dis. 2016 Jan;75(1):136-41. 2. Alexander T et al. Ann Rheum Dis 2023 (AB0512) 3. Arkema EV et al. ACR Open Rheumatol. 2023;5(8):426-432 4. Recalde M et al Int J Epidemiol. 2022 Dec 13;51(6):e324-e33

PV085 / #710

Poster Topic: ***AS11 - Epidemiology and Public Health***

DEFINING LUPUS TRIAL RECRUITMENT CHALLENGES AND IDENTIFYING COLLABORATIVE SOLUTIONS THROUGH THE LUPUS CLINICAL INVESTIGATORS NETWORK (LUCIN)

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Background/Purpose: Lupus Therapeutics (LT), the clinical affiliate of the Lupus Research Alliance, oversees the Lupus Clinical Investigators Network (LuCIN), a network of premier research sites in North America formed to accelerate and improve the conduct of clinical trials for the development of new therapies. Each year, a survey of LuCIN investigators and research teams is conducted to address broad topics, focusing on challenges and solutions to recruiting for lupus clinical trials.

Methods: The 2024 LuCIN annual survey collected data from January 7 to February 18, 2024. Questions focused on assessing views of challenges and solutions for conducting lupus clinical trials in North America. The survey methodology included the perspectives of investigators, study coordinators and other clinical site staff to broaden the perspectives of responses. Descriptive statistics were used to analyze the survey responses.

Results: 114 investigators and study coordinators identified industry regulatory or policy actions that could positively improve recruitment of underrepresented populations in lupus clinical trials which include increasing patient compensation to offset costs and burdens of participation (82%), providing additional funding or incentives for engagement efforts (70%), and revising eligibility criteria that may disproportionately exclude historically underrepresented populations (60%) **Table 1**. Most respondents affirmed that the inclusion/exclusion criteria are too restrictive (83%), and more than half find it difficult to recruit patients (57%) in the clinical trials they participate in. 70% of respondents also shared the existing or prior use of approved medications for lupus is a common reason for participant exclusion in industry-sponsored clinical trials. Most respondents utilize in-house referrals (92%) and their

own lupus clinic registries, biorepositories or databases (73%) to engage or recruit patients into clinical trials **Table 2**. Only 11% of respondents say they utilized social media for recruitment or other outreach communications for clinical trials, marking an area of strategic opportunity. According to the Investigators, most of their patients commute over 1 hour to their site (86%). Organizations like Lupus Therapeutics can best support sites to effectively engage and recruit historically underrepresented populations in clinical trials by partnering with community organizations (74%) and providing support in developing culturally sensitive outreach materials (73%). Almost half of respondents believe training to improve recruitment of underserved patients (48%) and disease activity/scale training (46%) would benefit their site staff teams. Investigators proposed solutions to recruitment challenges which included maintaining sufficient staff, providing additional stipends to support transportation, parking, food, hotel and childcare, as well as enhancing community-based interventions enhancing referral networks through provider collaboration, database filters, educating colleagues and creating incentives for physicians to refer patients.

Table 1

Total Investigator and Coordinator Respondents (N=114) **53 LuCIN Centers Surveyed**		%
Primary Role		
	Investigator	61
	Coordinator	39
Which of the following industry regulatory or policy actions do you believe could positively impact the recruitment of historically underrepresented populations for clinical trials?		
	Increasing participant compensation from pharmaceutical partner to offset costs and burdens of participation	82
	Providing additional funding or incentives for strategies and efforts focused on engaging historically underrepresented populations	70
	Revisiting and revising exclusionary eligibility criteria that may disproportionately exclude historically underrepresented populations	60
	Revising informed consent requirements to accommodate cultural/linguistic differences and/or literacy barriers	54
How do you think Lupus Therapeutics can best support LuCIN sites in effectively engaging and recruiting historically underrepresented populations in clinical trials at your site?		
	Partnerships with Community Organizations: Assistance in forging partnerships with community-based organizations, religious institutions, and local leaders to leverage existing networks and trusted community relationships.	74
	Culturally Sensitive Outreach Materials: Providing support in developing culturally sensitive and accessible recruitment materials, such as brochures, videos, and online resources, which resonate with historically underrepresented communities.	73
What difficulties has your site had in recruiting participants to LuCIN-sanctioned trials?		
	Restrictive inclusion/exclusion criteria	83
	I find it difficult to recruit patients	57
Is existing/prior use of approved medications for lupus a common reason for participant exclusion in industry-sponsored lupus clinical trials?		
	Yes	70
Which of the following approaches does your site utilize to engage or recruit patients?		
	In-house referrals	92
	Lupus Clinic Registries or Biorepositories or Databases	73
	Third-party referrals	45
	Community-based organization outreach/partnerships	32
Does your site utilize social media for recruitment or other outreach/ communications around clinical trial opportunities?		
	Yes	11
What educational topics or training would benefit site staff to be discussed/ presented?		
	Improve Recruitment of Underrepresented Participants	48
	Disease Activity/Scale Training	46

Table 2

Total Investigator Respondents (N=69) **53 LuCIN Centers Surveyed**		%
How long does it take the majority of your patients to commute to your site?		
	Less than 30 mins 1 hour 2 hours	14 72 13
Investigator Open Response (N=69)		
For overall study conduct, are there best practices or innovative solutions to challenges in clinical trials and/or research studies that you have implemented at your site that you would think would be beneficial for other sites to learn about and/or adopt?		
	"Culturally appropriate materials for recruitment; community-based interventions"	
	"For LN trials working with nephropathologists to identify LN cases from other institutions to increase our catchment area"	
	"Having dedicated team of lupus clinical trial with stable staff including coordinators is very helpful"	
	"Identify potentially eligible patients through EPIC EMR reporting tools has helped. Phenotype-specific reports can be generated for recruitment that include pertinent clinical details, date of last and next visit. Electronic invitations can be sent via the MyChart patient portal to individuals who allow contact for future research. We use patient portal messaging to increase awareness of potential research opportunities."	
	"Local site registries that help us identify potential study patients (criteria, disease activity, etc.)"	
	"Modifying trial design to address patients other than those with high disease activity"	
	"Paying coordinators adequately, providing transportation to and from study visits (built into study budget) and support for child-care"	
	"Recruit patients from my practice and from other practitioners in my group. This is much more dependable than advertising."	
	"Stipends for parking, transport and food which overcome important barrier to participating studies"	
	"Use of dedicated research personnel and space. Use of dedicated investigational pharmacy"	
	"We feel it important to appropriately support coordinators. If needed, we additionally provide transportation to participants for study visits, and can also support child-care."	
	"Develop a close network of referral"	

Conclusions: Survey findings highlight the need for tailored strategies to improve lupus trial recruitment, particularly among underrepresented populations. Perspectives provided by study teams across an omnipresent lupus clinical trials network in North America underscore the need to address challenges related to clinical trial conduct including revising eligibility criteria, increasing participant compensation and enabling better support for site teams to engage and recruit more patients. Future directions include a focus on understanding specific eligibility criteria that mitigate recruitment difficulties and implement new strategies in addition to social media outreach for clinical trials. This work highlights tangible opportunities in lupus research to promote equity in clinical trials and design future studies that enable easier recruitment to advance therapeutic options for lupus patients.

PV086 / #369

Poster Topic: ***AS11 - Epidemiology and Public Health***

VALIDATION OF AMERICAN COLLEGE OF RHEUMATOLOGY DIGITAL CLINICAL QUALITY MEASURES FOR LUPUS CARE IN THE RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) REGISTRY

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Background/Purpose: In collaboration with the Centers for Disease Control and Prevention (CDC), the American College of Rheumatology (ACR) recently developed digital clinical quality measures for lupus clinical care. These measures included 1) hydroxychloroquine use (yes/no), 2) limiting glucocorticoid use of doses above 7.5 mg/day of prednisone to fewer than six months (yes/no), and 3) kidney function and urine protein laboratory testing for monitoring/screening for lupus nephritis (yes/no). We aimed to assess the accuracy of calculating these quality measures in the ACR's Rheumatology Informatics System for Effectiveness (RISE) registry compared to manual medical record review.

Methods: Five practices that participate in the RISE registry were recruited to participate in this study. All eligible patients with systemic lupus erythematosus (SLE) (defined as ≥ 2 SLE codes ≥ 30 days apart in 2022) who were at least 18 years of age and had at least one visit with a participating practice in 2022 were identified from the RISE registry. Among those patients, stratified random sampling was used to select 35 patients from each practice based on patients' glucocorticoid and hydroxychloroquine use in 2022. Practice staff were asked to complete a structured medical record review for at least 25 of the 35 patients at each site. Data related to the SLE quality measures were abstracted for the measurement year 2022, including hydroxychloroquine use and its contraindications, glucocorticoid use, including dose and duration of use, end-stage kidney disease (ESKD), and laboratory testing for kidney function and urine protein excretion. Corresponding electronic health record data on these patients were extracted from the RISE registry. Cohen's Kappa statistic and percent agreement were calculated for each measure component.

Results: We included 121 patients with SLE, of whom 92% were female, 21% were Black or African American, and 13% had lupus nephritis (**Table 1**). Agreement between the practice medical record review and RISE data varied across the measure components, with higher Kappa statistics and percent agreement for medication use

than for laboratory testing (**Table 2**). The Kappa for hydroxychloroquine use and glucocorticoid use were 0.70 (95% CI 0.60- 0.90) and 0.90 (95% CI 0.82-0.98), respectively. Glucocorticoid use over 7.5 mg/day for longer than 6 months was infrequent, with 97% agreement, but lower kappa 0.48 (95% CI (0.05-0.92). One patient was identified with ESKD, with 100% agreement between data sources, and was excluded from the kidney monitoring measure. Kidney function measurement was reported at least once in 2022 for 93% per medical record review and 83% of patients per RISE data, with Kappa 0.27 (95% CI 0.04-0.50). Urine protein measurement was reported at least once in 2022 for 72% per medical record review and 49% of patients per RISE data, with Kappa 0.35 (95% CI 0.21-0.50).

Table 1. Characteristics of Patients with Systemic Lupus Erythematosus

Characteristics	Total N=121
Age, years, mean (SD)	53.0 (14.9)
Female, n (%)	111 (91.7)
Race and Ethnicity n (%)	
Asian	2 (1.7)
Black or African American	25 (20.7)
Hispanic	4 (3.3)
Other/Unknown	41 (33.8)
White, non-Hispanic	49 (40.5)
Rheumatology Encounters in 2022, mean (SD)	3.6 (2.7)
Health Insurance, n (%)	
Medicaid	12 (9.9)
Medicare	46 (38.0)
Private	57 (47.1)
Other/Unknown	6 (5.0)
Lupus nephritis, n (%)	16 (13.2)
End Stage Kidney Disease, n (%)	1 (0.8)
Charlson Comorbidity Index*, mean (SD)	1.4 (0.8)

All patients were required to have at least 2 visits in 2022 and to meet the SLE definition of ≥2 SLE codes ≥30 days apart, including ICD-9 CM 710.0 or ICD-10 M32.x (excluding 32.0). Lupus nephritis defined by ≥1 lupus nephritis code (M32.14 or M32.15) or ≥2 nephritis codes, including ICD-9 580-586, 791.0; ICD-10 N00, N03, N04, N05, N17, N18, N19, R80. End-stage kidney disease identified by ≥1 ICD-9 585.6; ICD-10 N18.6, Z 99.2, Z49, V42.0 V56.0 V56.8; access device ICD-10 Z45.2 Z49, or CPT HD 90951-90970, 90935-90947, 90921, 90925

*Based on all RISE data through 2022.

Table 2. Agreement between RISE data and Medical Record Review

Survey Items for Structured Medical Record Review	Denominator	"Yes" According to Medical Record Review	"Yes" According to RISE Data	Kappa (95% CI)	Percent Agreement
Hydroxychloroquine Measure					
Did the patient use hydroxychloroquine in 2022?*	120	92	81	0.70 (0.60-0.90)	89.3%
Among patients who did not use hydroxychloroquine in 2022:					
Does the patient have a history of allergy, intolerance, or adverse event to hydroxychloroquine?	28	12	5	0.45 (0.15-0.74)	75.0%
Did the patient use chloroquine in 2022?	28	0	0	-	100%
Did the patient use quinacrine in 2022?	28	0	0	-	100%
Glucocorticoid Measure					
Did the patient use oral glucocorticoids in 2022?	121	49	49	0.90 (0.82-0.98)	95.0%
Was the dose of oral prednisone (or equivalent) greater than 7.5 mg per day for ≥ 6 months in 2022?	121	4	4	0.48 (0.05-0.92)	96.7%
Kidney Monitoring Measure					
Did the patient have a diagnosis of ESKD in 2022?	121	1	1	-	100%
Among patients without a diagnosis of ESKD/eligible for the measure:					
Did the patient have kidney function measurement completed in 2022?	120	111	100	0.27 (0.04-0.50)	84.2%
Did patient have protein excretion measurement completed in 2022?	120	86	59	0.35 (0.21-0.50)	67.5%

*One practice skipped this question for 1 patient. Oral glucocorticoid use includes prednisone, cortisone, prednisolone, triamcinolone, methylprednisolone, dexamethasone, or betamethasone. ESKD, end-stage kidney disease. ESKD is an exclusion from the kidney monitoring measure. Kidney function measurement included creatinine, creatinine clearance/ glomerular filtration rate, Chem7 or basic metabolic panel with creatinine, or serum cystatin-C. Urine protein excretion measurement included urinalysis with protein, protein to creatinine ratio, albumin to creatinine ratio, 24 hr urine protein, and timed urine protein.

Conclusions: In this initial validation study of digital clinical quality measures for lupus applied to five rheumatology practices in the RISE registry, we found good agreement for hydroxychloroquine and glucocorticoid use between medical record review and RISE data. Discrepancies in glucocorticoid dosing rarely led to misclassification for the glucocorticoid measure. Agreement was lower for the capture of kidney monitoring tests. Further work will include additional measure validity testing between RISE and Medicare data and will examine strategies to more accurately capture kidney monitoring for patients with lupus.

PV087 / #47

Poster Topic: ***AS11 - Epidemiology and Public Health***

CERVICAL CANCER SCREENING RATES AMONG KOREAN WOMEN OF CHILDBEARING AGE WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Women with systemic lupus erythematosus (SLE) face an increased risk of cervical cancer (CC), yet their CC screening rates are reportedly low. This study aimed to examine the CC screening rates and identify potential predictors influencing CC screening uptake in Korean women of childbearing age with SLE.

Methods: Prevalent cases of women of childbearing age (20-49 years) with SLE were identified using the National Health Insurance Service-National Health Information Database (NHIS-NHID) (2016-2017). Age-matched women without rheumatic diseases, including SLE, seropositive rheumatoid arthritis, and ankylosing spondylitis randomly selected at a 1:5 ratio served as controls. For those eligible for CC screening in 2018-2019, Papanicolaou (Pap) test rates were calculated from NHIS-National Health Screening Database. Logistic regression was used to estimate odds ratios (ORs) for factors associated with CC screening.

Results: Among 10,981 women with SLE and 54,905 age-matched controls eligible for CC screening, Pap test rate was significantly lower in the SLE group compared with the control group (49.6% vs 52.1%, p=<0.0001). Logistic regression analysis revealed that younger age, lower income, self-employment and medical aid insurance types, and rural residence were associated with lower likelihood of Pap test uptake in both the SLE and control groups. The presence of comorbidities increased the likelihood of Pap test uptake in the control group (OR 1.18, 95% CI 1.13-1.23), but had no significant impact on the SLE group (OR 0.95, 95% CI 0.87-1.04).

Conclusions: CC screening rates were significantly lower in women with SLE compared with their age matched controls. To lower the risk of CC in women of childbearing age with SLE, it is crucial to implement strategies that reinforce adherence to national CC screening programs for these women, particularly for those who are younger, have lower incomes, have self-employment and medical aid insurance types, or reside in rural areas.

PV088 / #423

Poster Topic: ***AS11 - Epidemiology and Public Health***

CARDIOVASCULAR AND CEREBROVASCULAR OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH CORONAVIRUS DISEASE 2019: A NATIONAL INPATIENT ANALYSIS

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Background/Purpose: While Systemic Lupus Erythematosus (SLE) patients are known to be at increased risk for severe Coronavirus Disease 2019 (COVID-19) outcomes, specific cardiovascular risks remain poorly defined. We aimed to quantify acute cardiovascular and cerebrovascular complications in hospitalized SLE patients with COVID-19 using 2021 nationally representative data.

Methods: Using the 2021 National Inpatient Sample, we identified adult SLE patients (International Classification of Diseases, 10th Revision code M32) stratified by COVID-19 status. Primary outcomes included cardiac arrest, intubation, and stroke. Using survey-weighted logistic regression, we calculated adjusted odds ratios (aOR) for these outcomes, controlling for demographics and comorbidities.

Results: Among 170,085 hospitalized SLE patients, 12,710 (7.47%) had COVID-19. SLE patients with COVID-19 had higher rates of cardiac arrest (335/12,710 [2.64%] vs 1450/157,375 [0.92%], $p < 0.001$), intubation (1430/12,710 [11.25%] vs 4340/157,375 [2.76%], $p < 0.001$), and mortality (1655/12,710 [13.02%] vs 3510/157,375 [2.23%], $p < 0.001$). After adjustment, COVID-19 remained an independent predictor of cardiac arrest (aOR 2.98, 95% CI 2.28-3.90, $p < 0.001$), intubation (aOR 4.87, 95% CI 4.22-5.62, $p < 0.001$), and mortality (aOR 7.27, 95% CI 6.28-8.42, $p < 0.001$). Substance use was lower in COVID-19 patients: nicotine (1120/12,710 [8.81%] vs 24,299/157,375 [15.44%], $p < 0.001$) and alcohol (145/12,710 [1.14%] vs 4768/157,375 [3.03%], $p < 0.001$).

Conclusions: This comprehensive analysis reveals markedly increased risk of severe cardiovascular outcomes in hospitalized SLE patients with COVID-19, including a nearly threefold higher risk of cardiac arrest and nearly fivefold higher risk of respiratory failure requiring intubation. Notably, this elevated risk persists despite lower rates of traditional cardiovascular risk factors such as alcohol and tobacco use. These findings emphasize the critical need for targeted cardiovascular monitoring in SLE patients with COVID-19.

PV089 / #330

Poster Topic: ***AS11 - Epidemiology and Public Health***

SEASONAL VARIATION IN MORTALITY AND CARDIOVASCULAR OUTCOMES AMONG HOSPITALIZED SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A NATIONWIDE ANALYSIS

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Background/Purpose: While seasonal variation affects many autoimmune conditions, its impact on hospitalized Systemic Lupus Erythematosus (SLE) patients remains poorly understood. We aimed to evaluate seasonal patterns in mortality and major clinical outcomes among hospitalized SLE patients using a nationally representative database.

Methods: Using the 2021 National Inpatient Sample, we identified adult SLE patients (International Classification of Diseases, 10th Revision code M32). Seasons were defined as Spring (March-May), Summer (June-August), Fall (September-November), and Winter (December-February). Primary outcomes included in-hospital mortality, cardiac arrest, and respiratory failure requiring intubation. We employed survey-weighted multivariable logistic regression to calculate adjusted odds ratios (aOR), controlling for age, sex, race, Elixhauser comorbidity index, hypertension, diabetes, chronic kidney disease, prior myocardial infarction, and prior stroke.

Results: Among 170,085 hospitalized SLE patients, we observed even seasonal distribution (Spring 25.85%, Summer 25.94%, Fall 24.43%, Winter 23.78%). Unadjusted mortality rates demonstrated a progressive increase from Spring (2.36%) through Summer (2.89%) and Fall (3.35%), peaking in Winter (3.59%). After adjusting for demographics and comorbidities, this pattern persisted with significantly increased risk in Summer (aOR 1.24, 95% CI 1.03-1.49, p = 0.025), Fall (aOR 1.41, 95% CI 1.18-1.70, p < 0.001), and Winter (aOR 1.54, 95% CI 1.28-1.87, p < 0.001) compared to Spring. Cardiac arrest risk was highest in Summer and Winter (both aOR 1.54, 95% CI 1.13-2.08, p = 0.006 and 95% CI 1.14-2.09, p = 0.005, respectively). Respiratory failure requiring intubation showed a similar pattern, with risk increasing through Fall (aOR 1.22, 95% CI 1.02-1.45, p = 0.026) and peaking in Winter (aOR 1.34, 95% CI 1.12-1.59, p = 0.001). Mean length of stay increased from Spring (5.54 days, 95% CI 5.40-5.69) to Fall (5.93 days, 95% CI 5.78-6.08), with Fall showing significantly higher total hospital charges compared to Spring (adjusted incidence rate ratio [aIRR] 1.08, 95% CI 1.03-1.14, p = 0.003).

Conclusions: This first comprehensive analysis of seasonal variation in SLE hospitalizations reveals clinically and statistically significant increases in mortality and adverse outcomes during Fall/Winter months, with effect sizes ranging from 24% to 54% increased odds of mortality. These findings suggest the need for heightened vigilance and potentially adjusted monitoring strategies during higher-risk seasons.

PV090 / #421

Poster Topic: ***AS11 - Epidemiology and Public Health***

RISK OF ACUTE KIDNEY INJURY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH CORONAVIRUS DISEASE 2019: A NATIONAL INPATIENT ANALYSIS

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Background/Purpose: While studies have shown increased adverse outcomes in Systemic Lupus Erythematosus (SLE) patients with Coronavirus Disease 2019 (COVID-19), detailed analysis of acute kidney injury (AKI) risk factors remains limited. We aimed to assess AKI risk in hospitalized SLE patients with COVID-19 using 2021 nationally representative data.

Methods: Using the 2021 National Inpatient Sample, we identified adult SLE patients (International Classification of Diseases, 10th Revision code M32) stratified by COVID-19 status. The primary outcome was AKI. We employed survey-weighted logistic regression to calculate adjusted odds ratios (aOR), controlling for demographics, comorbidities, and substance use.

Results: Among 170,085 hospitalized SLE patients, 12,710 (7.47%) had COVID-19. AKI occurred more frequently in SLE patients with COVID-19 compared to those without (3725/12,710 [29.31%] vs 33,640/157,375 [21.38%], $p < 0.001$). COVID-19 independently predicted AKI (aOR 1.61, 95% CI 1.46-1.77, $p < 0.001$). Substance use was lower in COVID-19 patients: nicotine (1120/12,710 [8.81%] vs 24,299/157,375 [15.44%], aOR 0.71, 95% CI 0.64-0.78, $p < 0.001$) and alcohol (145/12,710 [1.14%] vs 4768/157,375 [3.03%], aOR 0.59, 95% CI 0.47-0.74, $p < 0.001$). Each year increase in age increased risk (aOR 1.01 per year, 95% CI 1.01-1.01, $p < 0.001$). African American patients had higher risk compared to Caucasian patients (aOR 1.18, 95% CI 1.09-1.28, $p < 0.001$), while females had lower risk than males (11,215/12,710 [88.24%] vs 138,905/157,375 [88.33%], aOR 0.76, 95% CI 0.70-0.82, $p < 0.001$). Compared to low comorbidity burden, Elixhauser categories strongly predicted risk: moderate (aOR 2.59, 95% CI 2.24-3.00, $p < 0.001$) and severe (aOR 4.32, 95% CI 3.73-4.99, $p < 0.001$). Prior cardiovascular conditions showed lower risk: myocardial infarction (aOR 0.79, 95% CI 0.71-0.88, $p < 0.001$) and stroke (aOR 0.85, 95% CI 0.73-0.98, $p = 0.029$).

Conclusions: This study demonstrates that COVID-19 significantly increases AKI risk in SLE patients, with 61% higher odds compared to non-COVID SLE patients. Our findings

reveal complex interactions between COVID-19 status, demographics, comorbidities, and substance use. The unexpected protective associations of cardiovascular conditions and substance use patterns suggest potential pre-emptive medical management effects. These insights can inform targeted preventive strategies and heightened monitoring protocols for this vulnerable population during the ongoing pandemic, particularly for identified high-risk subgroups such as older and African American patients.

PV091 / #536

Poster Topic: ***AS11 - Epidemiology and Public Health***

ECONOMIC IMPACT AND RESOURCE UTILIZATION OF CORONAVIRUS DISEASE 2019 IN HOSPITALIZED SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A NATIONAL INPATIENT ANALYSIS

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Background/Purpose: The economic impact of Coronavirus Disease 2019 (COVID-19) in Systemic Lupus Erythematosus (SLE) patients remains incompletely characterized. We aimed to analyze healthcare resource utilization and costs among hospitalized SLE patients with COVID-19 compared to those without, using a nationally representative database.

Methods: Using the 2021 National Inpatient Sample, we identified adult SLE patients (International Classification of Diseases, 10th Revision code M32) and stratified by COVID-19 status. Primary outcomes included length of stay (LOS) and total hospital charges. We employed survey-weighted Poisson regression for LOS analysis and generalized linear models for cost analysis, adjusting for demographics, comorbidities, and clinical factors.

Results: Among 170,085 hospitalized SLE patients, 12,710 (7.47%) had COVID-19. Mean LOS was significantly longer in SLE patients with COVID-19 versus without (8.48 vs 5.57 days, $p < 0.001$). After adjustment, COVID-19 was associated with a 53% increase in LOS (incidence rate ratio [IRR] 1.53, 95% CI 1.47-1.60, $p < 0.001$). Total hospital charges were substantially higher in COVID-19 patients versus non-COVID-19 patients ($103,126 vs $77,628, $p < 0.001$), with an adjusted cost ratio of 1.34 (95% CI 1.26-1.42, $p < 0.001$). Stratified analyses revealed higher rates of mechanical ventilation (11.25% vs 2.76%, $p < 0.001$) and acute kidney injury (29.31% vs 21.38%, $p < 0.001$) in COVID-19 patients. Among SLE patients with COVID-19, females versus males (88.24% vs 11.76%) showed lower hospital charges (IRR 0.91, 95% CI 0.85-0.98, $p = 0.015$) and shorter LOS (IRR 0.92, 95% CI 0.88-0.96, $p < 0.001$). African American versus Caucasian patients (29.50% vs 48.03%) demonstrated higher resource utilization (IRR 1.29, 95% CI 1.23-1.36, $p < 0.001$). Patients with severe versus mild comorbidity burden (41.03% vs 9.87%) had significantly higher costs (IRR 2.15, 95% CI 2.03-2.28, $p < 0.001$).

Conclusions: COVID-19 in SLE patients is associated with substantially increased healthcare resource utilization, manifesting as longer hospitalizations and higher costs. The economic burden is particularly pronounced in patients requiring mechanical ventilation or developing acute kidney injury. These findings highlight the significant economic impact of COVID-19 in SLE patients and can inform healthcare resource allocation and policy decisions for this high-risk population.

PV092 / #527

Poster Topic: ***AS11 - Epidemiology and Public Health***

ANALYSIS OF RACIAL DISPARITIES IN CORONAVIRUS DISEASE 2019 OUTCOMES AMONG HOSPITALIZED SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A NATIONAL INPATIENT STUDY

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Background/Purpose: While racial disparities exist in both Systemic Lupus Erythematosus (SLE) and Coronavirus Disease 2019 (COVID-19) independently, their combined impact remains understudied. We aimed to analyze differences in clinical outcomes and complications across racial groups among hospitalized SLE patients with COVID-19.

Methods: Using the 2021 National Inpatient Sample, we identified adult SLE patients with COVID-19. We analyzed outcomes across racial categories using survey-weighted regression models, adjusting for demographics, comorbidities, and socioeconomic factors. Primary outcomes included mortality, mechanical ventilation, acute kidney injury (AKI), and length of stay (LOS).

Results: Among 12,710 SLE patients with COVID-19, the racial distribution was: African American (29.50%), Caucasian (48.03%), Hispanic (14.59%), Asian (1.69%), and Other (6.18%). Compared to Caucasian patients, African American patients showed higher rates of mechanical ventilation (13.3% vs 9.8%, $p < 0.001$), AKI (33.2% vs 27.4%, $p < 0.001$), and longer mean LOS (9.2 vs 7.8 days, $p < 0.001$). After adjustment, African American patients maintained higher odds of mechanical ventilation (adjusted odds ratio [aOR] 1.17, 95% CI 1.00-1.37, $p = 0.045$) and AKI (aOR 1.18, 95% CI 1.09-1.28, $p < 0.001$). Hispanic patients compared to Caucasian patients demonstrated increased odds of mechanical ventilation (12.4% vs 9.8%, aOR 1.13, 95% CI 1.04-1.23, $p = 0.038$). Notably, comorbidity patterns differed significantly: African American versus Caucasian patients had higher rates of hypertension (34.7% vs 28.9%, $p < 0.001$) and obesity (31.9% vs 25.8%, $p < 0.001$). Healthcare resource utilization also varied, with African American patients experiencing higher total charges compared to Caucasian patients ($112,340 vs $98,450, $p < 0.001$). Social determinants analysis revealed disparities in insurance status, with African American patients more likely to have Medicaid compared to Caucasian patients (32.4% vs 24.6%, $p < 0.001$).

Conclusions: This comprehensive analysis reveals significant racial disparities in COVID-19 outcomes among hospitalized SLE patients, with African American patients experiencing higher rates of complications and resource utilization. These findings highlight the need for targeted interventions addressing both clinical and socioeconomic factors to improve outcomes across all racial groups in this high-risk population.

PV093 / #304

Poster Topic: ***AS11 - Epidemiology and Public Health***

DELAY IN DIAGNOSIS AND TREATMENT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN LATIN AMERICA. A MIXED METHODS STUDY

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex disease associated with significant early morbidity and mortality. Approximately 30% of patients with SLE experience diagnostic delays, with means ranging from 3 to 5 years. In Latin America (LA), the disparities in healthcare access and availability of specialized consultations across countries underscores the need to establish timelines and evaluate factors impacting key stages in the patients' healthcare journey. This study aims to describe the process of seeking care, as well as delays in diagnosis and treatment, and to identify associated factors—barriers, facilitators, and patient needs—among SLE patients receiving care at various rheumatology centers in LA.

Methods: This is a mixed methods (qualitative and quantitative) study in four phases with a sequential design, in which research outputs from each phase will serve as the foundation for subsequent phases. Phase 1: Evidence Generation - Identify the process of seeking care and define the concept of diagnostic delay through a systematic literature review and development of an interview guide for patients and rheumatologists. Phase 2: Qualitative Analysis - Describe and analyze the patient journey in SLE from the perspectives of both patients and rheumatologists. Phase 3: Questionnaire Development and Validation - Develop and validate a questionnaire to measure care delays and associated factors. Phase 4: Quantitative Analysis - Use the validated questionnaire to assess diagnostic and treatment delays in SLE patients across LA with a representative patient sample. The project is scheduled for the 2023-2027 period and is funded by a grant from PANLAR and the Latin American Lupus Study Group (GLADEL).

Results: Seventeen countries in LA are currently participating: Argentina, Bolivia, Chile, Colombia, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay, and Venezuela. Quantitative and qualitative systematic reviews been completed, and interview guides for rheumatologists and patients have been developed (Phase 1). Focus groups and in-depth patient interviews are currently underway, simultaneous with qualitative data analysis (Phase 2). Based on a sample design aligned with the epidemiological data of each country, the following activities will be conducted: Phase 2 - 23 focus groups with rheumatologists (an average of 8 participants per country), and 153 individual in-depth patient interviews; Phases 3 and 4 - 150 patients for the pilot test, 450 patients for questionnaire validation, and 13,369 patients for the measurement of diagnostic delays.

Conclusions: SLE is a heterogeneous disease that is challenging to diagnose and requires early treatment initiation. Patients and rheumatologists agree that delays in SLE diagnosis have specific characteristics, including disease variability, diversity of healthcare systems, educational factors among health professionals and the general population, and sociocultural and economic conditions. Measuring these delays is essential to provide evidence for informed decision-making in health policies at both national and regional levels.

PV094 / #450

Poster Topic: ***AS11 - Epidemiology and Public Health***

DEVELOPMENT OF A NOVEL FRAMEWORK TO INFORM COST-EFFECTIVENESS MODELS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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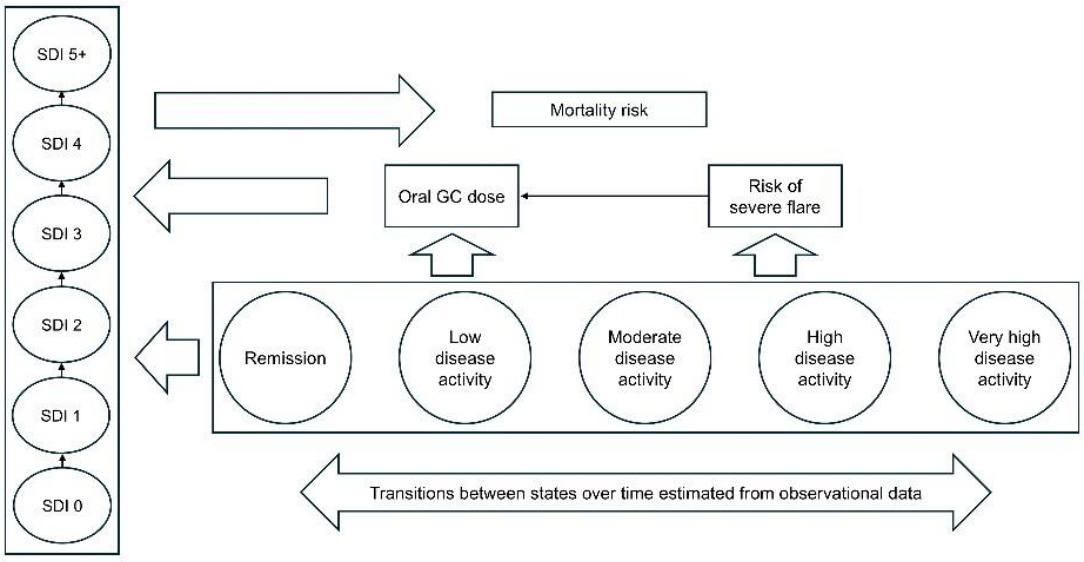
Background/Purpose: Cost-effectiveness models (CEMs) play a significant role in health technology assessments (HTAs). However, existing CEMs for systemic lupus erythematosus (SLE) are often complex and have limited face validity. Evolving clinical practices and new therapeutic regimens with different modes of action necessitate profound changes to prior publicly available models in SLE and the development of a new conceptual modeling framework [1–5].

Methods: A targeted literature review was conducted to identify treatment guidelines, standard of care, disease progression, outcome measures, drivers of health-related quality of life (HRQoL), costs, and existing CEMs in SLE. Following this, one-on-one virtual interviews were conducted with three international expert rheumatologists specializing in treating patients with SLE, to validate critical clinical components and their relationships identified in the literature review for use in the CEM. Additionally, two rounds of virtual advisory board meetings were convened with the same rheumatologists, two HTA experts, and two SLE patients to reach consensus on key assumptions and the conceptual model structure.

Results: Seven key components were identified as important for developing a CEM for SLE: disease activity, organ damage, flares and remission, oral glucocorticoid (GC) use, mortality, HRQoL, and healthcare resource use. An individual patient simulation approach was deemed necessary to reflect disease heterogeneity in patient disease trajectories and to facilitate interactions between different components of the disease process, such as disease activity, oral GC dosage and organ damage. Existing individual simulation models have used a regression equation to reflect disease activity over time that poorly captures patient heterogeneity. This new model structure categorizes disease activity into discrete levels (3–5 levels, including remission and low disease activity state). Existing models simulated organ damage by organ class, which adds complexity but poorly captures treatment benefits in slowing organ damage. The new model structure simplifies organ damage progression into six levels. Furthermore, severe flares are captured in this model, simulated as a function of disease activity, and influence the risk of organ damage (Figure 1). The face validity was confirmed by clinical, HTA and patient experts. The inclusion of distinct clinical states such as remission, low disease activity and severe flare are an important improvement of this new model framework as they are considered relevant to clinical practice and HTA decision making.

Conclusions: The new SLE CEM framework better reflects the impact of treatment on patient disease trajectories to facilitate improved technology assessment. This CEM concept can be utilized to assess the value of investigational treatments for SLE in the future, ensuring that they adequately address key unmet needs in SLE. **Figure 1:** Proposed SLE cost-effectiveness model structure



GC, glucocorticoid; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLE, systemic lupus erythematosus. [1.]

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PV095 / #822

Poster Topic: *AS11 - Epidemiology and Public Health*
Late-Breaking Abstract

HARNESSING VOLUNTEER NETWORKS TO DEVELOP A NEEDS ASSESSMENT PROTOCOL FOR PEER SUPPORT IN LUPUS CARE IN JAMAICA

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Background/Purpose: Background In Jamaica, an estimated 6,000 individuals are living with Lupus, yet fewer than 2,000 are enrolled in national health benefit programs, and only 300 are actively engaged as members of the Lupus Foundation of Jamaica (LFJ), a 40 year old education, support and advocacy group. Despite the growing recognition of peer support as an important and effective addition to comprehensive lupus management, lupus-specific peer support is underdeveloped in Jamaica due to limited funding, limited research capacity within lupus organizations, and low national priority. The LFJ set out to develop a peer support curriculum for lupus patients in Jamaica through a volunteer-led, participatory needs assessment, designed to identify the specific challenges faced by Jamaicans living with lupus.

Methods: A volunteer-led, multi-stakeholder collaboration guided the development of a needs assessment protocol to inform the peer support curriculum for persons living with lupus. LFJ volunteers, including persons living with lupus, caregivers, clinicians, and researchers worked together to ensure the study captured diverse patient experiences and priorities. The team conducted a brief literature review to understand the key considerations for designing and implementing peer support programs and to identify validated tools for assessing disease activity and experiences of persons with lupus. The draft survey was updated after a series of cognitive debriefing interviews with lupus patients, a caregiver, and a physician to ensure clarity, cultural relevance, and comprehensiveness. Additionally, the team established ethical and procedural guidelines, aligning with best practices in community engaged research. Strategies were developed to recruit participants through a range of networks including treatment centres, community and professional groups, and social media to maximise reach and diversity. The protocol was reviewed and approved by the medico-legal advisory committee of the Ministry of Health and Wellness, Jamaica.

Results: The final protocol incorporated qualitative in-depth interviews, focus group discussions (FGDs), and a self-administered electronic survey to identify gaps in lupus care and support. Data collection will include 6 to 8 in-depth interviews and 3 to 5 FGDs with persons with lupus, caregivers, and healthcare providers. Additionally, a target

sample of 196 lupus patients, 33 healthcare workers, and 49 caregivers will be recruited to complete the electronic questionnaire. The tool was designed to be accessible and inclusive. Volunteer team of researchers and LFJ staff will lead recruitment, data collection, data analysis and synthesis to formulate recommendations for the peer support curriculum.

Conclusions: This project, the first of its kind in the Caribbean, provides a model for integrating peer support into lupus care in low-resource settings. It demonstrates the potential for volunteer-driven research to address capacity and funding limitations in non-academic lupus organizations, and drive impactful health research, providing a model for other low-resource settings seeking to improve comprehensive lupus management. The finalized needs assessment protocol is a critical step towards developing a culturally relevant, patient-driven peer support program that is tailored to the specific needs of lupus patients in Jamaica. Findings from the needs assessment will guide the development of LFJ's peer support training curriculum, helping the Foundation to prioritize limited resources while also establishing baseline data for future evaluations.

PV096 / #835

Poster Topic: *AS11 - Epidemiology and Public Health*
Late-Breaking Abstract

INVESTIGATING CANADIANS' INFORMATION NEEDS RELATED TO LUPUS: A GOOGLE TRENDS ANALYSIS OF ONLINE SEARCH QUERY DATA

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Background/Purpose: SLE impacts 1 in 2000 Canadians, with indirect impacts on caregivers, households, family members, and healthcare professionals. SLE is idiosyncratic, with largely invisible symptoms that vary significantly from person to person, and disproportionately impacts groups considered vulnerable such as women, racialized, and low-income populations. These inequities are further underscored by a lack of public education and awareness about SLE, leading to delays in diagnosis and critical care and support. Indeed, lack of knowledge surrounding SLE has been identified as a main challenge for patients, particularly those seeking a diagnosis or recently diagnosed. Facing this challenge, many turn to online sources for information, where they risk encountering misleading or even endangering mis- or disinformation. The purpose of this research is to investigate public awareness of SLE and how this varies spatially across Canada using health geographical approaches to examine Google Trends (GT) data.

Methods: This research employs a health geographical approach to exploring spatial and temporal trends in information-seeking behaviours and associated knowledge gaps related to SLE in Canada. Using GT, relative search volumes (RSV), associated topics and queries were collected from 2004-present, using key words for "lupus". The top 25 search terms were collected from each province and territory, and these search terms were analyzed thematically. The research process leveraged an integrated knowledge translation approach (iKT), in which a patient partner living with SLE was a core member of the research team.

Results: Search volumes for the search term "lupus" in Canada hit an all-time peak in October 2015 (RSV=1.0). This peak occurred in all provinces simultaneously, correlating with celebrity Selena Gomez's diagnosis with SLE. Additional peaks were observed across Canada in July 2009 (RSV=0.58), September 2016 (RSV=0.69), and September 2017 (RSV=0.78), all of which were correlated with milestones in the development and eventual approval of belimumab for SLE. Similarly, a peak in August 2016 (RSV=0.66) was associated with positive Phase II trials for voclosporin. A national peak in June 2010 (RSV=0.60) was associated with the 9th International Congress on SLE held in

Vancouver. There was a marked trough across all provinces in November and December of 2020 (RSV=0.28), perhaps reflecting that SLE-related concerns were overshadowed by the ongoing COVID-19 pandemic. Overall interest was highest in Newfoundland (RSV=1.0), New Brunswick (RSV=0.83) and Manitoba (RSV=0.80), though the top related topics and queries varied spatially among provinces. The most frequently searched terms typically fell within the following themes: causes of lupus, diagnosis, symptoms, medication, and treatment. Some search terms were spatially unique, only appearing in one province, including search terms in French ("lupus maladie", Quebec), and Indonesian ("penyakit lupus", Newfoundland) languages.

Conclusions: An understanding of the information needs of the general public related to SLE, and how they vary spatially, is critical for designing and implementing targeted and effective patient education interventions. To this end, these research results will be shared and triangulated with the knowledge needs of advocacy organizations, and the realities of lived SLE experience, through a deliberative dialogue with key stakeholders from across Canada. This will set a foundation for the design and implementation of relevant interventions to effectively reduce SLE-related health disparities and improve SLE-related quality of life nationwide.

PV097 / #349

Poster Topic: ***AS11 - Epidemiology and Public Health***

COMORBIDITY BURDEN AND DEMOGRAPHICS OF PATIENTS ACROSS SUBTYPES OF CLE FROM A LARGE US ELECTRONIC HEALTH RECORD DATABASE STUDY

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Background/Purpose: Cutaneous lupus erythematosus (CLE) is an autoimmune disease with various skin manifestations, which can occur with or without systemic lupus erythematosus (SLE) [1.]. Few population-based observational studies have examined demographic and clinical characteristics of patients with CLE since four new CLE codes were introduced in the International Classification of Disease-10, Clinical Modification (ICD-10 CM) system in 2015. Electronic Health Record (EHR) databases are a rich source of data with large numbers of patients with CLE. This cross-sectional study evaluated demographics and comorbidities in a large cohort of US patients with CLE, and CLE subtypes stratified by coexisting SLE, from 2016 to 2022.

Methods: This analysis was performed using the Optum® de-identified EHR data set (N = ~113 million people in the US). CLE, SLE [2.], and comorbidities were defined using ICD-9/10-CM codes. Informed by a recent study validating EHR-based algorithms to identify CLE patients [3.], CLE patients were defined as having ≥ 2 ICD-10-CM codes for CLE, with ≥ 1 code from a dermatologist or a rheumatologist during the study period (2016–2022).The date of the first CLE diagnostic code on record (index date) was considered the diagnosis date. Comorbidities were identified by ≥ 1 ICD-10 CM code. Descriptive statistics for demographics and comorbidity frequency were summarized.

Results: Demographics: Among the 10,025 identified patients with CLE, 47.1% had coexisting SLE (CLE+SLE). Discoid lupus erythematosus (DLE) occurred in 56.8% and 72.0% of the CLE-only and CLE+SLE patients, respectively, while subacute CLE (SCLE) occurred in 13.3% and 5.7% of those same patient groups. Demographic findings by CLE subtype, as reported in CLE-only and CLE+SLE patients, respectively, included proportion of female patients (DLE: 76.8%, SCLE: 81.1%; DLE: 89.9%, SCLE: 87.1%), median age-of-onset (years) (DLE: 52, SCLE: 61; DLE: 48, SCLE: 56), and proportion of African-American patients (DLE: 29.1%, SCLE: 4.8%; DLE: 33.9%, SCLE: 8.9%) (**Table 1**). **Comorbidities:** Among the comorbidities of interest, the frequency of some cardiovascular risk factors and mental health disorders in patients with CLE by subtype, as reported in CLE-only and CLE+SLE patients, respectively, included: hypertension (DLE: 35.7%, SCLE: 34.1%; DLE: 54.2%, SCLE: 47.2%), obesity (DLE: 21.9%, SCLE:

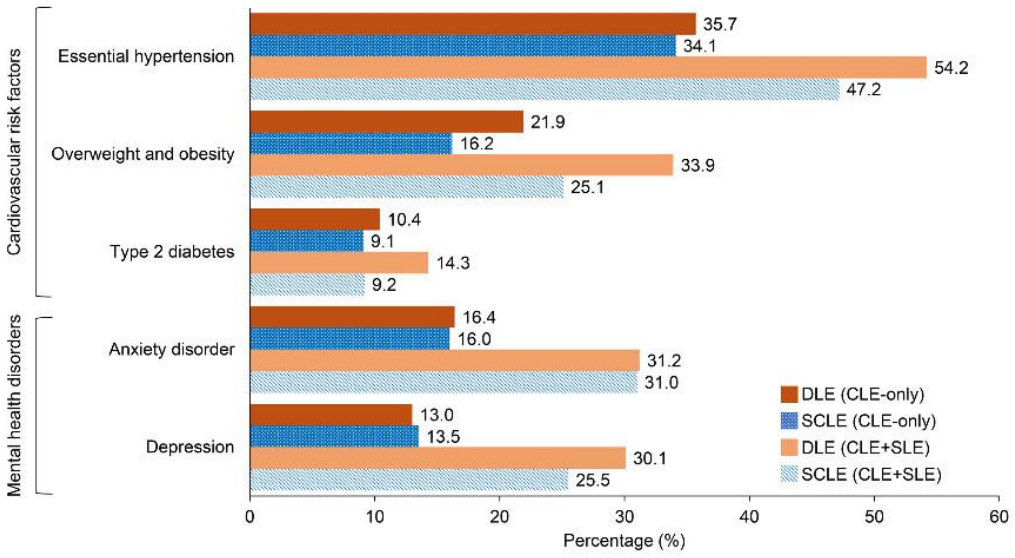
16.2%; DLE: 33.9%, SCLE: 25.1%), type 2 diabetes (DLE: 10.4%, SCLE: 9.1%; DLE: 14.3%, SCLE: 9.2%), depression (DLE: 13.0%, SCLE: 13.5%; DLE: 30.1%, SCLE: 25.5%), and anxiety disorder (DLE: 16.4%, SCLE: 16.0%; DLE: 31.2%, SCLE: 31.0%) (**Figure 1**).

Table 1: Demographic characteristics of patients with CLE, by CLE subtype, in the Optum® EHR database 2016–2022

	CLE-only		CLE+SLE	
	DLE	SCLE	DLE	SCLE
Characteristic	**(n = 2,200)**	**(n = 519)**	**(n = 3,399)**	**(n = 271)**
Sex, n (%)				
Female	1,706 (76.8)	421 (81.1)	3,056 (89.9)	236 (87.1)
Male	513 (23.1)	98 (18.9)	340 (10.0)	35 (12.9)
Unknown	1 (0.0)	0	3 (0.1)	0
Age at index date, years, median (min, max)	52 (18, 87)	61 (18, 88)	48 (18, 85)	56 (20, 84)
Race, n (%)				
African American	647 (29.1)	25 (4.8)	1,153 (33.9)	24 (8.9)
Asian	73 (3.3)	7 (1.3)	99 (2.9)	2 (0.7)
Caucasian	1,215 (54.7)	447 (86.1)	1,787 (52.6)	226 (83.4)
Other/Unknown	285 (12.8)	40 (7.7)	360 (10.6)	19 (7.0)

CLE, cutaneous lupus erythematosus; DLE, discoid lupus erythematosus; EHR, Electronic Health Record; SCLE, subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus.

Figure 1. Comorbidities of interest in patients with CLE occurring anytime between 2016–2022, by CLE subtype, in the Optum® EHR database



CLE, cutaneous lupus erythematosus; DLE, discoid lupus erythematosus; EHR, Electronic Health Record; SCLE, subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus.

Conclusions: CLE patients across all subtypes, and with or without SLE, experience serious comorbidities including cardiovascular risk factors and mental health disorders, underlining the seriousness of CLE. Characterizing this comorbidity burden could encourage earlier screening and treatment and improve understanding of CLE beyond cutaneous manifestations. First presented at AAD 2025. **References**: [1.] Durosaro O. Arch Dermatol 2009;145:249–253. [2.] Barnado A. Arthritis Care Res

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PV097a / #117

Poster Topic: ***AS11 - Epidemiology and Public Health***

SOCIAL DRIVERS OF HEALTH IN A LARGE ACADEMIC LUPUS CLINIC

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Background/Purpose: Adverse social drivers of health (SDoH) in systemic lupus erythematosus (SLE) are associated with worse health outcomes and quality of life. The aim of this initiative was to provide support to SLE patients with SDoH needs. To respect patient autonomy, financial support was given as $100 cash to spend as they deemed best. Herein, we report the clinical characteristics of those who received financial support as well as the patient and staff perspective of the program.

Methods: Adult Duke Lupus Clinic (DLC) patients are screened annually for SDoH insecurities. From January 2024 to October 2024, SLE patients were with food and/or transportation insecurity by routine SDoH screening, lupus nephritis patients with federally funded (Medicare and/or Medicaid) or no insurance, and patients with a SDoH need as determined by the treating clinician's discretion qualified for financial support. These patients were offered 1) $100 cash at the end of visit 2) a referral to NCCare360, a statewide community social support program, and 3) a referral to DukeWell, an internal healthcare navigation program. After the visit, patients completed an anonymous survey on barriers to healthcare and experience with the program. Feedback was obtained from the clinic team. The clinical and demographic data of participants in the Duke Lupus Registry (DLR) who did and did not receive cash assistance were analyzed.

Results: Cash was distributed to 101 DLC patients; 27 patients received cash at more than one visit. Of the 276 DLR patients seen during this time, 74 patients (26%) received cash assistance and underwent analysis. There was no difference in age, disease duration, gender, and Hispanic ethnicity between participants who had identified SDoH barriers and those who did not (Table 1). However, patients with identified SDoH barriers were more likely to have lower educational attainment, federally-funded insurance or no health insurance, and a low annual income. Nearly half of patients with an identified SDoH barrier reported food insecurity and over a quarter reported transportation insecurity. Nearly three-quarters identified difficulty paying for a variety of basic needs such as food, housing, medical care, and heating. Participants with an identified SDoH barrier were more likely to have a history of brain fog, fatigue, waking unrefreshed, and anxiety in the previous 18 months.

Over three-quarters of patients completed the anonymous survey. Over half of patients had never worked with a case manager or social worker. The most frequently reported barriers to managing and accessing healthcare included the cost of food (55%), cost of utilities (45%), and cost of medications (43%). Feedback from patients was overwhelmingly positive (Table 2), with patients frequently sharing emotions such as “grateful” or “blessed”. Quotes from the clinical team highlight the profound, positive impact of the program, with team members noting how the cash assistance has addressed tangible needs of patients with SLE.

Table 1. Demographics and Disease Manifestations

	SDoH Recipients n=74	Non Recipients n=202
Demographics		
Age, mean (SD)	44.3 (14.4)	44.0 (14.5)
Female (n=272)	68 (92%)	183 (92%)
Black race (n=269)	60 (83%)	100 (51%)
Ethnicity Hispanic (n=261)	2 (3%)	6 (3%)
Education (4-year College degree or more) (n=268)	21 (29%)	96 (49%)
Federally funded or no insurance (n=267)	54 (75%)	82 (42%)
Annual Income <$50,000 (n=259)	53 (77%)	89 (47%)
Social support 2 or more people (n=269)	56 (78%)	154 (78%)
Documented Social Drivers of Health		
Food insecurity (% yes) (often or sometimes true) (n=241)	32 (49%)	12 (7%)
Transportation insecurity (% yes) (n=243)	17 (26%)	5 (3%)
Daily stress (% yes) (to some extent, rather much, or very much) (n=81)	22 (67%)	19 (40%)
Difficulty paying for basics like food, housing, medical care, and heating (% yes) (somewhat hard to very hard) (n=126)	32 (70%)	24 (30%)
Disease Activity During Previous 18 Months		
Type 1 PGA (longitudinal mean) (n=261)	0.7 (0.6)	0.5 (0.5)
Type 2 PGA (longitudinal mean) (n=258)	1.0 (0.6)	0.7 (0.6)
Patient Reported Symptoms During Previous 18 Months		
Polysymptomatic Distress (PSD ≥12 ever) (n=263)	37 (52%)	87 (45%)
Depression (ever) (n=261)	36 (51%)	80 (42%)
Mod-Severe Brain Fog (ever) (n=262)	32 (46%)	60 (31%)
Mod-Severe Fatigue (ever) (n=262)	54 (76%)	113 (59%)
Mod-Severe Waking unrefreshed (ever) (n=261)	48 (69%)	103 (54%)
Mod-Severe Anxiety (ever) (n=261)	30 (43%)	46 (24%)

Table 2. Patient and clinical team quotes about the cash assistance program.

Patient Quotes
"Grateful and hope to be able to get in contact with someone who can help with resources."
"It's a blessing to have."
"It's a really great help"
"I think it helps the community"
"Great because we need help"
"I think it will help a lot of people"
Clinical Team Quotes
"This is amazing! What a wonderful impact to our community!" -Nurse Manager
"I think that this has been a terrific project. The experience of giving patients $100 has been remarkable, with many surprised and so appreciative. I feel like this is really having an impact on the people with lupus that we serve." -Physician
"This past week, when I gave a patient her $100, she responded with tears. As she hugged me and cried, she explained that she hadn't known how she was going to afford to get out of the hospital parking garage. My lupus patient puts everyone else's needs first, often to the detriment of her lupus care and health. It was wonderful to be able to ease her financial burdens, even if just a little, and send her home glad she had come to see her medical team." -Physician
"I was really excited to hear that such a program would exits for our Lupus patients. For some that I have had the pleasure of being the one to hand the money to them was an eye opener of just how much one small gift meant to some. They were so thankful and excited at the same time. We never know what struggles some may have but just to know that for one moment, day we can offer just a little to go a long way. Great program so far." -Clinic staff
The process has been really easy for me. It has helped me pay attention to certain patient needs that I wasn't accustomed to think about on a regular basis, and that is important because these needs have real and significant impact on patients' health outcomes. It is gratifying to know that we are helping these patients with tangible needs that they care about." -Physician

Conclusions: A financial support program was implemented to address SDoH needs that are identified upon routine clinic screening. A range of SDoH needs and financial difficulty affording food, utilities, and medications are not uncommon in SLE. Those with SDoH needs experienced a greater burden of fatigue, pain, and mental health suggesting a connection between social, environmental, and physical health. Patients and the clinical team expressed gratitude and appreciation for program. Sustainable programs that screen and address SDoH could impact disparities in lupus outcomes.

PV098 / #559

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

CYTOKINES GENES POLYMORPHISMS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with multisystemic involvement. SLE results from the interaction between genetic and environmental factors that cause loss of tolerance to self-antigens and the synthesis of autoantibodies. The aim of our study was to assess genetically the involvement of cytokines in the pathogenesis of SLE in a group of Algerian patients.

Methods: Our study was carried out on 156 lupus patients and 104 healthy subjects. Polymorphisms of the genes cytokine of IL-6 (-174 G/C), IL-1 (-31 C/T, -511 C/T), TNFα (-308 G/A, -208 G/A), IRF5 (-13176 A/C, -3835 G/T) and IL-8 (-251 T>A) were evaluated by real-time PCR (Taqman technology).

Results: The immunogenetic study revealed a significant association between G allele of the -3835 G / T polymorphism of the IRF5 gene and the risk of genetic susceptibility to the lupus ($p = 0.012$). Stratification according to clinical has showed that the G allele of the -31 C/T polymorphism of the IL-1 gene is associated with joint damage ($P = 0.024$) in lupus patients and the allele A of -511 C/T polymorphism predisposes to hematological damage ($p = 0.041$). Also, the allele A of the polymorphism-238 G/A of the TNFα gene is associated with neuropsychiatric impairment ($p = 0.036$) and the allele A of -251A/T SNP of the IL-8 gene at joint damage ($p = 0.04$).

Conclusions: Cytokines could be very useful genetic marker for diagnosing SLE, assessing disease systemic disorders.

PV099 / #84

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

NUCLEOLAR DISRUPTION IN AUTOIMMUNE AND NEURODEGENERATIVE DISEASES

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Background/Purpose: Autoimmune disease tautology (i.e. common features of autoimmune diseases such as female predominance among patients) suggests there may be similar cellular level mechanisms in many autoimmune diseases with the subsequent symptoms varying based on the cell type, triggers involved, and immune system accessibility. This tautology can also include Alzheimer's and other neurodegenerative diseases. The purpose of this project was to search published research to develop a mechanistic hypothesis based on synergies among these diseases.

Methods: The author's previously published hypothesis, the "X chromosome-nucleolus nexus" which focused primarily on lupus, provided a starting point. That hypothesis proposed that nucleolar dynamics during extraordinary cellular stress could disrupt the inactive X chromosome (Xi; aka, the "nucleolar satellite" or Barr body). This could open expression of normally silent X-linked polyamine enzyme alleles and an abundance of Alu elements on the Xi. Increased polyamine metabolism could drive further nucleolar dynamics. RNA polymerase III generated Alu RNA transcripts could competitively bind nucleolin, disrupting the nucleolar shell normally stabilized by nucleolin and structural RNAs. Disruption of the nucleolar shell could release autoantigenic material leading to the lupus autoimmune reaction. Online queries (e.g., PubMed) with key word combinations (e.g., nucleolin, lupus, Alzheimer's) were used and retrieved research results that supported potential abnormalities in polyamine metabolism, disruption of peri-nucleolar chromatin, abnormal expression of Alu elements, and loss of nucleolar integrity.

Results: It was found that many aspects of Alzheimer's and other diseases could be explained by expansion of the original "X chromosome-nucleolus nexus" hypothesis and such expansion gives further details for the original lupus hypothesis. When key genes in Alzheimer's were queried, it was found that they were in peri-nucleolar chromatin: presenilin-1 on chromosome 14; amyloid precursor protein on chromosome 21; tau on chromosome 17, and ApoE4 on chromosome 19. Chromosomes 14 and 21 with nucleolar organizing regions are in the nucleolar shell and chromosomes 17 and 19, with DNA repair genes, are associated with the nucleolus (i.e.,TADs, topological associated domains) to assist in the nucleolar function of DNA repair. Therefore, nucleolar dynamics could potentially adversely impact epigenetic control in these peri-nucleolar chromosomes. Alu elements comprise 11% of the human genome, with more

than one million Alu copies, whereas non-primate animals do not have Alu elements. Alu elements account for 28.8% of the pseudo-autosomal region 1 (PAR1) of the X chromosome (~2,500 Alu copies). The chromosome 22 long arm (22q) in the nucleolar shell is 18% Alu, chromosome 19 is 25.8% Alu, chromosome 17 is 18% Alu with 30% in 17p13.3. Such Alu clusters could have a significant role in disruption of the nucleolus in lupus, Alzheimer's and other autoimmune and neurodegenerative diseases.

Conclusions: The hypothesis proposes mutual disruption of the nucleolus and peri-nucleolar chromatin in these diseases with loss of epigenetic control that allows altered expression of Alzheimer's related genes and, in lupus, formation of autoantigens, many of which are components of the nucleolus. Increased polyamine metabolism (e.g., triggered by EBV or UV light) can reduce S-adenosylmethionine (SAM) which, at low levels seen in Alzheimer's, can induce tau phosphorylation by p38 kinase followed by polyamine-induced aggregation of hyperphosphorylated tau. Polyamine recycling can reduce acetyl-CoA leading to low acetylcholine seen in Alzheimer's. This hypothesis suggests new directions for therapeutic research in autoimmune and neurodegenerative diseases.

PV100 / #484

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

DYSREGULATION OF THE EXPRESSION OF HUMAN RETROVIRUSES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease characterized by dysregulation of the immune system. Although many etiologies have been suggested for SLE, the possibility that active or latent viruses may contribute has been entertained. A family of viral elements, the Human Endogenous Retroviruses (HERVs), remnants of ancient viral infections comprising ~8% of the human genome, are possible etiologic factors in SLE. Previous studies have suggested that HERVs contribute to SLE pathogenesis by being differentially expressed in people with the disease — triggering the sensing mechanisms that detect cytoplasmic viral-like RNA and, thereby, inducing an interferon response.[1.] For decades, HERVs have been classified and named by molecular and genomic features. This legacy system has little bearing on the evolutionary history and sequence features of HERV elements. We hypothesized that features of HERV immunogenicity and the role of HERVs in SLE pathogenesis would be more apparent upon regrouping HERVs in a taxonomically-robust manner followed by a set of in-silico RNA-binding analyses and transcriptomic HERV quantification in SLE patients.

Methods: We employed sequence alignment and phylogenetic inference to align 14,000+ HERV sequences in the human genome and calculate a distance matrix for these sequences. We clustered HERVs into groups with shared sequence similarity and common evolutionary history. We characterized the sequences in these clusters using RNA binding prediction to identify how RNA HERV transcripts would be expected to bind with sensors of innate immunity relevant to SLE pathophysiology: Rig-I, MDA5, ADAR, and ZBP. We further classified HERV sequences according to viral similarity by performing a BLAST against a database of exogenous viral genomes. HERV expression in RNA-Seq data from human keratinocytes stimulated with various cytokines relevant to SLE pathophysiology (TWEAK, TNF, IL-17A IFNa2, IL18, IFNa6, IFNb, and IFNg) was quantified and HERV expression was similarly quantified in 124 SLE patients and 41 healthy controls.

Results: We identified HERV clusters of shared evolutionary history that are dysregulated in SLE. Clusters of HERVs with specific expression patterns in SLE were also exhibited dysregulated expression in keratinocytes stimulated with inflammatory cytokines and increased binding with sensors of innate immunity. Those families of

HERVs upregulated upon cytokine stimulation are the same HERVs that seem to be immunoactive, especially in terms of binding with ADAR — an intracellular enzyme known to be involved in RNA editing and regulation of interferon production. Finally, families of HERVs upregulated in SLE share sequence similarity with extant infectious viruses with known rheumatologic consequences, including alphavirus,Chikungunya.

Conclusions: HERVs can be separated into families based on sequence similarity. Specific families are up-regulated in SLE, are induced by specific cytokines in-vitro and are enriched in sequences that bind intracytoplasmic RNA sensors. Our findings support the existence of positive-feedback loops in the pathophysiology of SLE, whereby cytokines induce the expression of HERVs with molecular motifs that bind to sensors of cytoplasmic RNA and lead to further cytokine production, inflammation, and an interferon signature in SLE. Finally, these families of HERVs share sequence similarity with infectious viruses known to cause rheumatologic manifestations.

References: Stearrett, N. *et al.* Expression of Human Endogenous Retroviruses in Systemic Lupus Erythematosus: Multiomic Integration With Gene Expression. *Front. Immunol.* **12**, 661437 (2021).

PV101 / #418

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

GENETIC ASSOCIATIONS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SUDANESE POPULATION

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Background/Purpose: Previous genome-wide studies have revealed >130 loci linked to systemic lupus erythematosus (SLE), primarily in European populations.[1] Research on East Asian groups has shown different genetic associations related to SLE. This study contributes to understanding genetic risk factors for SLE across various ancestries, focusing on the Sudanese population. This study aimed to assess genetic associations with SLE in a cohort of Sudanese individuals. We sought to determine if the *HLA* alleles found in this cohort align with those identified in other studies.

Methods: The study involved 483 Sudanese participants, 96 of whom were diagnosed with SLE based on the revised 1982 ACR criteria and 387 age- and sex-matched healthy controls. Genotyping was performed using the Infinium® Expanded Multi-Ethnic Genotyping Array (MEGAEX). *HLA* alleles and amino acids were imputed using a modified 1000G African panel in SNP2HLA.[2] Genetic markers with a minor allele frequency (MAF) below 1%, genomic missingness over 5%, or imputation quality under 75% were excluded. After quality control, 453 unrelated samples and 1,183,339 variants were analyzed statistically. Genetic associations were examined using logistic regression models adjusted for age, sex, and the first five principal components with PLINK 2.0.[3] Significant associations were defined using Bonferroni correction for *HLA* alleles and amino acids, while a conventional genome-wide significance threshold was applied to other genetic associations.

Results: The strongest association within the MHC region was found with the *HLA-DRB1*03* allele (frequency = 12%), which was linked to an increased SLE risk (OR = 1.95, 95% CI = 1.19–3.16; p = 0.007). More specifically the *HLA-DRB1*0301* allele was associated with a two-fold risk increase (OR = 2.00; 95% CI = 1.22–3.29; p = 0.006). Additionally, a novel association was identified with the rs12953472 marker located

within the intronic region of the *ZNF236-DT* gene, associated with a significant increase in SLE risk (OR = 5.6, 95% CI = 2.86–10.9; p = 4.5 × 10^{-07}; Figure 1). Intriguingly, there are no prominent association signals from the MHC compared to other studies.

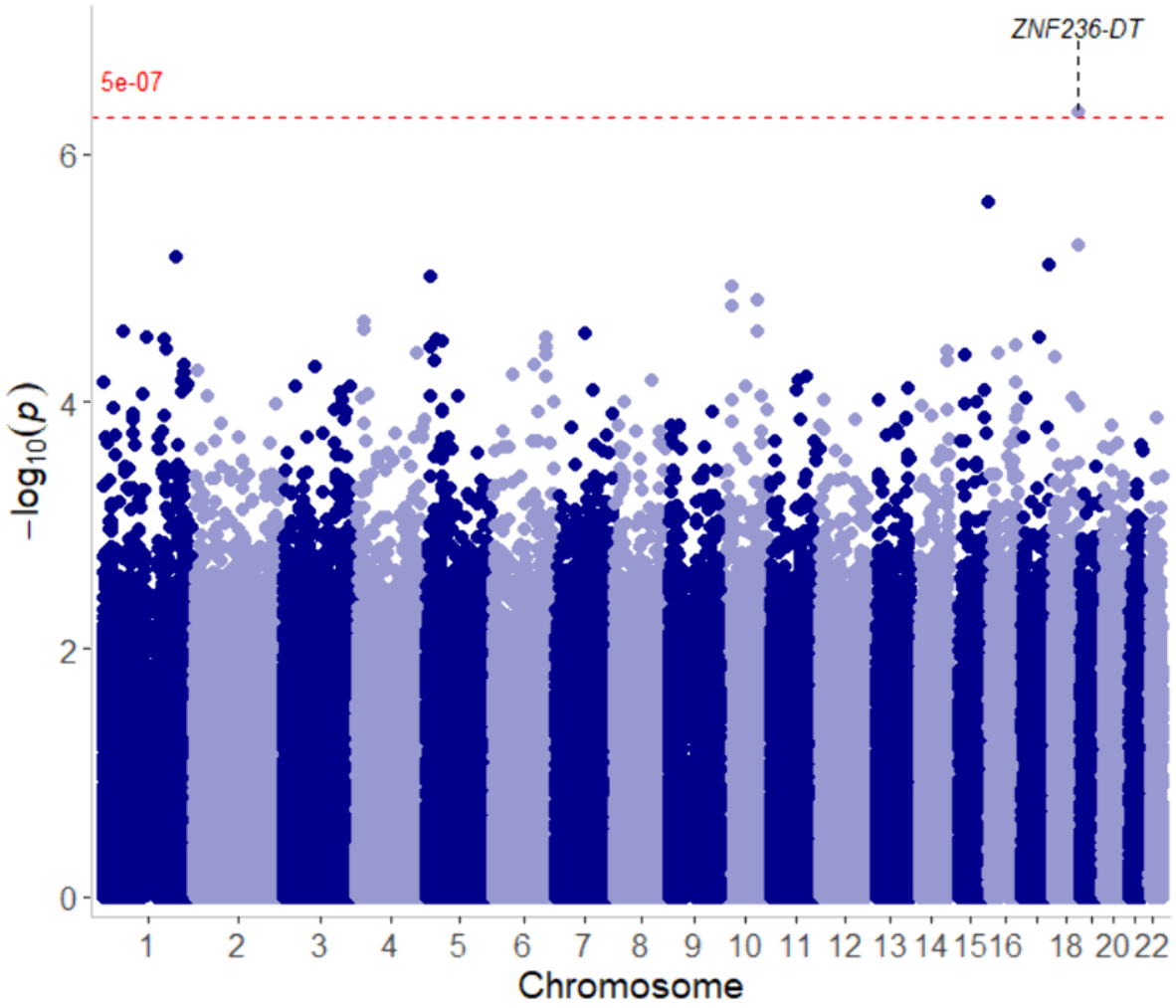

Figure 1. Manhattan plot showing genetic associations with lupus. X and y-axes display chromosomal positions and log-transformed p-values, respectively. Genome-wide significance threshold is shown as a red dashed line.

Conclusions: This study represents the first GWAS focused on genetic factors influencing SLE in the Sudanese population. It confirms the association of *HLA-DRB1*03* with SLE and reveals a novel suggestive signal within the *ZNF236-DT* gene that significantly increases SLE risk. These associations need to be validated in independent studies. Future research will also focus on genetic associations to clinical manifestations of SLE in individuals of African ancestry. **References** 1. Khunsriraksakul, C. *et al. Nat Commun* **14**, 668 (2023). 2. Jia, X. *et al. PLoS One* **8**, e64683 (2013). 3. Chang, C.C. *et al. Gigascience* **4**, 7 (2015).

PV102 / #625

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

OPHTHALMIC INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS IS ASSOCIATED WITH INTERFERON ALPHA GENE SIGNATURE: A CROSS-SECTIONAL STUDY

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Background/Purpose: Interferon Pathways studies have highlighted the role of type I interferons, especially interferon-alpha (IFN-α), in driving inflammatory pathways in lupus. Elevated levels of IFN-α are often associated with disease activity. However, few studies have been performed to clarify the role of IFN-α in ocular involvement, including dry eye and retinal changes in Systemic Erythematosus Lupus (SLE). We aimed to assess the association between IFN-α genes signature and ophthalmological involvement in SLE patients.

Methods: We evaluated patients aged 18 years or older at the Rheumatology unit of Professor Alberto Antunes University Hospital – Federal University of Alagoas, Brazil, who fulfilled 2019 EULAR/ACR criteria for SLE and attended medical routine consultation. A retinal specialist performed Clinical Ophthalmologic evaluation. In this analysis, we excluded eye problems related to treatment, such as cataracts or Hydroxychloroquine retinopathy. We utilized SLEDAI-2K to measure disease activity and blood samples were obtained from patients on the same day of clinical evaluation. Isolation of mononuclear cells (PBMC) and RNA extraction were performed, followed by cDNA synthesis. The expression of the IFI27, IFI44L, IFIT1, ISG15, RSAD2, and SIGLEC1 genes was performed via real-time PCR, using the reference genes RPLP0 and EEF1A1 for normalization. The median of the normalized relative quantity (NRQ) of the genes of each patient was used to calculate the fold change (FC) of the "Interferon Score". Statistical analysis was performed with GraphPad Prism® 8.0, using the Mann-Whitney test for group comparisons and the Spearman test for correlation analysis.

Results: The group sample consisted of 38 SLE patients. We identified SLE eye involvement in 57.89% (22/38). Of these, 36.6% (8/22) had lupus retinopathy, 68% (14/22) dry eye, and 18% (4/22) Lupus choroidopathy. 65% of the patients had active

disease measured by SLEDAI-2K. We verified higher expression levels of IFN-a gene signature in SLE patients with eye involvement (FC= 2,52 ±1,96; p=0,0027).

Conclusions: Upregulation of Interferon alpha genes was observed in SLE patients with ocular involvement, supporting the hypothesis that Interferon alpha may be an important factor in the inflammatory ophthalmic conditions associated with SLE.

PV103 / #629

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

DOES SLEDAI-2K REFLECT THE INTERFERON ALPHA GENE SIGNATURE IN SYSTEMIC LUPUS ERYTHEMATOSUS? PRELIMINARY RESULTS FROM A COHORT

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Background/Purpose: Interferon pathways studies have highlighted the role of type I interferons, especially interferon-alpha (IFN-α), in driving inflammatory pathways in systemic lupus erythematosus (SLE). Elevated levels of IFN-α are often associated with disease severity and IFN-regulated gene expression have been described as correlated with lupus disease activity, including more severe manifestations. We aimed to verify the association and correlation between IFN-α genes signature and disease activity in SLE patients in a cohort of northeast region of Brazil.

Methods: In this cross-sectional observational study, we evaluated patients aged 18 years or older at the Rheumatology unit of Professor Alberto Antunes University Hospital – Federal University of Alagoas, Brazil, who fulfilled 2019 EULAR/ACR criteria for SLE, attended clinical follow-up outpatient visits and provided written consent to participate. We measured disease activity using SLEDAI-2K. Blood samples were obtained from patients on the same day of clinical evaluation. Isolation of mononuclear cells (PBMC) and RNA extraction were performed, followed by cDNA synthesis. The expression of the IFI27, IFI44L, IFIT1, ISG15, RSAD2, and SIGLEC1 genes was performed via real-time PCR, using the reference genes RPLP0 and EEF1A1 for normalization. The median of the normalized relative quantity (NRQ) of the genes of each patient was used to calculate the fold change (FC) of the "Interferon Score". Statistical analysis was performed with GraphPad Prism® 8.0, using the Mann-Whitney test for group comparisons and the Spearman test for correlation analysis.

Results: The group sample consisted of 32 SLE patients (female =94%; mean age = 38.47 (IQR = 7)). At time of assessment, median SLEDAI-2K was 5.5 (IQR = 19). Of these patients, 65.6% (21/32) had active disease (76.19% with moderate or severe disease activity) and 9 patients had nephritis (42.8%). We verified no statistical differences in expression levels of IFN-a gene signature in SLE patients with active disease (FC= 1,48 ±1,33; p=0,3415) and nephritis (FC= 1,60 ±1,38; p=0,2448). We also did not find a

correlation between SLEDAI-2K total score and expression levels of Interferon alpha ($r = -0.02848$; $p>0.05$).

Conclusions: No statistically significant association or correlation was observed between the SLEDAI-2K and IFN-α gene signature. However, the small sample size is a limitation of this study.

PV104 / #455

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

HLA HOMOZYGOSITY IS ASSOCIATED WITH INCREASED RISK AND SEVERITY OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: The risk of systemic lupus erythematosus (SLE) involves both environmental and genetic factors, yet the etiology remains largely unknown. Previous genome-wide association studies have revealed strong associations between SLE and the major histocompatibility complex (MHC) region. Meanwhile, loss of heterozygosity at the human leukocyte antigen (HLA) loci has been extensively studied in the field of oncology, correlated with dysregulated immune response and an elevated susceptibility to various malignancies. The aim of this study was to identify the association between homozygosity of HLA genes and the onset and clinical manifestations of SLE.

Methods: MHC-targeted sequencing or whole exome sequencing (WES) was performed for 1409 SLE patients and 6084 healthy controls. HLA alleles and amino acid sequences were identified, and rate of homozygosity was compared between SLE patients and healthy controls. The results were validated in an independent cohort consisting of 1303 SLE patients and 4832 healthy controls. Data on disease activity, organ damage and autoantibody profile were collected during a follow-up of over 5 years for the discovery cohort, and the association between HLA homozygosity and clinical manifestations was investigated.

Results: Homozygosity of HLA-A, B, C, DQA1, and DRB1 was associated with increased risk of SLE in both the discovery and validation cohort. Among SLE patients, homozygosity of HLA-A, DQA1, and DRB1 was associated with an earlier age of onset. Homozygosity of HLA-DQA1 and homozygosity across all HLA alleles were associated with greater maximum SLE Disease Activity Score (SLEDAI) during the course of disease. With respect to organ involvement, homozygosity of certain HLA genes was identified as risk factor for myopathy, serositis, ophthalmic diseases, while homozygosity of certain other HLA genes conferred protection against alopecia, leukopenia, thrombosis, etc. Homozygosity of certain amino acid loci within the peptide binding groove was also associated with increased risk of SLE.

Conclusions: Homozygosity of certain class-I and class-II HLA genes is associated with increased risk of SLE, earlier age of onset, and exacerbated clinical manifestations among SLE patients.

PV105 / #92

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

DNA CIRCULOMICS IN MURINE DNASE KNOCKOUT MODELS OF SLE REVEALS ENRICHMENT OF CALCIUM SIGNALING PATHWAYS IN LIVER

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Background/Purpose: Liver function test abnormalities occur in nearly 60% of patients with SLE, compared with 1-4% in the general population. While the inositol/calcium signaling pathway has been intensely studied in immune cells in health and disease, how the dysregulation of calcium signaling may contribute to the pathogenesis of SLE in particular is not well understood. Deficiencies in two endonucleases, DNASE1 and DNASE1L3, have been shown to cause SLE. Previously, we analyzed the genic profiles of cf-eccDNA in the plasma of Dnase1$^{-/-}$ and Dnase1l3$^{-/-}$ compared to wild-type (WT) mice. Here, we performed circulomics analyses in liver of the same groups.

Methods: eccDNA libraries were generated from livers of five WT, Dnase1$^{-/-}$ and Dnase1l3$^{-/-}$ mice, respectively, based on short-read sequencing data amplified by rolling circle amplification (Sin et al., JCI Insight, 2022). We downloaded the dataset from the EGA (accession EGAS00001005873) and applied our computational pipeline and differential analysis method, DifCir, to identify eccDNA from the liver DNA circulomics data. Each eccDNA was defined by two split reads, and coupled to a fold change of 1 on a $\log_2$ scale at a 0.05 significance level to filter out non-significant genic eccDNA. Gene Ontology (GO) enrichment analysis was applied on the statistically significant eccDNAs.

Results: For Dnase1l3$^{-/-}$ versus WT, we identified 304 up- and 92 down-differentially produced per gene circles (DPpGCs). The top up-DPpGC originated from the RAS protein-specific guanine nucleotide-releasing factor 1, Rasgrf1 ($p=2.53e^{-05}$). It has been suggested that Rasgrf1 plays a role in the differentiation of plasma cells from B cells when confronted with factors of T cell-derived humoral immune responses. The most enriched GO term of up-DPpGCs was "positive regulation of GTPase activity", followed by "GTPase activator activity", and "nucleoside triphosphatase regulator activity". The highest ranked down-DPpGC derived from the calmodulin binding transcription activator 1, Camta1 ($p=0.0010$). The encoded protein is a transcription factor and tumor suppressor. Camta1 participated as a member of the top-ranked GO terms in down-DPpGCs, "calcineurin mediated signaling" and "inositol phosphate mediated signaling". For Dnase1$^{-/-}$ versus WT, we identified 291 up- and 104 down- DPpGCs. The top up-DPpGC arised from the sodium/potassium transporting ATPase interacting 3, Nkain3 ($p=0.00077$). GO terms statistically enriched in up-DPpGCs included "ion homeostasis",

"calmodulin binding", and "glutamate receptor activity". The top ranked down-DPpGC came from phospholipase C like-1 (inactive), Plcl1 ($p=1.18e^{-05}$), with PLCL1 known as a suppressor of tumor progression in renal cell carcinoma. GO terms in down-DPpGCs included "cyclic gmp-amp transmembrane", "response to interleukin 3", "histone dephosphorylation', and "calcineurin-mediated signaling". Intra-organ comparison of eccDNA in the liver of Dnase1$^{-/-}$ and Dnase1l3$^{-/-}$ mutants revealed an enrichment of the GO term "calcineurin-mediated signaling" in both models. Eight genes, Asic2, Bnc2, Cacna2d2, Farp2, Osbpl10, Pcca, Prdm16 and Tg, were identified as up-excising eccDNA in both liver and plasma of Dnase1l3$^{-/-}$ mice (Gerovska et al., Biomedicines, 2023). Remarkably, we found that oxysterol binding protein like-10, OSBPL10, predominantly expressed in B cells and plasma cells, is also a specific and up-producing cf-eccDNA in DNASE1L3-deficient SLE patients (Gerovska et al., Cells, 2023).

Conclusions: We found a functional enrichment of inositol/calcium signaling pathways for the genes excising eccDNA in the liver of SLE mouse models. More targeted research is needed to elucidate the precise mechanisms linking inositol calcium signaling, lupus, and liver pathology. Circulomics research might reveal new genes and cascades that elucidate the pathology and provide candidates for treatment interference.

PV106 / #522

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

GENETICS AND PROTEOMICS IN AUTOANTIBODY-DEFINED SUBGROUPS OF PATIENTS WITH SLE

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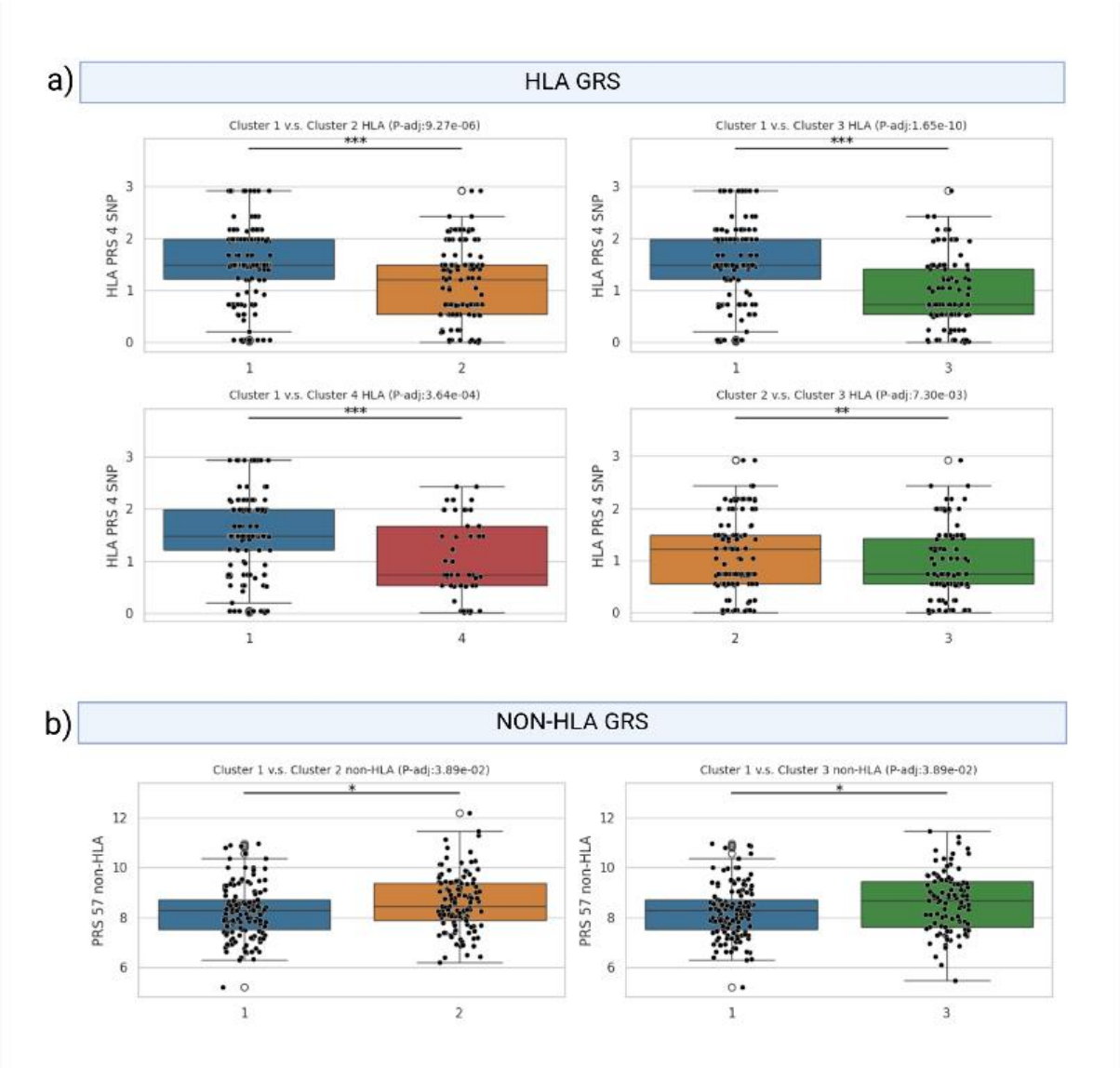
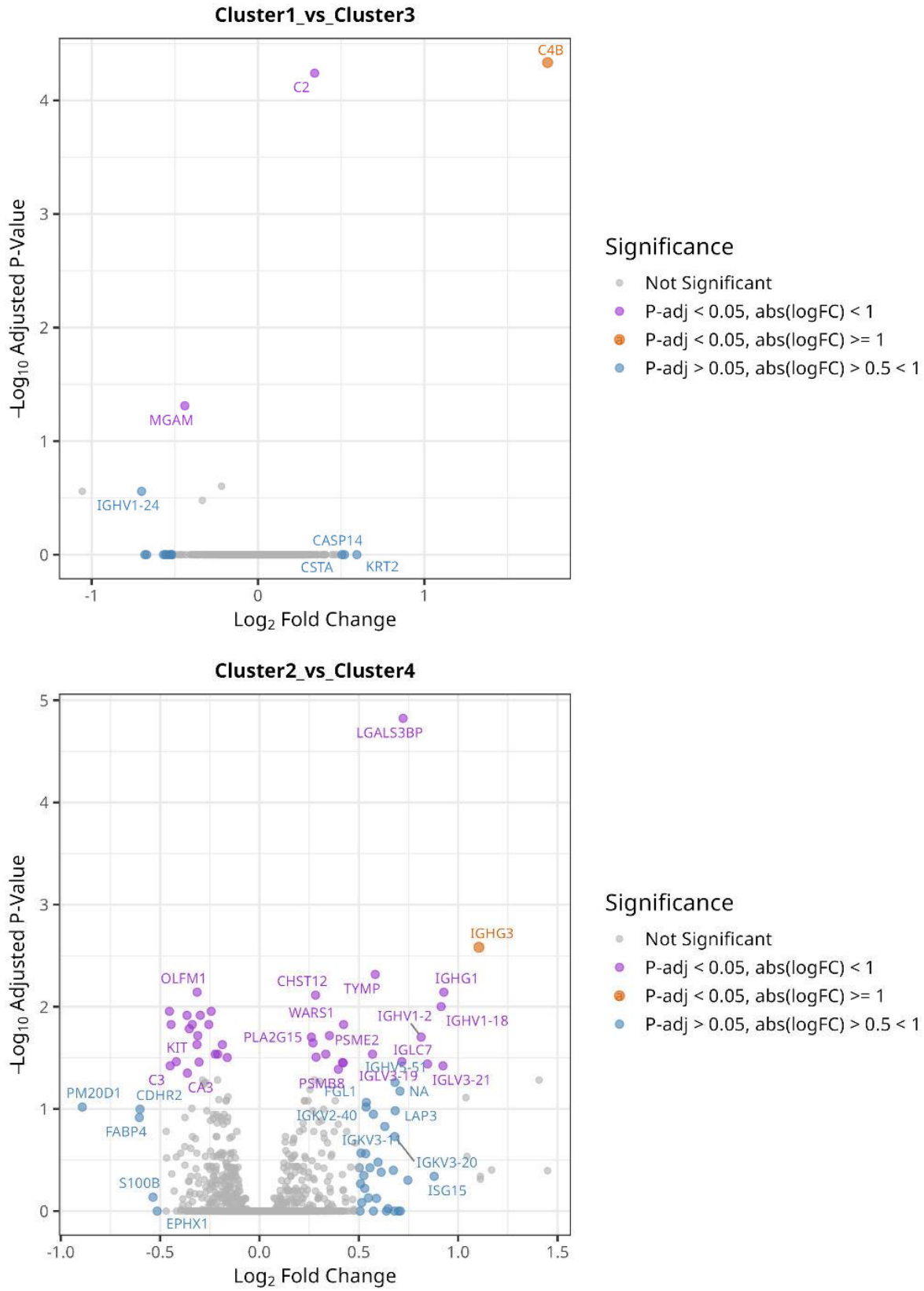
Background/Purpose: Using their autoantibody profile, patients with systemic lupus erythematosus (SLE) can be grouped into four less heterogeneous subgroups [1] Subgroup 1 was dominated by anti-SSA/SSB, Subgroup 2 by anti-nucleosome/Sm/RNP/dsDNA, Subgroup 3 by aPL, and Subgroup 4 was negative for 13 antibodies tested, but ANA ever positive. Those subgroups differed in cytokine levels, clinical manifestations, and *HLA-DRB1* gene associations.[1] Therefore, we hypothesize that the pathogenic mechanisms are different among these subgroups of patients. We aimed to evaluate whether there are differences in known SLE genetic risk factors and protein levels among antibody-defined SLE subgroups.

Methods: We analyzed 448 patients from our previous study[1] to address differences in genetic risk factors. We compared the SLE polygenic risk scores (PRS) previously described by Reid *et al.* 2020.[2] Using a double-sided Mann-Whitney U test, we tested differences in the distribution of two PRS: one including four Single Nucleotide Polymorphisms (SNPs) in the *HLA* region or fifty-seven non-*HLA* SNPs across the subgroups. Furthermore, untargeted liquid chromatography-mass spectrometry (LC-MS) was implemented using plasma samples from 100 SLE patients, 25 representing each subgroup. Differential expression analysis was performed using linear modeling with the limma package,[3] and pairwise comparisons were conducted among the subgroups. P-values for both approaches were corrected using a False Discovery Rate (FDR) multiple-testing correction. Adjusted values (P-adj) lower than 0.05 were considered significant.

Results: Subgroup 1 displayed significantly higher *HLA-P*RS compared to subgroup 2 (P-adj = 9.27e-06), subgroup 3 (P-adj =1.65e-10), and subgroup 4 (P-adj =3.64e-04) (**Fig1**). Similarly, subgroup 2 had a significantly higher i-PRS than subgroup 3 (P-adj =

7.3e-03). Conversely, for PRS calculated using SNPs outside the HLA region, scores of subgroup 1 were significantly lower than scores from subgroups 2 (P-adj = 3.89e-02) and 3 (P-adj = 3.89e-02), suggesting a higher contribution of SNPs in the HLA region to the overall higher genetic risk of subgroup 1. Differential expression analysis of proteins (n=2625) between the subgroups revealed that an isoform of Complement C4-B (C4B) was significantly overexpressed (P-adj 3.72e0-5) in subgroup 1 compared to subgroup 3, followed by C2, which indicates involvement of the complement system in this subgroup. Likewise, an isoform of Immunoglobulin heavy constant gamma 3 (*IGHG3*) was significantly overexpressed (P-adj 2.3e-03) in subgroup 2 compared to subgroup 4 (**Fig2**). These preliminary results support the concept that unanalyzed or unknown autoantibodies and B-cell involvement may be present in patients of subgroup 4.





Conclusions: Subgroup 1 exhibited higher *HLA*-PRS than the other subgroups and elevated C4b levels compared to Subgroup 3. This is consistent with the high linkage disequilibrium between *C4* gene and *HLA* risk variants. These preliminary findings

support the hypothesis of subgroup-specific pathogenic mechanisms among antibody-defined SLE subgroups of patients. We will further analyze this dataset to incorporate PRS relevant to immune cell phenotypes and calculate PRS targeted to SLE-subgroups. We will also validate these findings in independent populations. **References** 1. Diaz-Gallo LM, et al. ACR Open Rheumatol. 2022;4(1):27-39. 2. Reid S, et al. Ann Rheum Dis. 2020;79(3):363-9. 3. Ritchie ME, et al. Nucleic Acids Res. 2015;43(7):e47

PV107 / #499

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

GENETICS OF EGFR VARIABILITY AS A PROXY FOR LUPUS NEPHRITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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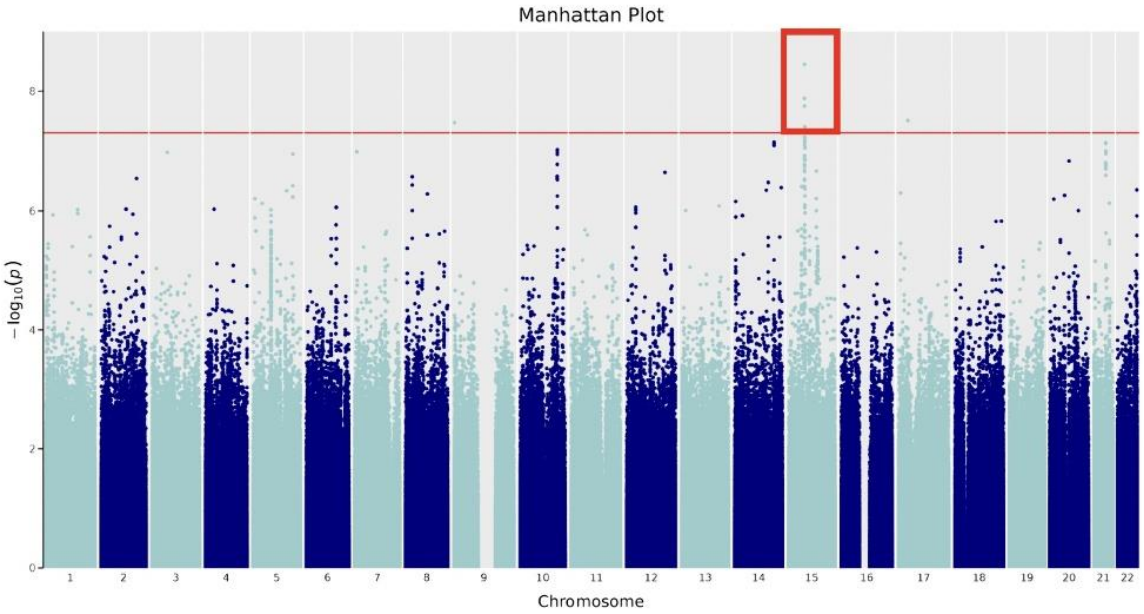
Background/Purpose: Lupus nephritis (LN) is one of the most common and severe manifestations of systemic lupus erythematosus (SLE). We performed genome wide association studies (GWAS) for lupus nephritis and kidney function measures over time. We hypothesized that analyzing a person's eGFR variability over time would be a good proxy for LN and improve power for detecting genetic loci for LN. We also used local ancestry estimation to facilitate inclusion of admixed individuals.

Methods: We included SLE patients from several child and adult dedicated lupus databases and the Systemic Lupus International Collaborating Clinics (SLICC) cohort. All met American College of Rheumatology and/or SLICC SLE criteria and were genotyped on a multi-ethnic Illumina array. Ungenotyped SNPs were imputed to the Trans-Omics for Precision Medicine program (TopMed), and local ancestry of chromosomal information was estimated using RFMix and Tractor software. LN was

defined by SLE criteria, with a subset confirmed by kidney biopsy. Kidney function (estimated glomerular filtration rate, eGFR) was calculated using the Schwartz formula for measures <18 years and CKD-EPI for >18 years of age. Wilcoxon rank sum or Chi-square tests were used to compare characteristics between LN and Non-LN patients. We completed separate GWAS for the outcomes of LN, mean eGFR and eGFR variability over time (log of the mean absolute deviation from mean eGFR per participant), in marginal and multivariable adjusted regression models with sex, site and local principal components using Regenie. Local ancestry analysis was restricted to individuals of European, African and East Asian ancestry using Tractor. We meta-analyzed ancestry-specific results with METAL software (significance $p<5x10^{-8}$).

Results: We studied 2981 individuals with SLE, 88% female, 46% of European ancestry, 27% childhood-onset SLE, and 45% with LN (Table). Kidney failure was observed in 25 patients over a median follow-up time of 8.9 years (IQR: 4.1,14.8). Within-person eGFR was similar between people with and without LN, but eGFR variability was significantly greater in people with LN (*P*-value= 2.2e-16). Variability was calculated using a median of 16 [IQR: 8,35] eGFR measurements per person. GWAS of LN did not identify a significant LN locus, yet GWAS of eGFR variability demonstrated a significant peak on chromosome 15, downstream of *SCH4* and intronic to *SECISBP2L* (Figure). The variant was found in a genomic region of African ancestry.

Patient Characteristics	**All SLE Patients (n=2981)**	**LN Patients (n=1351)**	**Non-LN Patients (n=1630)**	***P***
Female	2628 (88.2)	1138 (84.2)	1490 (91.4)	$1.6e^{-09}$
Age diagnosis	25.6 [16.4, 37.8]	22.6 [15.7, 33.0]	28.3 [17.3, 41.3]	$2.2e^{-16}$
cSLE diagnosis	814 (27.3)	484 (35.8)	440 (27.0)	$2.1e^{-07}$
Ancestry European East Asian African Ameridian South Asian Admixed	1367 (45.9) 459 (15.4) 555 (18.6) 151 (5.1) 131 (4.4) 317 (10.6)	493 (36.5) 252 (18.6) 316 (23.3) 80 (5.9) 68 (5.0) 141 (10.4)	874 (53.6) 207 (12.7) 239 (14.7) 71 (4.4) 63 (3.9) 176 (10.8)	$2.2e^{-16}$



Conclusions: We completed GWAS of LN, eGFR mean and variability over time, generating ancestry specific estimates and identified a genome-wide significant locus for variability in measures of renal function over time, in a multiethnic cohort of children and adults with SLE. This locus was only found in an African ancestry portion of the genome. Variability in measures of renal function is correlated with LN, yet GWAS of LN did not identify significant loci. Future work includes repeating analyses to include all global ancestries, and to investigate the biologic link between the loci and LN.

PV108 / #408

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

MECHANISMS PROTECTING MALES FROM DEVELOPMENT OF SLE

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Background/Purpose: Among the autoimmune rheumatic diseases, the highest female prevalence is observed in SLE, suggesting that sex-related pathways are important contributors to disease pathogenesis. Several hypotheses have been presented to explain the extreme 9-10:1 female:male skewing of SLE, with a role for sex hormones, X chromosome dose, and incomplete X chromosome inactivation (XCI) currently dominating this field of research. We have taken a novel experimental approach by investigating the cellular and molecular factors that protect males from development of SLE. Our goal is to gain new understanding of the skewed sex-related occurrence of SLE, thereby identifying new therapeutic approaches.

Methods: The study groups included 15 females with SLE, 15 males with SLE, all from our longitudinal SLE cohort established at Hospital for Special Surgery, and 15 female and 15 male healthy donor subjects, well matched for age and ancestry with the SLE patients. RNA sequencing of PBMC was performed and data analyzed using principal component analysis (PCA) and determination of differentially expressed gene transcripts.

Results: PCA showed a larger difference in RNA transcripts between SLE males and healthy males than between SLE females and healthy females. Weighted gene co-expression analysis identified 24 groups of co-expressed and functionally related transcripts, with female and male SLE patients demonstrating considerable overlap of common disease-associated genes, including type I interferon-stimulated genes, neutrophil-related genes, and B cell/plasmablast transcripts. However, transcripts associated with the NF-kB and epidermal growth factor receptor pathways were expressed at a significantly higher level in SLE males than in healthy males, while those pathways were expressed at comparable levels between SLE and healthy donor females. In contrast, gene transcripts typically expressed in natural killer (NK) cells, including *KLRK1, KLRC3, KLRC4 and CADM1,* were expressed at a significantly lower level in SLE males than in healthy males. In addition, several Y chromosome-encoded genes, namely *KDMD5D,* encoding a histone demethylase that is expressed in NK cells, and *TXLNGY* were expressed at a significantly lower level in SLE males than in healthy males (adjusted $p < 0.01$ for comparison with healthy males for both genes).

Conclusions: Our data suggest that NK cells may represent an important protective cell type that limits development of SLE in most males. Moreover, our data point to

several Y chromosome-encoded genes that are decreased in expression in SLE males and may contribute to altered epigenetic regulation of immune system cells, including NK cells, leading to impaired control of autoimmunity and development of SLE in some males. Further characterization of these alterations in SLE males may identify novel approaches for limiting development or severity of SLE in both males and females.

PV109 / #563

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

RARE VARIANTS OF PAH RISK GENES ASSOCIATE WITH A DISTINCT VASCULOPATHY PHENOTYPE AND WORSE OUTCOMES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

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Background/Purpose: Systemic lupus erythematosus (SLE)-associated pulmonary arterial hypertension (PAH) displays significant clinical heterogeneity; Presently, more than twenty risk genes have been identified to be closely linked to the pathogenesis and prognosis of idiopathic and familial PAH. However, the role of rare variants of PAH risk genes in SLE-associated PAH remains largely unknown.

Methods: Based on the Chinese SLE Treatment and Research Group (CSTAR)-PAH cohort, 241 patients with SLE-associated PAH were recruited and screened for rare deleterious variants in 28 known PAH risk genes by whole exome sequencing. Clinical features, hemodynamic characteristics and outcomes were compared between variant carriers and noncarriers. Another 87 patients with SLE-associated PAH were included as genetic replication cohort.

Results: 51 patients of SLE-associated PAH (21.5%) carried rare variants of PAH risk genes, which is significantly higher than control group (13.9%, P=0.009). This finding was replicated in the independent validation cohort. Among patients with SLE-associated PAH, carriers had a shorter PAH duration from SLE onset, a higher proportion of PAH as the onset symptom of SLE and lower SLE disease activity. Carrying rare variants of PAH risk genes was identified as an independent prognostic factor of mortality (hazard ratio [HR]=3.13, 95% CI, 1.10-8.97; P=0.005) and of poor treatment response to immunosuppressants, defined as the proportion of patients reaching a low risk profile of PAH according to the ESC/ERS guidelines (HR=0.56, 95% CI 0.34-0.94, P=0.027).

Conclusions: We showed for the first time that rare variants of PAH risk genes associated with a distinct vasculopathy phenotype and worse outcomes in patients with SLE-associated PAH, highlighting the significant clinical value in molecular classification and supporting future research on personalized strategies based on genetic and clinical characteristics in SLE-associated PAH.

PV110 / #608

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

EPIGENETIC PROFILING OF CHILDHOOD-ONSET LUPUS REVEALS DISTINCT EPIGENETIC CLUSTERS AND SUGGESTS EPIGENETIC DRIVERS OF DISEASE ACTIVITY

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Background/Purpose: Systemic lupus erythematosus, or lupus, is a chronic autoimmune disease that can affect multiple organ systems. Childhood-onset lupus is typically associated with a more severe disease course compared to adult-onset lupus. DNA methylation alterations play an important role in the pathogenesis of lupus. We have previously demonstrated a higher genetic risk for lupus in childhood-onset compared to adult-onset disease. However, epigenetic studies in childhood-onset lupus have been limited. The aim of this study was to investigate DNA methylation changes in childhood-onset lupus.

Methods: A total of 64 patients with childhood-onset lupus and 47 healthy controls from Turkey were included in this study. DNA from peripheral blood mononuclear cells (PBMCs) was isolated to assess DNA methylation patterns using the Infinium MethylationEPIC v2.0 array (Illumina). Quality controls and statistical analyses were performed using *minfi* and *limma* R packages. Methylation differences among groups were tested through linear regression, adjusting for age, sex, medication use, and cell subset compositions. Differences in clinical manifestations were assessed using Fisher's exact tests. Gene ontology (GO) enrichment analyses were performed with the online tools Metascape and GREAT.

Results: Case-control differential DNA methylation analysis revealed significant hypomethylation in interferon-regulated genes, such as *DTX3L*, *PARP9*, *IFI44L*, and *MX1*, in patients compared to controls. The enrichment analysis confirmed the presence of type I interferon signature-related biological processes, consistent with our previous findings in adult-onset lupus. The association of DNA methylation levels and disease activity in lupus, as measured by SLEDAI scores, revealed progressive hypomethylation in genes related to B cell activation and cellular senescence as the disease becomes more active. K-means clustering analysis of lupus patients based on DNA methylation patterns identified 3 distinct lupus clusters. Cluster 1 was characterized by the enrichment of hypomethylated genes involved in cell adhesion and response to growth

factor pathways; Cluster 2 exhibited hypomethylation in genes related to regulation of cell differentiation and cell fate determination; and Cluster 3 showed enrichment in response to oxidative stress and Rap1 signaling pathway in hypomethylated genes.

Conclusions: We identified significant hypomethylation in interferon-regulated genes, consistent with the type I interferon epigenetic signature observed in adult-onset lupus. Furthermore, the relationship between DNA methylation changes and disease activity, particularly in genes associated with B cell activation and cellular senescence, suggests that these alterations may play a role in disease progression. The identification of distinct DNA methylation clusters also underscores the heterogeneity of childhood-onset lupus, offering potential avenues for personalized therapeutic strategies. These findings emphasize the need for further investigation into the epigenetic mechanisms driving childhood-onset lupus to improve diagnosis and treatment approaches.

PV111 / #471

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

HLA GENOTYPES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN RUSSIAN FEDERATION

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multiorgan damage mediated by immune complexes and the autoantibodies production. Human leukocyte antigen (HLA) gene polymorphisms play an important role in the pathogenesis of SLE, however, the observed susceptibility alleles vary across ethnic groups and geographic regions [1]. The current study aims to describe the spectrum of HLA class I and HLA class II alleles in Russian patients with SLE.

Methods: The study was approved by the local ethics committee and included 130 patients (110 women/20 men), average age was 34.0 [26.0; 42.0] yars and 235 healthy controls. All enrolled patients were diagnosed with SLE according to the 2012 SLICC classification criteria. All patients signed informed consents to be included in the study. The duration of the disease was 7.0 [4.0; 13.0] years. Eighteen (14%) patients had secondary APS. SLEDAI-2K was 6.0 [4.0; 10.0]. Clinical and laboratory characteristics are presented in Table 1. **Table 1.** Clinical and laboratory characteristics of the SLE patients.

SLICC 2012 criteria	**In past history, n (%)**	**Baseline, n (%)**
Clinical criteria		
Acute cutaneous lupus	85 (65)	26 (20)
Chronic cutaneous lupus	33 (25)	18 (14)
Oral ulcers	42 (32)	9 (7)

Nonscarring alopecia	71 (55)	46 (35)
Arthritis	102 (78)	40 (31)
Serositis	52 (40)	17 (13)
Renal involvement	66 (51)	44 (34)
Neurologic involvement	15 (12)	4 (3)
Hemolytic anemia	49 (38)	18 (14)
Leukopenia	97 (52)	19 (15)
Thrombocytopenia	28 (22)	7 (5)

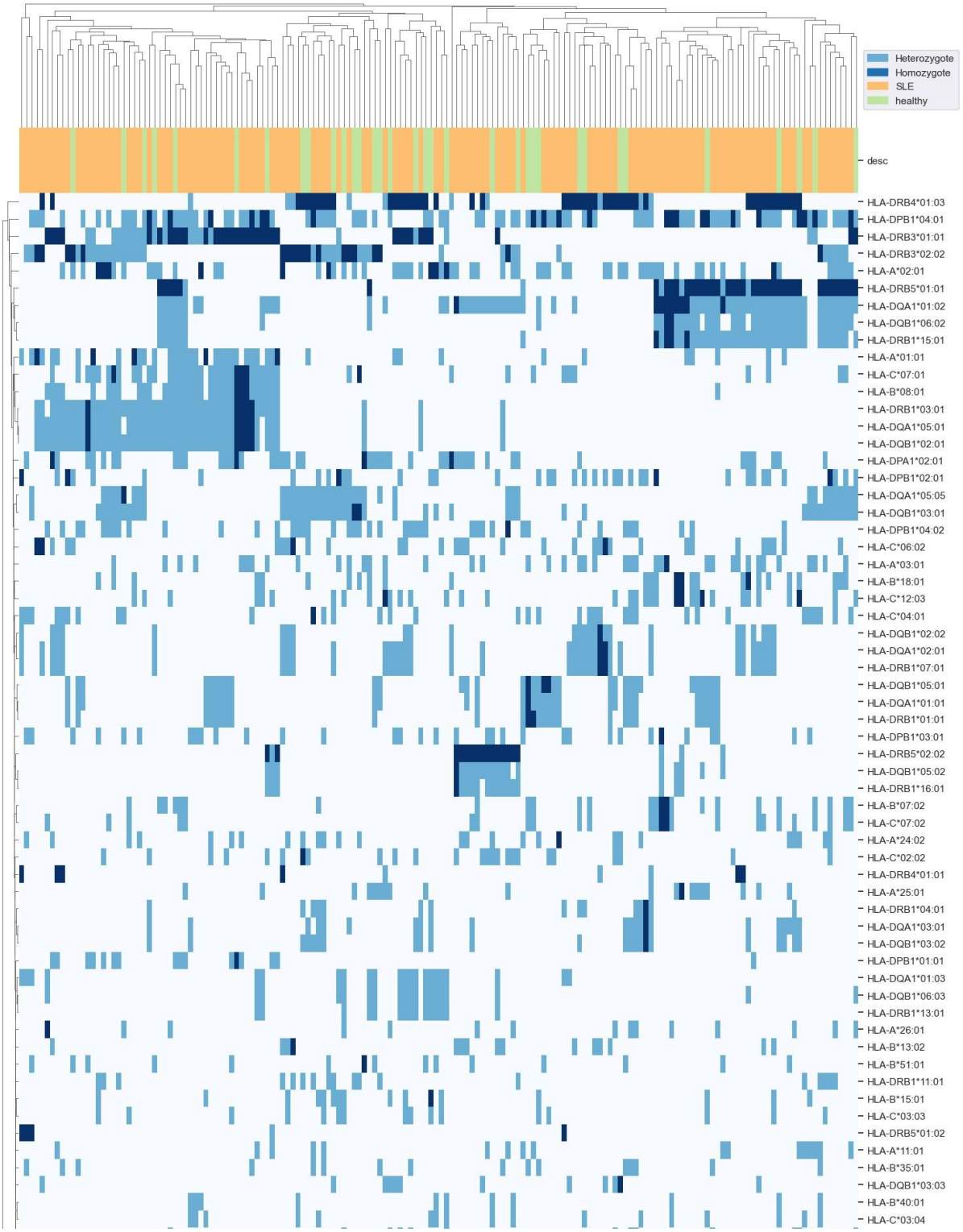
Immunological Criteria at the baseline	**n (%)**
ANA	130 (100)
Anti-dsDNA	80 (62)
Anti-Sm	28 (22)
Anti-Ro/SS-A	48 (37)
Anti-La/SS-B	12 (9)
Anti-RNP70	18 (14)
Antiphospholipid antibody -aCL IgG/IgM -aB2-GP1 IgG/IgM	15 (12) / 11 (9) 12 (9) / 12 (9)
Low complement -↓C3 -↓C4 -↓C3 and C4	66 (51) 36 (28) 10 (8)

HLA-typing of HLA-A, B, C, DRB1 and DQB1 alleles from whole genome sequencing data was conducted using the HLA-HD tool with a reference panel from the IPD-IMGT/HLA database [2]. All statistical analyses were performed using Python module statsmodels. Chi-square tests were performed to evaluate the differences in HLA allele frequencies between SLE patients and healthy controls. Alpha level was set at 0.05; *p*-values were corrected for multiple comparisons using Benjamini-Hochberg procedure.

Results: A total of 37 HLA-A, 58 HLA-B, 37 HLA-C, 34 HLA-DRB1 and 19 HLA-DQB1 4-digit allelic groups were detected in the patients with SLE. We found two alleles associated with increased risk for developing SLE in the Russian population: 1) HLA-DRB1*03:01 (OR = 2.31, 95% CI = 1.47-3.62, p-value = 0.03) 2) HLA-DQB1*02:02 (OR = 15.8, 95% CI = 4.72-53.1, p-value = 0.002) According to literary data HLA-DRB1:03:01

allele is a major risk factor for SLE in Europeans, in addition, it was shown that the short epitope encoded by this allele activates SLE-characteristic cellular aberrations [3]. We also noted the overrepresentation of HLA-B*13:02, HLA-DRB1*15:01, HLA-DQB1*06:02 alleles in SLE patients (fig. 1).

Figure 1. Cluster analysis of patients with SLE and healthy controls



Conclusions: Combinations of alleles identified as a result of cluster analysis were also considered. We observed that frequency of five-loci haplotype HLA-A*01:01 ~ HLA-B*08:01~ HLA-C*07:01 ~ HLA-DQB1*02:01~ HLA-DRB1*03:01 was significantly increased in SLE patients when compared to controls. **References:** [1.] Lewis MJ. Rheumatology (Oxford). 2017;56(suppl_1):i67-i77. [2.] Kawaguchi S. Hum Mutat. 2017;38(7):788-797. [3.] Miglioranza Scavuzzi B. Commun Biol. 2022;5(1):751.

PV112 / #584

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

METHYL-RICH DIET SUPPRESSES THE DEVELOPMENT OF LUPUS-LIKE SYMPTOMS IN HUMANIZED MOUSE MODEL OF THE DISEASE

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Background/Purpose: SLE is a chronic autoimmune disease with complex involvement of organs and systems. A body of evidence confirmed the central role of environmental factors in lupus pathogenesis with special place assigned to the dietary components. Although a genetic predisposition is required for the onset of SLE, epigenetic factors also play a central role in this process. Having in mind that methyl-containing nutrients are key participants in the DNA methylation processes, and that lupus patients' DNA shows alterations in this major epigenetic modification, it is intriguing to study the therapeutic effect of these components on SLE progression and clinical manifestations. In the present study we report that the methyl-supplemented diet ameliorates the development of SLE in NSG/Rag2-γc-mice humanized with lupus patients' PBMCs.

Methods: Two types of rodent diet were used: normal (standard) rodent diet and supplemented diet containing the following ingredients for 8 g of daily portion per mouse (Table 1).

	Normal diet mg/8g diet	High-dose methyl diet mg/8g diet
L-methionine	137	295
Betaine	0	375
Choline	33.5	485
Zn/ZnO	0	7.5
Folic Acid	0.075	0.412
VitB12	0.00125	0.039

Table 1. Amounts of the components (mg/8g diet) in the normal diet and in the high-dose methyl diet. PBMCs from each SLE patient were isolated from peripheral blood. After PBMCs separation, 10 weeks old mice were injected *i.p.* with one billion cells/mouse (two mice per patient). Two groups of female NSG/Rag2-γc- mice were engrafted with PBMCs from SLE patients. One group was put on a normal rodent diet, the other – on methyl-supplemented diet. Two groups of control non-humanized mice were also put on either of the diets. The animals were monitored for 8 weeks with blood and urine samples being collected once a week. At the end of the dietary course the mice were sacrificed, and kidneys were examined for glomerular pathology. Assays for appearance of anti-dsDNA antibodies and proteinuria were performed.

Results: The results showed a decrease in anti-dsDNA antibody and proteinuria levels in the mice put on the supplemented diet, compared to the mice put on normal diet. In addition, histopathological changes in the structure of the glomeruli were observed in the kidney of mice fed with the normal diet but not the supplemented group. The results showed statistically insignificant decrease in the percent atrophic glomeruli of humanized mice put on normal diet (ND group) and of humanized mice put on supplemented diet (SD group). However, the percentages of glomeruli with mesangial proliferation were significantly decreased in mice humanized with PBMCs from patients and put on supplemented diet compared to the humanized mice fed with control diet. Kidney analysis of mice engrafted with lupus patients' PBMCs and put on normal diet showed moderate mesangial proliferation. On the contrary, mice put on supplemented diet displayed only mild cellular proliferation in the glomeruli. Kidney preparations from non-humanized mice put on normal diet or on supplemented diet did not significantly differ.

Conclusions: The observed beneficial effect of the methyl-rich diet may be related to the potential modulation of DNA methylation levels and subsequent changes in gene expression. These results point to the importance of DNA methylation as one of the major epigenetic factors responsible for the progression of SLE.

PV113 / #260

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

TRANSCRIPTOMIC ANALYSIS REVEALS A SYNERGY OF HYDROXYCHLOROQUINE AND GLUCOCORTICOIDS IN MODULATING B CELL-RELATED IMMUNE PROCESSES

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Background/Purpose: Hydroxychloroquine (HCQ), glucocorticoids (GC), and their combination are common treatments in autoimmune rheumatic diseases. Their effects at the molecular level and potential synergistic effects remain unclear, which formed the scope of this work, including investigation of specific gene sets that are involved in this potential interaction.

Methods: We analyzed bulk RNA sequencing data from 591 samples from the PRECISESADS project. [1.] The patients were diagnosed with systemic lupus erythematosus (SLE), Sjögren's disease (SjD), undifferentiated connective tissue disease (UCTD), and mixed connective tissue disease (MCTD), and were grouped into four categories based on treatment status: no current exposure to HCQ or GC (off-treatment; n = 244), on HCQ (n = 198), on GC (n = 47), or on HCQ and GC combined (n = 102) (Table 1). Patients were not on any immunosuppressive treatment at the time of sampling. We performed differential gene expression (DGE) analysis across treatment groups (HCQ, GC, and HCQ+GC) with the off-treatment group of patients serving as the comparator. Overrepresentation analysis (ORA) was conducted on genes with amplified effects (absolute $\log_2$ fold change (FC) < 0.5 for the individual treatments; absolute $\log_2$FC > 0.5 for the combination treatment), using Chaussabel's gene set modules to identify enriched pathways. [2.] The activity of the modules was estimated using gene set variation analysis (GSVA). Statistical comparisons of gene activities within modules between treatment groups (GC vs. HCQ+GC) for steroid dosages (low, medium, high) were conducted using the Mann Whitney *U* test. [1.] Barturen G. Arthritis Rheumatol 2021;73:1073–85. [2.] Rinchai D. Bioinformatics 2021;37:2382-89.

Table 1. Number of samples per patient diagnosis and treatment category.

Diagnosis	Off-treatment	HCQ	GC	HCQ+GC
SjD	134	66	18	16
SLE	48	91	16	71
UCTD	45	28	6	9
MCTD	17	13	7	6

Results: Combination of HCQ and GC generated a synergistic molecular response, with a higher number of differentially expressed genes and greater effect size compared to the individual treatments, regarding both differentially overexpressed and downregulated genes. The ORA of genes with amplified effect size pointed to numerous immune-related pathways, consistent with the GSEA analysis results. Notably, B cell-related gene proliferation and activity modules were significantly suppressed (ORA adj. p-value < 0.05, GSEA adj. p-value < 0.05) in the group of patients on combination treatment. The B cell proliferation module was significantly lowered by the addition of HCQ to GC at a daily average dose of 4-6 mg of prednisone equivalents compared to GC alone at the same doses ($p = 0.014$). Pathways related to DNA damage and DNA replication were also reduced.

Conclusions: The combination of HCQ and GC results in a synergistic molecular response. ORA and GSEA revealed significant involvement of immune-related pathways, with a notable suppression of B cell-related gene modules. While the suppression of the B cell proliferation module was significantly amplified by the addition of HCQ to GC treatment, the influence of GC dosage requires further investigation. Overall, these findings suggest a synergy at the molecular level when HCQ and GC are administered concurrently in combined regimens, enhancing the modulation of key immune processes.

PV114 / #325

Poster Topic: ***AS12 - Genetics, Epigenetics, Transcriptomics***

EXTRACELLULAR VESICLES FROM LUPUS NEPHRITIS PATIENTS INDUCE CHANGES IN THE TRANSCRIPTIONAL PROFILE OF MONOCYTES THAT RESEMBLE SLAN+ MONOCYTES

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Background/Purpose: Extracellular Vesicles (EVs) are a source of autoantigens that can be recognized by circulating monocytes and can also form immune complexes. Lupus nephritis (LN) is the most frequent and severe manifestation in patients with systemic lupus erythematosus (SLE). Renal injury is attributed to the deposition of immune complexes in the glomerulus. SLAN+ monocytes, a fraction of non-classical monocytes considered the most inflammatory, have been detected in renal tissue. We analyzed the transcriptional profile and functional characteristics of monocytes and SLAN+/- monocyte fractions circulating in patients with LN and controls. Additionally, we studied the effect of EVs from the plasma of patients on the transcriptional profile of the SLAN- fraction.

Methods: We included three active LN female patients who meet the American College of Rheumatology/European Alliance of Associations for Rheumatology 2019 diagnosis criteria, with lupus nephritis confirmed by kidney biopsy following the International Society of Nephrology/Renal Pathology Society (ISN/RPS) parameters and in the initial phase of treatment and three healthy female donors (HD) of similar age in the study. Circulating monocytes SLAN+/- were purified from peripheral blood using FACS sorting. EVs were isolated from plasma using a differential centrifugation protocol. The SLAN- fraction was seeded with the isolated EVs for six hours. RNA from circulating monocyte SLAN+/- fractions and post-EV incubation samples was extracted using a commercial column kit. Transcriptomes were assessed by next-generation RNA sequencing on the Illumina Novaseq platform. Differential expression analysis was performed using the DESeq2 package. GeneCodis, GeneAnalytics, and GSEA platforms were employed for functional enrichment analysis of the most significant and differentially expressed

genes (padj < 0.05 and FC > 1) between SLAN+/- fractions and to explore the effect of the EVs on the transcriptional profile of SLAN- monocytes.

Results: Gene expression profiling of monocytes from patients identified 51 genes that were differentially expressed between SLAN+ and SLAN- fractions. The SLAN+ monocytes from LN patients exhibited significant molecular changes, reflecting an inflammatory profile and pathways related to cell adhesion and differentiation. In contrast, the SLAN- fraction demonstrated a strong response to IFN-I. Additionally, EVs from LN patients prompted the SLAN- fraction from healthy donors to express 206 genes associated with an inflammatory profile and enriched SLAN+ signature, indicating differentiation potential.

Conclusions: These findings highlight the pathogenic potential of SLAN+ monocytes and EVs in lupus nephritis, suggesting they may serve as therapeutic targets. By altering the transcriptional profile of monocytes, EVs from LN patients could contribute to disease progression and inflammation. Targeting these pathways may offer new strategies for intervention in lupus nephritis.

PV115 / #373

Poster Topic: ***AS14 - Innate Immunity***

MEMBRANE-LOCALIZED ESTROGEN RECEPTOR ALPHA (ERA) IS REQUIRED FOR BOTH NORMAL AND TLR7-INDUCED DEVELOPMENT OF CD11B+LY6C+ INFLAMMATORY MONOCYTES

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Background/Purpose: Lupus is a disease that disproportionately affects females. We previously showed that selective expression of an ERα short variant in lupus prone mice resulted in significantly reduced renal disease and increased survival. The mechanism of this protective effect, which required estradiol, is not known but may relate to the role of ERα in innate immune cells since dendritic cell subsets were significantly impacted.

Methods: We investigated the immunophenotype of mice expressing ERα that is selectively targeted to the cytosolic membrane (MOER) vs. nuclear-restricted ERα (NOER) to further explore the role of ERα in innate immune cells from these mutant mice (on a C57/B6j background). We subsequently stimulated these mice *in vivo* with a TLR7 agonist (topical R848) for 4 weeks and analyzed *ex vivo* bone marrow and spleen cell populations as well as manifestations of lupus-like disease (ex. autoantibodies, splenomegaly, blood counts, kidney function).

Results: Total BM cells were surprisingly reduced in NOER mice when compared to MOER in ovary intact animals (p=0.037). A significant decrease was also observed in CD11b+ cells from NOER BM and a trend towards decreased CD11c+ and MHCII+ cells, but not CD19+ cells, suggesting that membrane ERα rather than nuclear ERα is required for normal development of CD11b+ cells and perhaps other myeloid cells, but is not required for B cell development. When assessing spleen, there was a significant increase in CD11b+Ly6C+ cells (inflammatory monocytes) in MOER mice. NOER mice had reduced numbers of CD11b+Ly6C+ cells, suggesting an inability to mount a robust response to TLR7 stimulation when compared to WT and MOER mice. In BM, Ly6C+ and Ly6C+CD11b+ cells had similar trends with statistically significant enrichment from MOER mice regardless of treatment status. R848-treated MOER mice also had a significant leukocytosis (increased WBCs, p=0.0077) and increased blood urea nitrogen (BUN) reflecting an early change in renal function compared to NOER mice (p=0.002) , suggesting that membrane ERα mediates these physiologic effects. Renal pathology and immunohistochemistry demonstrated significantly increased glomerular IgG deposition in R848-treated mice, which was also mildly increased in TLR7-stimulated MOER mice.

Conclusions: These findings suggest nuanced interactions between estradiol, ERα, and immune regulation. The study underscores the pivotal roles played by both nuclear and membrane ERα in both immune cell development and function. Further investigations are warranted to elucidate the precise mechanisms through which distinct ERα isoforms and their subcellular localization exert influence on immune responses.

PV116 / #181

Poster Topic: ***AS14 - Innate Immunity***

DISTINCT CELL-BOUND COMPLEMENT ACTIVATION PRODUCTS ASSOCIATE WITH DISEASE ACTIVITY AND IMMUNE TRANSCRIPTIONAL SIGNATURES IN SLE

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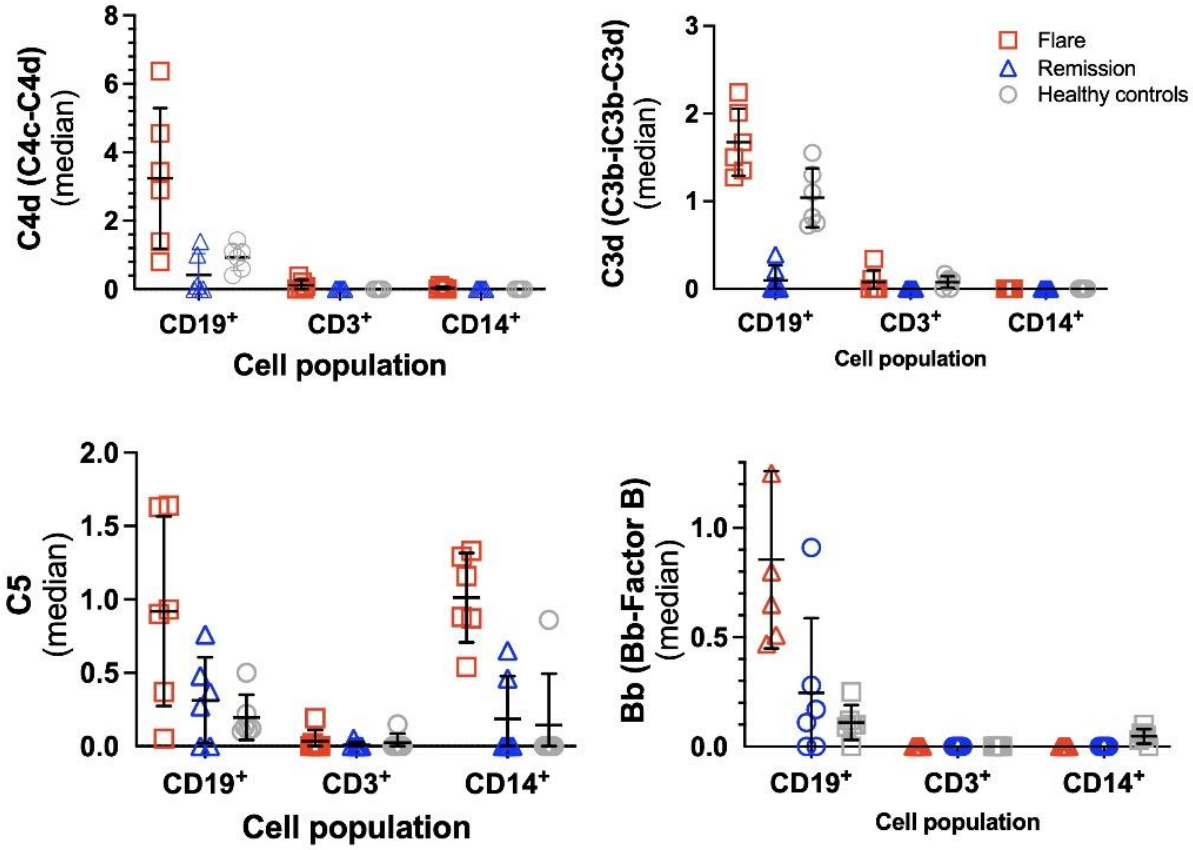
Background/Purpose: Complement plays a central role in SLE, generating an array of bioactive soluble and cell-bound complement activation products (CB-CAPs) during disease activity. Data are lacking though detailing the types, quantities, and impacts of the numerous CB-CAP on SLE immune cells, especially with respect to disease activity. We applied a mass cytometry (MC) panel that can detect over 20 CB-CAPs and complement receptors to PBMCs from paired flare and remission samples from 6 patients with classified SLE. Furthermore, we analyzed single-cell transcriptional profiles on flaring samples using antibodies to the most prevalent CB-CAPs using cellular indexing of transcriptomes and epitopes (CITE)-seq.

Methods: Adults with ACR- or SLICC-classified SLE were consented for PBMC collection at Washington University School of Medicine. Isolated PBMCs were subjected to single cell MC (n = 6) and CITE-seq (n = 3). MC data analysis was performed with Cytobank. CITE-seq data analyses was performed with Seuret, gProfileR, and Comprehensive Multi-omics Platform for Biological InterpretatiOn (COMPBIO).

Results: We found the highest frequency of C4d, C3d, C5, and Bb deposition on B cells compared to T cells and monocytes during SLE flares (Fig 1).



During disease remission, low levels of all CB-CAPs were observed in these cells. Compared to controls, transitional B cells from flaring patients with SLE had high levels of C5 and Bb with little C4d or C3d. CD11c$^+$ B cells from flaring patients also had elevated Bb deposition compared to controls. CITE-seq transcriptional profiling identified Bb- and C3d-bearing CD11c$^+$ B cells possessing a type I interferon signature, with Bb-bearing B cells further possessing a TNF/NF-κB transcriptional signature (Fig 2).

Pathway	Adjusted p-value
TNF-alpha signaling pathway	1.804E-03
Canonical NF-kB pathway	2.406E-03
T-cell receptor signaling pathway	6.253E-03
protease binding	8.229E-03
IL-18 signaling pathway	8.288E-03
RNA polymerase II transcription repressor complex	1.314E-02
B cell receptor signaling pathway	1.716E-02
STING pathway in Kawasaki-like disease and COVID-19	1.794E-02
hsa-miR-337-3p	1.811E-02
hsa-miR-202-5p	2.244E-02
C-C chemokine receptor activity	2.564E-02
positive regulation of miRNA transcription	2.641E-02
C-C chemokine binding	2.797E-02
aspartic-type endopeptidase inhibitor activity	2.873E-02
G protein-coupled chemoattractant receptor activity	3.292E-02
chemokine receptor activity	3.292E-02
Factor: NFKB2; motif: NGGGGAWTCCCCN	3.932E-02
Factor: NFKB2; motif: NGGGGAWTCCCCN; match class: 1	3.932E-02
positive regulation of miRNA metabolic process	4.173E-02

Conclusions: A high level of CB-CAP deposition was observed in B cells obtained from flaring subjects with a SLE, which was absent during disease remission. The types of CB-CAPs found on PBMCs were not uniform between cell types, potentially opening a previously undescribed heterogeneity in SLE. Additional heterogeneity was observed in the transcriptional profiles associated with specific CB-CAPs on B cells. These pilot data demonstrate the feasibility of the MC complement panel on human samples, and

the potential insights CITE-seq has using CB-CAPs in discovering novel mechanisms of complement activation and regulation.

PV117 / #372

Poster Topic: ***AS14 - Innate Immunity***

EXPLORING THE ROLE OF ESTROGEN RECEPTOR ALPHA VARIANTS IN TLR7-INDUCED LUPUS PATHOGENESIS

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Background/Purpose: Lupus is a classical autoimmune disease affecting mainly women of reproductive age, which has led to investigations into the role of sex hormones and their receptors in its pathogenesis. Our previous research has shown that a functional knockout of estrogen receptor alpha (expressing ERα short, similar to endogenous ERα46), but *not* complete ERα deletion, protected lupus-prone mice from disease development, suggesting complex effects of ERα variants on lupus pathogenesis. This study aims to investigate the role of two ERα variants, the classic full-length ERα66 and a short variant ERα46, in modulating the inflammatory response to Toll-like receptor 7 (TLR7) stimulation, which is involved in the pathogenesis of lupus.

Methods: Raw 264.7 cells (a mouse macrophage cell line) were transfected with a plasmid containing ERα66 or ERα46, with an empty plasmid as a control. After 24h, cells were treated with 0.2 mM loxoribine (Lox), a TLR7 agonist, or an equal volume of DMSO (vehicle) for 1h or 18h. The expression of ERα66 and ERα46 was validated by RT-qPCR and western blot. RNA levels of pro-inflammatory cytokines (IL-6, IL-1β, and TNF-α, among others) were then assessed.

Results: Compared to plasmid control (pc), where no endogenous expression of ERα66 or ERα46 was detected by western blot, Raw 264.7 cells transfected with ERα66 or ERα46 plasmids successfully overexpressed ERα66 or ERα46 protein. RT-qPCR showed consistent results: ERα mRNA was only increased in cells overexpressing ERα66 using primers to exon 1-2 (only exists in ERα66), and in parallel experiments, ERα mRNA level was increased in both ERα66 and ERα46-over-expressing cells when using primers to exon 4-5 (shared by both). Unexpectedly, our pilot data showed that both ERα46 and ERα66 overexpression promoted IL-6, IL-1β, and TNF-α by macrophages in response to TLR7 stimulation, contrary to our hypothesis that ERα46 might antagonize the pro-inflammatory influence of ERα66 in lupus.

Conclusions: Two main ERα variants, ERα66 and ERα46, both promote the activation and inflammatory response of macrophages in the setting of low/no estrogen. Since our previous *in vivo* studies demonstrated a requirement for estrogen in the protective effect of ERα46 in disease expression, further studies are needed to systemically elucidate the respective roles of ERα66 and ERα46 in lupus pathogenesis in the setting of estrogen.

PV118 / #653

Poster Topic: *AS15 - Lupus Nephritis-Clinical*

DELAYED ONSET OF MALE INFERTILITY AFTER TREATMENT WITH HIGH DOSE OF CYCLOPHOSPHAMIDE FOR LUPUS NEPHRITIS

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a classical autoimmune disease with manifestations in multiple organs. Urgent immune modulation and immunosuppressive therapy, particularly with cyclophosphamide (CYC), are essential in cases of diffuse vasculitis and involvement of critical organs like the central nervous system or the kidneys. However, due to its significant side effects, particularly on fertility, alternative regimens such as mycophenolate mofetil (MMF) have been used, especially in childbearing population. In the last years, the induction therapy for active lupus nephritis (LN) with intravenous cyclophosphamide (IV CYC) has been changing from high doses (NIH protocol) to lower cumulative doses (EUROLUPUS) with comparable efficacy, but less adverse events such as infections and toxicity. Gonadal function is severely affected following CYC in both sexes. In male SLE patients, the risk of sterility after CYC is higher than in female, due to greater mitotic activity in the testis. The sperm count in SLE males is inversely influenced by disease activity, and worsens with exposure to CYC, and typically declines within a few weeks of therapy. This toxic effect is less in youger age and pre-puberty, following lower dose and shorter treatment duration. Male sterility is usually sustained for several years after end of CYC therapy, so it reinforces the need for sperm cryopreservation. Most of the known data regarding CYC toxicity is based on the onco-hematologic literature, while in SLE patients the actual timing of clinically toxic effect on fertility, of IV CYC for LN, is still unclear and needs to be identified.

Methods: Presenting a case-series of three males, of arab origin with SLE who received IV CYC (NIH protocol) for active LE (mainly diffuse and proliferative glomerulonephritis, Type IV) at a young age (ages 20-23). Their fertility records included available sperm tests and their actual reproductive capability was estimated by number of their spouses' successful pregnancies. These pregnancies occurred naturally without the use of frozen semen samples and their timing after end of IV CYC courses was recorded.

Results: After semen cryopreservation, age at administration of IV CYC was 20-23 years old,. It was given monthly in 1g doses for six consecutive months, and later every 2-3 months for a total of 9-11g. All cases were followed-up in rheumatology clinic for a period of 13-17 years. During the initial 3-4.5 years after CYC therapy, all patients

exhibited normal fertility status and their wives conceived and gave birth without complications to a total of 7 babies. Surprisingly, oligospermia and azoospermia emerged subsequently in all patients, with continuous infertility requiring the use of frozen semen specimens for in-vitro fertilization in two additional pregnancies. Despite difficulty to childbearing after the third year post-chemotherapy, one successful pregnancy was recorded with tests showing abnormal semen count, motility and morphology with clear oligospermia.

Conclusions: SLE-related nephritis requires urgent induction therapy with cyclophosphamide being a cornerstone, despite concerns about gonadal failure and infertility. A presented case-series suggests a different pattern of fertility following IV CYC use for Lupus nephritis, with more reassuring results in the first 3-4 years post therapy. The onset of clinical infertility and findings of oligo/ azospermia after cyclophosphamide treatment may occur several years later, providing a natural window of opportunity for normal fertilization and family planning. This unique finding in SLE male patients is noteworthy and mandates investigation and confirmation with further observational studies.

PV119 / #87

Poster Topic: *AS15 - Lupus Nephritis-Clinical*

A PHASE 1, MULTICENTER, OPEN-LABEL STUDY OF CB-010, A NEXT-GENERATION CRISPR-EDITED ALLOGENEIC ANTI-CD19 CAR-T CELL THERAPY, IN PATIENTS WITH REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS (GALLOP)

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Background/Purpose: Autologous CD19-directed CAR-T cell therapy led to deep depletion of aberrant B cells in lupus patients, leading to prolonged treatment-free remission in recent publications [Muller F. N Engl J Med 2024;390:1631-1632]. However, autologous CAR-T cell therapy is characterized by logistical challenges, including the need for leukapheresis, prolonged manufacturing and QC, and manufacturing failures. These may contribute to treatment delays and extended periods of treatment washout, compounding the risk for flares. Furthermore, the manufacturing time and logistics of autologous CAR-T cell therapies can limit their real-world feasibility and/or access for patients. CB-010 is an allogeneic, off-the-shelf anti-CD19 CAR-T cell therapy derived from healthy donor T cells. Patients receiving CB-010 do not require leukapheresis, thus eliminating the need for treatment washout preceding leukapheresis. CB-010 uses a next-generation genome-editing technology (chRDNA) to generate 3 genome edits: (i) knockout of the *TRAC* gene to eliminate TCR expression to reduce the risk of graft-versus-host disease, (ii) site-specific insertion of a CD19-specific CAR into the *TRAC* locus, and (iii) knockout of the gene encoding PD-1, designed to increase cytotoxic activity against B cells. Importantly, PD-1 knockout in CB-010 has demonstrated a statistically significant benefit in efficacy in *in vivo* preclinical studies.

CB-010 also features an FMC63 scFv and a 4-1BB costimulatory domain, a combination used in recently published cases [Muller F. N Engl J Med 2024;390:1631-1632]. In the Phase 1 ANTLER trial in 46 relapsed or refractory B cell non-Hodgkin lymphoma patients, CB-010 was generally well tolerated, with no Grade 3 or higher CRS [Hu B J Clin Onc 2024;42:7025]. CB-010 was readily available, with a median of 2 days between the time of eligibility confirmation and the start of lymphodepletion in ANTLER patients. CB-010 led to deep B cell depletion and extended B cell aplasia in the ANTLER trial. Furthermore, in preclinical studies, CB-010 demonstrated lupus specific B cell targeting both *in vitro* and *in vivo*, accompanied by suppression of autoantibody generation as a result of B cell targeting [Garner E, Accepted for presentation at ACR 2024]. The combination of these preclinical data and encouraging safety and efficacy data from the ongoing ANTLER clinical trial, support the evaluation of CB-010 in a Phase 1 clinical trial for refractory lupus nephritis (LN) and extra-renal lupus (ERL) patients (GALLOP).

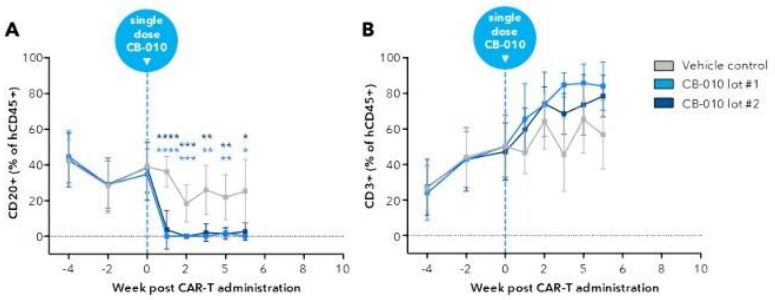
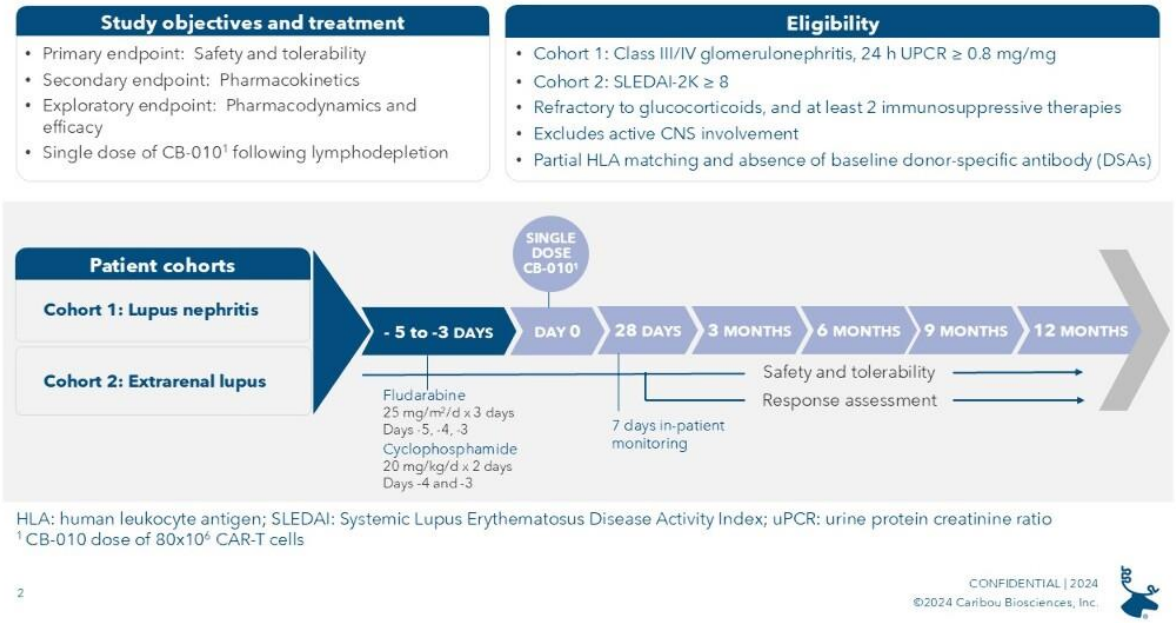


Fig 1. CB-010-mediated B cell aplasia in humanized mouse models NOG-EXL mice were engrafted with human CD34+ HSCs via tail vein injection. At 16 weeks post engraftment, animals were dosed intravenously with 1×10^7 CB-010 CAR+ T cells per animal. In-life sampling of peripheral blood was analyzed via flow cytometry every two weeks prior to CAR-T cell administration and every week post CAR-T cell administration. Human CD20+ cells as a percentage of total human CD45+ cells are plotted indicating B cell dynamics (**A**). Human CD3+ cells as a percentage of total human CD45+ cells are plotted indicating T cell dynamics (**B**). Significance determined by unpaired T test. *p < 0.05, **p< 0.01, ***p < 0.001, ****p< 0.0001.

Methods: CB-010 is being investigated in an open-label, multicenter Phase 1 clinical trial in adult patients with LN and ERL. The GALLOP study will enroll approximately 20 patients. The primary objective is safety. Additional key objectives include preliminary efficacy, pharmacokinetics, and biomarkers of response. After lymphodepletion therapy with fludarabine (25 mg/m^2/day on Days -5, -4, -3) and cyclophosphamide (20 mg/kg/day on Days -4, -3), patients receive a single infusion of 80 million CB-010 CAR-T cells and are followed for safety and efficacy. Initial efficacy including the SLEDAI-2K, DORIS, and PhGA scores, along with steroid usage and renal responses (LN cohort) will be evaluated.



Results: are not available for this trial-in-progress.

Conclusions: GALLOP is a Phase 1 clinical trial evaluating CB-010 in the treatment of LN and ERL, which has the potential to overcome key barriers to access to CAR-T cell treatment and rapidly deliver care to patients.

PV120 / #816

Poster Topic: *AS15 - Lupus Nephritis-Clinical*
Late-Breaking Abstract

RENAL BIOPSY DATA IN LUPUS PATIENTS WITH LOW PROTEINURIA

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Background/Purpose: Introduction:
Systemic lupus is an extremely protean, chronic disease, evolving in flares, the severity of which varies depending on the severity of the affected organs.
Renal involvement during lupus is a major prognostic factor.
The objective of our study is to evaluate histological renal involvement in lupus patients with proteinuria < 1.2 g/24 and to determine the impact on the therapeutic project.

Methods: This is a 2-year retrospective study from January 2023 to January 2025 including lupus patients with proteinuria between 0.7 and 1.2 g/24h who underwent a renal biopsy. We excluded those with renal failure

Results: We gathered 23 patients with an average age of 28 years +/- 22 years, the female gender predominates in our study, making up all the patients gathered.
The average proteinuria rate was 1g/24h.
The indication for renal biopsy was proteinuria in 86% of cases, as well as proteinuria associated with hematuria in 14% of cases.
Renal biopsy puncture showed class III lupus nephropathy in 17% of cases, class IV or IV+V in 40% of cases and class V found in 43% of cases
The use of immunosuppressants and full-dose corticosteroid therapy was imperatively instituted in 83% of cases
As a result, even low proteinuria can reveal advanced class lupus nephropathy, which underlines the absence of anatomoclinical correlation and joins the new KDIGO 2024 recommendations, a renal biopsy puncture should be considered in the event of proteinuria > or equal to 500mg/day and/or active urinary sediment.

Conclusions: As a conclusion, according to our study, a biopsy puncture is necessary in the event of even minimal urinary sediment abnormalities, given the absence of anatomoclinical correlation.

PV122 / #252

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

ATTAINMENT OF ULTRA-LOW LEVELS OF UPCR IN THE AURORA 1 STUDY ASSOCIATED WITH ALTERATIONS IN THE CIRCULATING LIPIDOME

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Background/Purpose: Lupus nephritis (LN) is an independent risk factor for cardiovascular disease (CVD) and is associated with a nearly 5-fold greater risk of cardiovascular mortality compared to non-renal systemic lupus erythematosus. In the Phase 3 AURORA 1 study of adult patients with active LN, the addition of voclosporin to mycophenolate mofetil (MMF) and low-dose glucocorticoids resulted in significantly greater and earlier urine protein creatinine ratio (UPCR) reduction as well as significant reductions in many classes of lipids within the circulating lipidome.[1,2] We hypothesized that patients who achieved an ultra-low UPCR (≤0.2 g/g) would have distinct changes in their lipidomes over time compared to patients achieving a partial renal response (PRR).

Methods: Patients enrolled in the 52-week AURORA 1 study were randomized to either voclosporin 23.7 mg twice daily or placebo (control), in combination with MMF (target 2 g/day) and low-dose glucocorticoids (starting dose 20-25 mg/day, tapered to ≤2.5 mg/day by Week 16). Serum samples were collected from each patient prior to treatment (baseline) and at the end of treatment (Week 52). A lipidomic analysis assessing 19 classes of lipids (935 individual lipids) was performed on a subset of 58 patients. Lipids were extracted from biofluid and quantified as previously described.[1] Changes in mean lipid levels from baseline to Week 52 were compared in patients who achieved a UPCR ≤0.2 g/g at Week 52 with patients who achieved a PRR (≥50% reduction in UPCR from baseline) at Week 52 but maintained UPCR levels >0.2 g/g.

Results: Overall, 115 (31.9%) patients (voclosporin, 72; control, 42) achieved a UPCR ≤0.2 g/g at any point during the 52-week study. Of the subset of patients with available lipidomic data, 7 (voclosporin, 4; control, 3) achieved a UPCR ≤0.2 g/g at Week 52; 22 patients achieved a PRR with UPCR >0.2 g/g. In patients achieving UPCR ≤0.2 g/g, mean levels of the following lipids decreased from baseline to Week 52 and were statistically different from corresponding levels in patients who achieved PRR: triacylglycerol (TAG; p=<0.0001), diacylglycerol (DAG; p<0.0001), phosphatidylcholine (PC; p<0.0001), phosphatidylethanolamine (PE; p<0.0001), phosphatidylinositol (PI; p=0.0122), lyso-PC (LPC; p=0.0170), and lyso-PE (LPE; p=0.0026; Figure 1). Mean levels of PE-O (p<0.0001), acylcarnitine (AC; p=0.0006), and PE-P (p=0.0011) were increased from baseline to

Week 52 in patients achieving UPCR ≤0.2 and statistically different from corresponding mean levels in patients achieving PRR.

Conclusions: Proteinuria confers CVD risk due to alterations in the lipidome. This analysis has revealed a distinct lipidomic profile in patients who achieved ultra-low UPCR compared to patients who achieved a PRR. ACs transport long chain fatty acid into mitochondria for β-oxidation, and the AC profiles change dynamically according to the completeness of β-oxidation.[3] In our previous work, AC levels decreased in patients with UPCR ≤0.5 g/g.[1] In the current analysis, the increase in AC levels in those who achieved UPCR ≤0.2 g/g suggests a possible restoration of fatty acid metabolism homeostasis with deeper UPCR reductions.[3] Taken together, our data suggest that differential modification of CVD risk in LN can be further modified with attainment of ultra-low UPCR targets. **References** 1. Afshinnia F, Rajendiran TM, Byun J, et al. *Kidney Int Rep*. 2024;9(8):2559-2562. 2. Rovin BH, Teng YKO, Ginzler EM, et al. *The Lancet*. 2021;397 (10289):2070-2080. 3. Makrecka-Kuka M, Sevostjanovs E, Vilks K, et al. *Scientific Reports*. 2017;7(1):17528.

Figure 1. Change in lipid level by UPCR Level

	Z-score standardized mean change in lipid level from baseline to Week 52		
	UPCR ≤0.2 g/g n=7	PRR (UPCR >0.2 g/g) n=22	P value
TAG	-0.447	0.012	<0.0001
DAG	-0.291	0.050	<0.0001
PC	-0.19	0.051	<0.0001
PE	-0.311	-0.010	<0.0001
PE-O	0.8272	-0.126	<0.0001
AC	0.103	-0.080	0.0006
PE-P	0.201	-0.044	0.0011
LPE	-0.289	0.085	0.0026
LPC	-0.121	0.132	0.0170
PI	-0.138	0.169	0.0122
LCER	0.1828	0.014	0.1525
DCER	0.0285	-0.136	0.1789
MAG	-0.106	0.002	0.1809
SM	-0.165	-0.016	0.2084
HCER	0.0583	-0.085	0.2561
FFA	-0.08	0.028	0.3697
CE	0.0295	-0.040	0.4020
CER	-0.037	-0.123	0.5111

Changes from baseline to Week 52 were calculated for each lipid followed by z-score standardization. Mean z-score standardized changes of lipids were used for comparison by group. Red bars represent increases and blue bars represent decreases in the corresponding lipid. AC, acylcarnitine; CE, cholesteryl ester; CER, ceramide; DAG, diacylglycerol; DCER, dihydroceramide; FFA, free fatty acid; HCER, hexosylceramide; LCER, lactosylceramide; LPC, lyso-PC; LPE, lyso-PE; MAG, monoacylglycerol; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PI, phosphatidylinositol; PRR, partial renal response (≥50% reduction in UPCR from baseline at Week 52); SM, sphingomyelin; TAG, triacylglycerol; UPCR, urine protein creatinine ratio.

PV123 / #804

Poster Topic: *AS15 - Lupus Nephritis-Clinical*
Late-Breaking Abstract

COMPARATIVE ANALYSIS OF DAMAGE ACCRUAL IN LUPUS NEPHRITIS STRATIFIED BY BIOLOGIC SEX

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Background/Purpose: Several studies in systemic lupus erythematosus (SLE) have suggested that males may experience greater damage accrual compared to females. However, this has not been adequately explored in cohorts focused specifically on lupus nephritis (LN), particularly with the separate consideration of renal and extra-renal damage. In this study, we aimed to investigate biologic sex-based differences in the accrual of both extra-renal and renal damage in a cohort of LN patients.

Methods: This retrospective study included patients with systemic lupus erythematosus (SLE) from an observational cohort who developed LN at or after clinic entry. Outcomes of extra-renal and renal damage were assessed. For extra-renal damage, the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) Damage Index (SDI) was used, excluding the renal item (non-renal SDI). For renal damage, a composite measure was used, defined as a sustained ≥ 30% decline in estimated glomerular filtration rate (eGFR) or end-stage kidney disease (ESKD). Univariable and multivariable Fine-Gray subdistribution hazard models were utilized to identify baseline features associated with the first outcome, an increase in non-renal SDI by ≥1, employing death as used as a competing risk. The models were adjusted for age, hypertension, baseline SDI, overall mean glucocorticoid dose, and 'LN before 2005 vs. 2005 or after' to account for the calendar effect; mycophenolate mofetil became available in our cohort after the year 2005 and it was around that time when a more glucocorticoid-conservative approach was followed. Likewise, univariable and multivariable Fine-Gray subdistribution hazard models were then utilized to identify baseline features associated with the composite outcome employing death as a competing risk. The models were adjusted for baseline serum creatinine level and calendar effect.

Results: The LN cohort included 460 patients, with a predominance of females (83.5%) and a median age of 33 years. Female patients were more likely to be Black, and there were no significant differences in baseline SDI or renal histology between males and females (**Table 1**). Over a median follow-up of 8.6 years [IQR: 4.1, 14.9], 45% of patients accrued extra-renal damage, while 32% experienced renal damage. Notably, the median time to extra-renal damage was numerically shorter than that for renal damage

(4.1 [1.6, 8.7] vs. 5.5 [1.7, 11.3] years). No significant differences in the accrual of either extra-renal or renal damage were observed between males and females, and the time to these outcomes was not statistically different between sexes (**Figure 1 A-B**). The most common SDI items identified in the 188 patients who accrued extra-renal damage were ocular (36.7%), diabetes mellitus (15.4%), skin (13.8%), musculoskeletal (9.6%), and neurologic (8.5%). Aside from neurologic damage, which was more prevalent in males (20.7% [6/29] in males vs. 6.2% [10/159] in females, p = 0.04), no significant differences based on sex were found. When examining the SDI organ items, peripheral neuropathy was more frequent in males (13.8 [4/29] % vs. 2.5% [4/159], p = 0.02). Multivariate analyses revealed that male sex was not associated with greater damage accrual, either extra-renal (HR 1.13, 95% CI 0.76–1.69) or renal (HR 1.34, 95% CI 0.73–2.48).

Figure 1. Baseline characteristics and therapeutic regimens in patients with LN

Variable		Overall (n=460)	Female (n=384)	Male (n=76)	p-value
Age in years	Median [IQR]	33.0 [25.5, 42.9]	33.5 [25.5, 42.5]	32.2 [25.2, 43.0]	0.75
Race	Black, n (%)	89 (19.5)	82 (21.5)	7 (9.3)	**0.02**
	White, n (%)	246 (53.8)	194 (50.8)	52 (69.3)	
	Chinese, n (%)	60 (13.1)	51 (13.4)	9 (12.0)	
	Other, n (%)	62 (13.6)	55 (14.4)	7 (9.3)	
SLE duration in years	Median [IQR]	5.0 [0.9, 10.4]	5.0 [0.9, 10.4]	5.3 [1.2, 10.3]	0.63
Creatinine, µmol/L	Median [IQR]	80.0 [63.0, 106.0]	76.5 [61.0, 104.3]	90.0 [75.0, 113.3]	**<0.01**
Serum albumin, g/L	Mean (SD)	33.0 (7.2)	32.69 (7.02)	34.79 (7.66)	**0.03**
Low complement levels	n (%)	287 (63.4)	238 (63.0)	49 (65.3)	0.80
Positive anti-dsDNA	n (%)	288 (62.6)	243 (63.3)	45 (59.2)	0.59
Proteinuria, g/day	Mean (SD)	2.8 (2.93)	2.7 (3.0)	3.0 (2.6)	0.54
	Median [IQR]	2.0 [1.0, 3.5]	2.0 [1.0, 3.5]	2.3 [1.3, 3.6]	0.22
SLEDAI-2K	Median [IQR]	13.0 [9.0, 19.0]	14.0 [10.0, 19.5]	12.0 [8.0, 17.3]	**0.04**
SDI	Median [IQR]	0.0 [0.0, 1.0]	0.00 [0.0, 1.0]	0.0 [0.0, 1.0]	0.41
Biopsy class, n=353	I or II, n (%)	47 (13.3)	41 (13.6)	6 (11.8)	0.53
	III, n (%)	64 (18.1)	53 (17.5)	11 (21.6)	
	IV, n (%)	103 (29.2)	89 (29.5)	14 (27.5)	
	III/VI+V, n (%)	66 (18.7)	60 (19.9)	6 (11.8)	
	V, n (%)	69 (19.5)	55 (18.2)	14 (27.5)	
	VI, N (%)	4 (1.1)	4 (1.3)	0 (0.0)	
NIH Activity index	Median [IQR]	3.0 [1.0, 7.0]	4.0 [1.0, 8.0]	2.0 [1.0, 6.0]	0.24
NIH Chronicity index	Median [IQR]	2.0 [0.0, 3.0]	2.0 [0.0, 3.3]	2.0 [0.3, 3.0]	0.61
Glucocorticoid use	n (%)	449 (97.6)	377 (98.2)	72 (94.7)	0.17
Average daily glucocorticoid dose during the first year in mg	Median [IQR]	21.3 [16.0, 29.0]	21.0 [16.0, 28.3]	22.3 [15.8, 30.3]	0.72
Use of immunosuppressives during the first year	n (%)	386 (83.9)	320 (83.3)	66 (86.8)	0.56
Immunosuppressives used during the first year	MMF, n (%)	212 (46.1)	171 (44.5)	41 (53.9)	0.17
	CYC, n (%)	45 (9.8)	40 (10.4)	5 (6.6)	0.41
	AZA, n (%)	198 (43.0)	176 (45.8)	22 (28.9)	**0.01**
	Other (including Cyclosporine, TAC, RTX, and/or BEL), n (%)	50 (10.9)	39 (10.2)	11 (14.5)	0.37
Antimalarial use	n (%)	281 (61.1)	232 (60.4)	49 (64.5)	0.59

LN, lupus nephritis; SLE, systemic lupus erythematosus; IQR, interquartile range; SD, standard deviation; eGFR, estimated glomerular filtration rate; dsDNA, double-stranded DNA; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SDI, Systemic Lupus International Collaboration Clinics (SLICC)/American College of Rheumatology Damage Index; NIH, National Institutes of Health; MMF, mycophenolate mofetil, CYC, cyclophosphamide, AZA, azathioprine, RTX, rituximab, BEL, belimumab

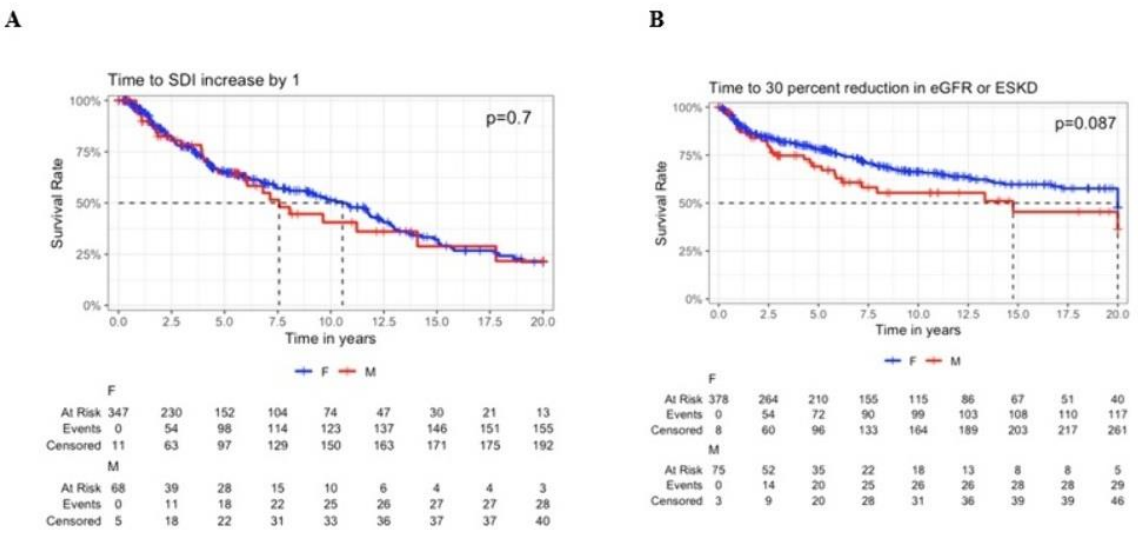

Figure 1 A-B. Kaplan-Meier curves showing the differences between the female and male lupus nephritis patients in:

A- Time to extra-renal damage (a ≥1 point increase in non-renal SDI)
B- Time to renal damage (a sustained ≥30% decline in eGFR or ESKD)

SDI, Systemic Lupus International Collaboration Clinics (SLICC)/American College of Rheumatology Damage Index; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease

Conclusions: Extra-renal and renal damage accrual are common in patients with LN but do not appear to occur more rapidly in males. We suggest that optimizing treatment protocols through multitargeted therapy and reducing glucocorticoid exposure may improve long-term outcomes.

PV124 / #678

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

INFLUENCE OF AGE OF ONSET OF LUPUS NEPHRITIS ON OUTCOMES: AN INCEPTION COHORT-BASED STUDY

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Background/Purpose: Renal involvement in systemic lupus erythematosus (SLE) most commonly occurs in women of the reproductive age group. However, it may theoretically start at any age. In this study, we aimed to explore the impact of early vs. late-onset lupus nephritis (EoLN vs. LoLN) on clinical presentation and disease outcomes.

Methods: We included 246 inception cohort patients who developed LN during follow-up. We classified patients based on the age of onset of LN into EoLN (before age 50; 205 patients) and LoLN (50 years or older; 41 patients). Outcomes included complete proteinuria recovery (CPR) at one year, an adverse composite outcome (end-stage kidney disease [ESKD], a sustained ≥40% decline in eGFR, or death), subsequent LN flares (doubling of proteinuria to ≥1 g/day after complete response or to ≥2 g/day partial response), and a ≥1 point increase in non-renal SLICC damage index (SDI). The association with outcomes was studied using Cox proportional hazards model.

Results: At baseline, the median [IQR] age was 31.4 [25.2, 38.5] years for EoLN and 58.4 [53.9, 63.5] years for LoLN. LoLN patients exhibited higher median creatinine levels, lower median eGFR, reduced proteinuria, and a lower median SLEDAI-2K score compared to EoLN patients. On long-term follow-up (median 8.5 years [IQR 4.2, 15.5]), the rates of achieving CRR, adverse composite outcomes, and renal flares were comparable between the two groups (**Table 1**). However, the LoLN group demonstrated a significantly higher incidence of a ≥1 point increase in non-renal SDI. Additionally, the time to damage accrual was notably shorter in the LoLN group (**Figure 1**) Cox proportional hazard models confirmed these results by showing no significant differences between the two groups in terms of achieving CRR (LoLN vs. EoLN, HR 1.29, 95% CI 0.76-2.18, p=0.35), developing adverse composite outcomes (LoLN vs. EoLN, HR 1.16, 95% CI 0.57-2.35, p=0.68), or experiencing renal flares (HR 0.54, 95% CI 0.23-1.28, p=0.16). Notably, LoLN was associated with significantly higher odds of a ≥1 point increase in non-renal SDI (HR 2.37, 95% CI 1.42-3.97, p<0.01).

Table 1. Rate and time to short and long-term outcomes of patients with early- and late-onset lupus nephritis.

Outcome	Overall (n=246)	Early-onset LN (EoLN) (n=205)	Late-onset LN (LoLN) (n=41)	p-value
Short-term outcomes, n=237				
CPR at 1 year, n (%)	114 (48.1)	93 (47.0)	21 (53.8)	0.54
Time to CPR, years	1.0 [0.4, 2.5]	1.0 [0.4, 2.6]	0.6 [0.3, 1.3]	0.20
Long-term outcomes, n=246				
Adverse composite outcome^, n (%)	83 (33.7)	69 (33.7)	14 (34.1)	1.00
Time to the adverse composite outcome, years	6.9 [2.2, 13.5]	6.9 [2.2, 13.7]	6.7 [1.7, 12.2]	0.80
LN Flare, n (%)	76 (31.0)	68 (33.3)	8 (19.5)	0.12
Time to LN flare, years	5.7 [2.5, 10.8]	5.6 [2.6, 10.8]	6.6 [1.6, 11.3]	0.13
≥1 point increase in non-renal SDI, n (%)	99 (42.9)	76 (39.0)	23 (63.9)	**0.01***
Time to SDI increase, years	4.2 [1.8, 9.1]	4.2 [1.8, 9.7]	3.9 [1.6, 7.1]	**0.01***

LN lupus nephritis; CPR, complete proteinuria recovery; SDI, Systemic Lupus Erythematosus International Collaboration Clinics (SLICC)/ACR Damage Index

^ End-stage kidney disease (ESKD), a sustained ≥40% decline in eGFR, or death

Non-renal SDI refers to damage not related to the renal component

*Statistically significant (p <0.05)

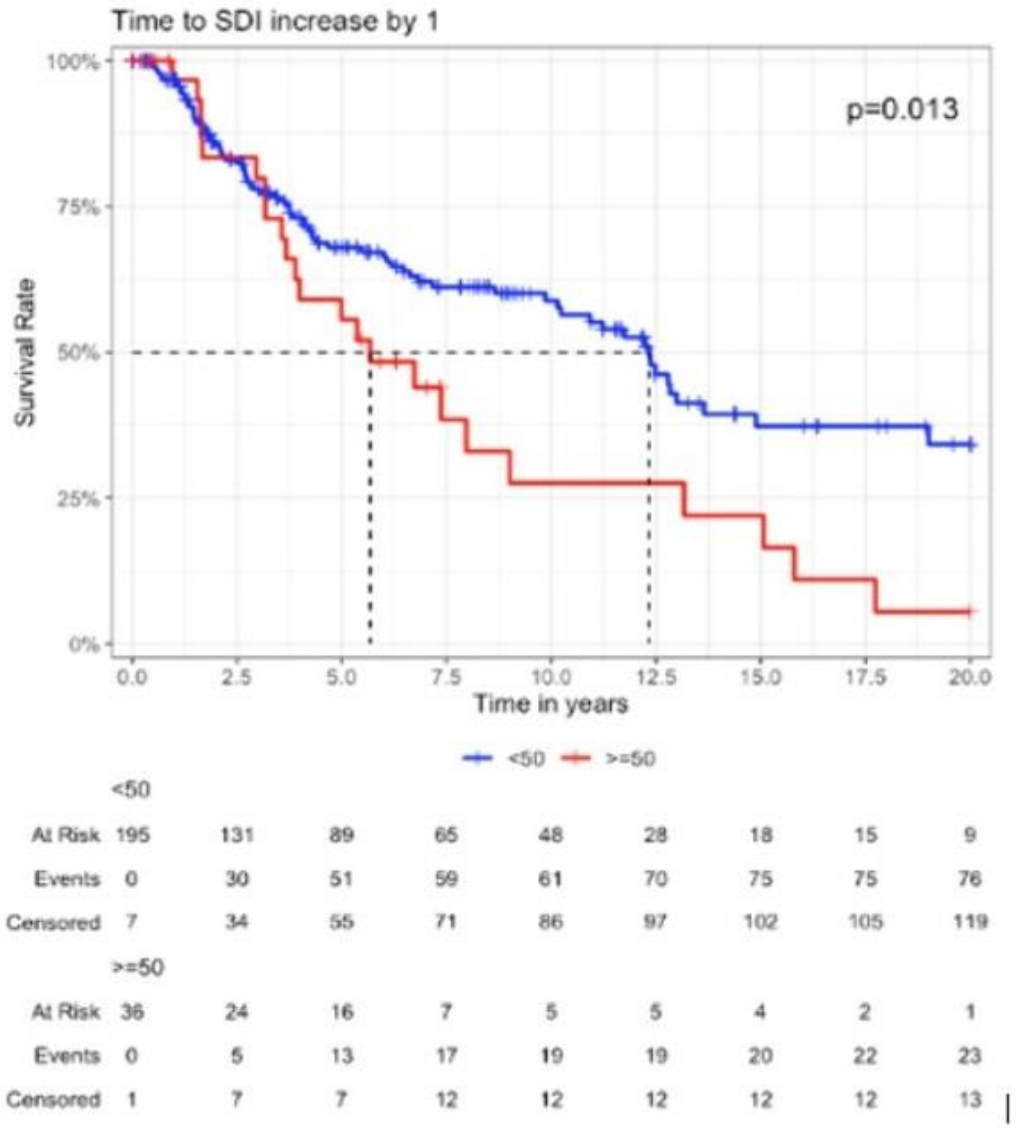

Figure 1. Kaplan-Meier curve showing the differences between the early- and late-onset lupus nephritis groups in time to a ≥1 point increase in non-renal SDI.

Conclusions: Late-onset lupus nephritis (LN) is not associated with significant differences in short- or long-term renal outcomes; however, it is associated with increased damage accrual over time.

PV125 / #23

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

EFFICACY AND SAFETY OF TACROLIMUS IN THE MAINTENANCE TREATMENT OF PATIENTS WITH LUPUS NEPHRITIS

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Background/Purpose: The treatment for lupus nephritis (LN) is associated with severe adverse effects and treatment failures. Calcineurin inhibitor such as tacrolimus has become increasingly interested as a therapeutic agent in LN. This study aims to evaluate the efficacy and safety of tacrolimus in maintenance treatment of patients with LN.

Methods: We retrospectively reviewed of medical records from the Ajou University Hospital included 179 patients who had biopsy-proven LN, with 92 in the tacrolimus and 87 in the non-tacrolimus. Clinical parameters were assessed at 6 months, 1 year, 2 years, 3 years, and 5 years. Complete (CR) and partial renal responses (PR) were defined based on established criteria. Adverse events, renal flares, and poor outcomes (ESRD or death) were documented.

Results: At 6 months, CR were 49.5% in the tacrolimus group and 56.6% in the non-tacrolimus group ($p = 0.308$). At 1 year, the non-tacrolimus group had a significantly higher CR rate (73.1% vs. 52.3%, $p = 0.006$), while the overall response rates were similar ($p = 0.15$). After 2 years, the non-tacrolimus group had higher CR rates (71.8% vs. 58.2%, $p = 0.031$) and higher overall response. However, at 3 and 5 years, the overall response rates were similar (75.3% and 72.9% in the tacrolimus and 83.1% and 85.5% in the non-tacrolimus, $p = 0.252$ and $p = 0.1$, respectively). Renal flare rates, poor outcomes, and adverse events showed no significant differences.

Conclusions: The efficacy and safety of tacrolimus in maintenance treatment have been demonstrated for patients with LN who have not achieved remission.

PV126 / #511

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

NOVEL URINARY BIOMARKER MODEL FOR DIFFERENTIATING LUPUS NEPHRITIS FROM ANCA ASSOCIATED VASCULITIS

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Background/Purpose: Urinary complement activation products (uCAP) and soluble CD163 (usCD163) are promising biomarkers that reflect active renal inflammation in lupus nephritis (LN). However, these urinary proteins alone are not specific to LN since they can be elevated in other disorders including ANCA-associated vasculitis (AAV). The goal of this study was to develop a model that can accurately differentiate between LN vs. AAV using a combination of uCAP, usCD163, and urine protein creatinine ratio (UPCR) levels.

Methods: We included patients with renal biopsy-confirmed cases of LN (n=12) and AAV (n=9) enrolled in the Biobank for Molecular Classification of Kidney Disease (BMCKD) as well as healthy controls (n=10). Their urine samples were collected anytime from 14 days pre-renal biopsy to 238 days post-renal biopsy. Each urine sample was tested for three different uCAP: C3a and C5a using the U-PLEX sandwich immunoassay (BD Biosciences, Franklin Lakes, United States)and sC5b9 using enzyme-linked immunosorbent assay (ELISA) (QuidelOrtho. San Diego, United States). usCD163 was tested using a commercial ELISA (Euroimmun, Luebeck, Germany) normalized to urine creatinine. UPCR levels were tested via conventional clinical methodologies. We compared six logistic regression models for LN vs. AAV prediction, each calculating the area under the receiver operating characteristic curve (AUC) utilizing: 1) C3a, 2) C5a, 3) sC5b9, 4) usCD163, 5) UPCR, and 6) all five urinary biomarkers.

Results: The mean levels of the three uCAPs, usCD163, and UPCR for LN, AAV, and healthy controls, are shown in Figure 1A-E. Among these urinary markers, mean usCD163 was significantly higher in LN (mean difference 776.80 ng/mmol, 95% CI 23.45 – 1530.15) and AAV (mean difference 502.34 ng/mmol, 95% CI 84.19 – 920.48) compared to healthy controls. UPCR was also significantly elevated among LN (mean difference 188.18 mg/mmol, 95% CI 54.80-321.55) and AAV (mean difference 93.0 mg/mmol, 95% CI 28.15-157.84) compared to controls. There were no differences among the uCAP biomarkers for LN/AAV compared to controls. When comparing LN and AAV, there were no significant differences in mean levels of any urinary biomarkers. Models 1-6 for differentiating LN vs. AAV yielded the following AUCs: C3a 0.62 (95%CI 0.34-0.90), C5a 0.56 (95%CI 0.29-0.84), sC5b9 0.56 (95%CI 0.30-0.83), usCD163 0.52

(95%CI 0.29-0.84), UPCR 0.67 (95%CI 0.42-0.92), and combined 0.79 (95%CI 0.57-1.00). (Figure 2).

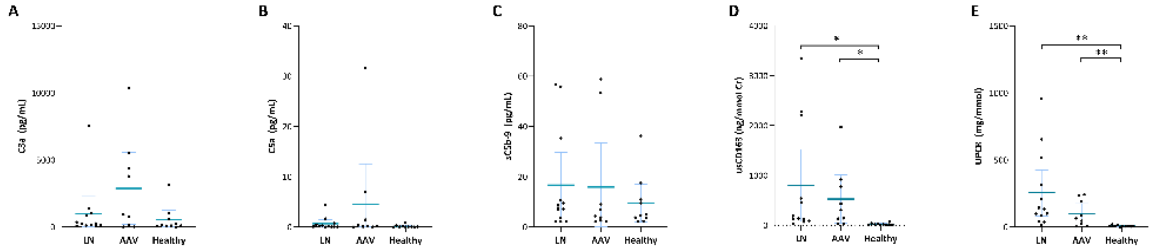

Figure 1. Mean concentration (95% confidence interval) of urinary biomarkers among patients with lupus nephritis (LN), ANCA-associated vasculitis (AAV), and healthy controls. A. C3a. B.C5a. C. sC5b9, D. usCD163 creatinine ratio, E. Urine protein creatinine ratio (UPCR). * denotes p <0.05, and
**p<0.01.

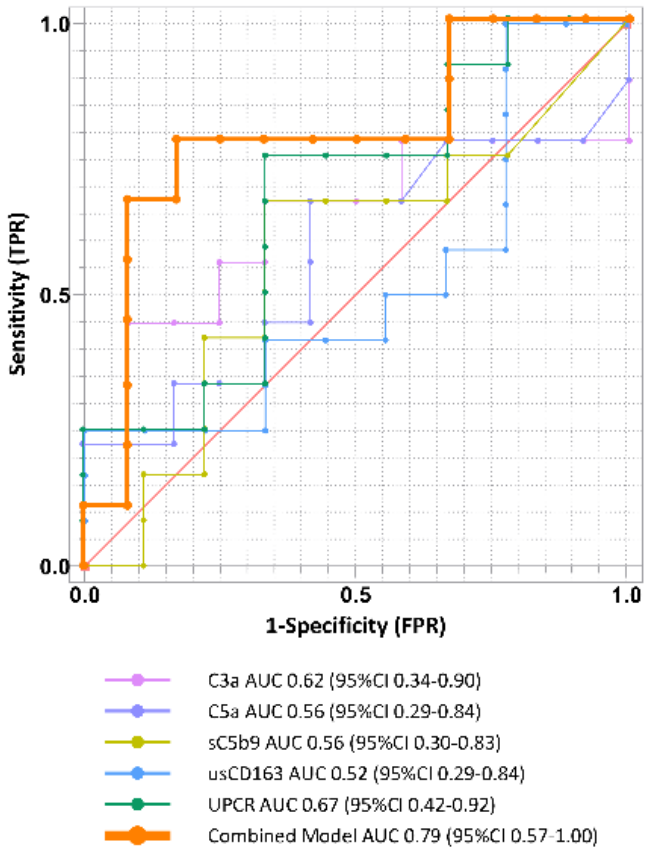

Figure 2. Receiver operator characteristic (ROC) curves of individual urinary biomarkers and a combined model of all 5 urinary biomarkers for the differentiation of lupus nephritis (LN) and ANCA-associated vasculitis (AAV). Area-under-the-curve (AUC) was based on logistic regression predicting LN vs. AAV for each urinary biomarker and the combination of all 5 biomarkers.

Conclusions: In this preliminary study, we demonstrated that both LN and AAV had higher concentrations of usCD163 compared to controls, but it was unable to differentiate between the two diseases. We developed a diagnostic model that combined uCAP, usCD163, and UPCR biomarkers that could differentiate between LN and AAV with an AUC of 79%. A study of larger disease and control cohorts to validate our model is underway. **Acknowledgment** We would like to thank the Biobank for the Molecular Classification of Kidney Disease for supporting this work.

PV127 / #823

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***
Late-Breaking Abstract

A SURVEY OF PATIENTS WITH SLE SUGGESTS LIMITED KNOWLEDGE OF NEPHRITIS UNLESS THERE IS ALREADY CHRONIC KIDNEY DISEASE

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Background/Purpose: Approximately 60% of patients with Systemic Lupus Erythematosus (SLE) will develop Lupus Nephritis (LN) during the course of their disease[1]. However, patients may have limited knowledge about LN, which could hinder participation in shared decision-making and lead to poor outcomes. This study examines the association between patients' self-reported knowledge of LN and factors that might influence their understanding of the disease.

Methods: Cross-sectional data was collected from an online survey of patients with SLE (48 women, 2 men) in the Piedmont Healthcare Rheumatic Disease cohort. Patients were aged 21 to 74, race included African 81.6%, Mixed (other) 12.2%, Asian 2%, and European 1%. Qualtrics®[XM] statistical software was used for analysis.

Results: Patient report of advanced general knowledge about LN was associated with having had a diagnosis of LN, chronic kidney disease (CKD), familiarity with the symptoms of LN, participation in LN support groups, and time spent researching LN online. The following had no impact: frequency of specialist visits, frequency of laboratory evaluations, or participation in LN education programs. The strongest indicators were CKD or participation in a LN support group (100% had knowledge of LN). Of those who did not report CKD, 100% had limited knowledge of LN. 100% of those who spent at least 6 hours searching for LN information on the internet reported advanced knowledge. [See Table 1].

Conclusions: SLE patients without a diagnosis of LN often have limited knowledge of the disease, raising concerns about their recognition of early symptoms and efficient access to definitive care. Many patients may not have optimal knowledge about their condition until they develop chronic kidney disease. These data point to possible

solutions stressing that the internet plays a large role in patient education, and it will be important to ensure that accurate information is available there.

	PATIENT-REPORTED KNOWLEDGE OF LUPUS NEPHRITIS (LN)			
CKD DIAGNOSIS KNOWLEDGE	**NONE**	**LIMITED**	**MODERATE**	**ADVANCED**
NO		**100%**	0	0%
YES		0	50%	**100%**
UNSURE		0	50%	0%
LN SYMPTOMS KNOWLEDGE	**NONE**	**LIMITED**	**MODERATE**	**ADVANCED**
NO	**100.0%**	68.4.0%	50.0%	11.8%
YES	0.0%	31.6.0%	50.0%	**88.2%**
LN DIAGNOSIS KNOWLEDGE	**NONE**	**LIMITED**	**MODERATE**	**ADVANCED**
NO	**100.0%**	75.0%	54.5%	16.6%
YES	0.0%	15.0%	18.2%	**76.5%**
I DO NOT RECALL	0.0%	10.0%	27.3%	5.9%
RACE DECENT	**NONE**	**LIMITED**	**MODERATE**	**ADVANCED**
EUROPEAN	**100.0%**	0.0%	0.0%	0.0%
MIXED, OTHER	0.0%	50.0%	0.0%	50.0%
ASIAN	0.0%	0.0%	0.0%	**100.0%**
AFRICAN	2.5%	42.5.0%	25.0%	30.0%
HOURS SPENT ON INTERNET SEARCHING LN INFO	**NONE**	**LIMITED**	**MODERATE**	**ADVANCED**
~1	0.0%	50.0%	35.7%	14.3%
2-5	0.0%	21.4%	28.6%	50
≥6	0.0%	0.0%	0.0%	**100**
0	14.3	**64.3%**	14.3%	7.1%
LN SUPPORT GROUP PARTICIPATION	**NONE**	**LIMITED**	**MODERATE**	**ADVANCED**
NO, NOT INTERESTED	7.4%	37.0%	29.6%	25.9%
NO, BUT INTERESTED	0.0%	**58.5%**	17.6%	23.5%
YES, INTERESTED IN OPTIONS	0.0%	0.0%	0.0%	**100.0%**

Table 1: Chi-Squared analysis results

References [1.] Saxena, R. Arthritis Res Ther 2011, 13:1-12.

PV128 / #610

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

LUPUS NEPHRITIS: THE RESPONSE TO A PROTEIN OVERLOAD IS DIFFERENT IN GLOMERULAR VERSUS INTERSTITIAL SCLEROSIS AND MAY HELP TO IDENTIFY PATIENTS WITH POOR KIDNEY PROGNOSIS

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Background/Purpose: The kidney response to protein overload (PO) has major diagnostic and prognosis implications in the evaluation of progressive kidney diseases, a frequent finding in patients (Pts) with lupus nephritis (LN). The contribution of the tubulo-interstitial damage (more than the glomerular sclerosis) to the progression towards severe kidney failure is well known. Given that creatinine undergoes considerable tubular secretion, the assessment of sequential glomerular filtration rate (eGFR) after a PO could be used as a test detector of the tubular functional mass. The aim of this trial was to evaluate the kidney response to PO in LN pts with mainly glomerular (GS) versus tubulo-interstitial (TIS) sclerosis and their long follow up. Time to achieve the composite event (CE), decrease of the eGFR ≥40% or needed of renal replacement therapy, was compared among both groups

Methods: All LN biopsies performed in Pts with pure Class III (n: 6) and Class IV (n: 20) LN from Jan 2011 up to Jun 2012 before withdrawing immunosuppression, were included. A total of 26 pts (14 with predominant GS and 12 with predominant TIS) underwent a protein load test to assess the functional kidney reserve (FKR). Test: After an overnight fast all the pts received an oral water load (20 ml/kg BW) and the urinary output was then replaced orally with equal volumes of water. In the morning, a 1.5 g/kg BW PO was provided. GFR was measured every 30 min. from 1 h before and up to 4 h following PO. The FKR index was calculated as the quotient between peak and baseline GFR. Variation of the eGFR by 30% from baseline was considered as a positive test or sufficient KFR meanwhile less than 30% was a negative one. Log-rank test was used to compare FKR test results. The Kaplan Meier product-limit estimator was used and the survival curves, showing the response to the previously performed renal reserve study were compared using the log-rank test. P-values < 0.05 were accepted as statistically significant. All data is expressed as media± SD.

Results: Both groups (GS and TIS) were homogeneous about demographic characteristics at baseline. Pre PO media GFR (ml/min) was similar in GS and TIS (100.6 ± 11.4 and 99.5 ± 10.8; respectively). GFR rose after PO to a peak of 135 ±22.0 and to 125 ±27.5 ml/min in GS and TIS groups respectively. The FKR index was lower in TIS than in GS and CG (1.22 0.04 and 1.42 0.06 respectively (p-value < 0.05). Time to the CE was 136.4 ±14 months in pts showing a positive test versus 89.9 ± 19 months in those with a negative test. (P-value < 0.05).

Conclusions: The results from this study suggest that in LN patients the presence of tubulo-interstitial damage drastically reduces the renal response to a protein overload in contrast with the almost normal response obtained in patients with predominant glomerular involvement. This lack of response to a protein overload is related to poor long-term evolution. The assessment of the functional kidney reserve may help to balance the decision whether to start/continue /enhance immunosuppression in those patients with kidney sclerosis.

PV128a / #66

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

CLINICAL CHARACTERISTICS AND OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WITH LUPUS NEPHRITIS: A SINGLE CENTER LONGITUDINAL STUDY FROM THE UNITED ARAB EMIRATES

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Background/Purpose: Lupus nephritis (LN) is a common manifestation of systemic lupus erythematosus (SLE), with 10–30% of patients progressing to end-stage renal disease (ESRD) and requiring hemodialysis (HD) [1]. Kidney transplantation (KT) is also a treatment option; however, long-term graft survival remains controversial [2]. The aim of this study is to evaluate the clinical characteristics of patients with LN who undergo KT, assess the disease course from SLE/LN diagnosis to KT, and estimate graft survival within a cohort from the United Arab Emirates (UAE).

Methods: Between April 2015 and April 2024, patients with LN who underwent KT were retrospectively studied at Cleveland Clinic Abu Dhabi. Data collected included sociodemographic information, clinical characteristics, laboratory investigations, lupus domain involvement, baseline KT variables, post-transplant complications, the timeline from SLE/LN diagnosis to KT, and immunosuppressive therapies. Descriptive statistics were used to analyze the data.

Results: Our database identified 37 patients with LN, of whom 26 were KT recipients, 4 were undergoing KT evaluation, and 7 were actively on the KT waitlist. The patients were predominately UAE nationals (94.59%), with 31 (83.78%) females and 6 (16.22%) males. The mean age of SLE diagnosis was 23.75 ± 11.80 years (mean ± SD), the mean age of LN diagnosis was 24.24 ± 9.13 years, and the mean age at HD initiation at 32.55 ± 11.43 years. The most common lupus domains involved were musculoskeletal (45.94%), seizures (18.92%), followed by oral ulcers (13.51%). The most common LN class was Class IV affecting 10 (27.03%) patients. Investigations revealed positive ANA in 23 patients (62.12%), positive anti-Smith in 7 (18.92%), a mean CRP of 26.58 ± 50.08 mg/L, a mean ESR of 43.59 ± 33.28 mm/hr, a mean C3 of 91.80 ± 38.21 mg/dL, and a mean C4 of 26.48 ± 14.63 mg/dL. Additionally, the mean dsDNA at clinic presentation and prior to KT were 23.59 ± 55.27 IU/mL and 11.89 ± 14.26 IU/mL, respectively (Table 1). Of those who underwent KT, 12 (46.15%) received a living donor kidney, while 10 (38.46%) received a deceased donor kidney. The mean age at KT was 32.35 ± 12.64 years, with an

average follow up of 91.77 ± 97.32 months. Post-transplant complications included re-transplantation in 3 (8.11%) patients, graft rejection in 7 (18.92%) patients, and death in 1 (2.7%) patient. Notably, there was an average time interval of 9.65 ± 6.66 years from LN diagnosis to KT, and 1.80 ± 7.59 years from HD initiation to KT. Regarding immunosuppressive medications, the majority of patients had a history of prednisone use, with 28 (75.68%) having used it previously and 31 (83.78%) currently using it. Additionally, mycophenolate mofetil was administered to 32 (86.49%) patients, tacrolimus to 24 (64.86%) patients, and hydroxychloroquine to 15 (40.54%) patients (Table 2).

Sociodemographic features of KT cohort	(n = 37)
UAE national, n (%)	35 (94.59)
Gender	
Female, n (%)	31 (83.78)
Male, n (%)	6 (16.22)
BMI, mean ± SD	26.39 ± 7.18
Age at time of initial symptoms, mean ± SD years	22.09 ± 11.02
Age at time of clinic presentation, mean ± SD years	35.46 ± 10.89
Age at time of SLE diagnosis, mean ± SD years	23.75 ± 11.80
Age at time of LN diagnosis, mean ± SD years	24.24 ± 9.13
Age at HD, mean ± SD years	32.55 ± 11.43
Laboratory investigations in KT cohort	
ANA, n (%)	23 (62.12)
Anti-Smith, n (%)	7 (18.92)
APS, n (%)	9 (24.32)
ESR, mean ± SD mm/hr [normal range: 2 – 37 mm/hr]	43.59 ± 33.28
CRP, mean ± SD mg/L [normal range: 0.0 – 4.9 mg/L]	26.58 ± 50.08
dsDNA at baseline, mean ± SD IU/mL [normal range: <4 IU/mL]	23.59 ± 55.27
dsDNA prior to KT, mean ± SD IU/mL [normal range: <4 IU/mL]	11.89 ± 14.26
C3, mean ± SD mg/dL [normal range: 82 – 167 mg/dL]	91.80 ± 38.21
C4, mean ± SD mg/dL [normal range: 14 – 44 mg/dL]	26.48 ± 14.63
Lupus domain involvement in KT cohort	
Photosensitivity, n (%)	4 (10.81)
Cutaneous lupus	4 (10.81)
Acute, n (%)	2
Subacute, n (%)	1
Discoid, n (%)	1
Raynaud's phenomenon, n (%)	3 (8.11)
Oral ulcers, n (%)	5 (13.51)
Musculoskeletal, n (%)	17 (45.94%)
Vasculitis, n (%)	3 (8.11)
Ocular involvement, n (%)	3 (8.11)
Autoimmune hepatitis, n (%)	0 (0)
Cardiac involvement, n (%)	4 (10.81)
Lung involvement, n (%)	4 (10.81)
PAH, n (%)	2 (5.41)
Seizures, n (%)	7 (18.92)
CNS lupus, n (%)	2 (35)

Table 1. Sociodemographic data, laboratory investigations, and lupus domains of KT patients with

Baseline KT variables	(n = 37)
Kidney biopsy performed, n (%)	25 (67.57)
Class I, n (%)	0 (0)
Class II, n (%)	1 (2.70)
Class III, n (%)	3 (8.11)
Class IV, n (%)	10 (27.03)
Class V, n (%)	3 (8.11)
>1 class, n (%)	1 (2.70)
Unknown class, n (%)	7 (28)
Undergoing transplant evaluation, n (%)	4 (10.81)
Actively on transplant waitlist, n (%)	7 (18.92)
KT recipient, n (%)	26 (70.27)
KT donor type	
Living donor, n (%)	12 (46.15)
Deceased donor, n (%)	10 (38.46)
Unknown donor type, n (%)	4 (15.38)
Age at KT, mean ± SD years	32.35 ± 12.64
Duration post-transplant, mean ± SD months	91.77 ± 97.32
Post-transplant complications	
Re-transplantation, n (%)	3 (8.11)
Graft rejection, n (%)	7 (18.92)
LN recurrence, n (%)	0 (0)
Death, n (%)	1 (2.70)
Timeline from SLE diagnosis to KT	
SLE diagnosis → LN diagnosis, mean ± SD years	1.97 ± 4.41
LN diagnosis → HD initiation, mean ± SD years	7.43 ± 6.02
LN diagnosis → KT, mean ± SD years	9.65 ± 6.66
HD initiation → KT, mean ± SD years	1.80 ± 7.59
Immunosuppressive therapies	
Prednisone	
Previous prednisone use	28 (75.68)
Current prednisone use	31 (83.78)
Initial prednisone dose, mean ± SD mg	21.33±23.86
Hydroxychloroquine	15 (40.54)
Methotrexate	1 (2.70)
Leflunomide	0 (0)
Mycophenolate mofetil	32 (86.49)
Cyclophosphamide	7 (18.92)
Rituximab	7 (18.92)
Cyclosporin	3 (8.11)
Tacrolimus	24 (64.86)
Anifrolumab	0 (0)

LN Table 2. Baseline KT-related variables, post-transplant complications, diagnostic time intervals, and immunosuppressive therapies of KT patients with LN

Conclusions: This study highlights the clinical profile and treatment outcomes of UAE patients with lupus nephritis undergoing kidney transplantation. The findings reveal significant time intervals from diagnosis to transplantation and initiation of hemodialysis. Despite high use of immunosuppressive medications, post-transplant

complications, including graft rejection and the need for re-transplantation, remain notable. These results emphasize the importance of tailored management approaches and continued monitoring to enhance patient outcomes in this unique cohort.

PV129 / #332

Poster Topic: *AS15 - Lupus Nephritis-Clinical*

RESPONSE TO PLACEBO IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS: A SYSTEMATIC REVIEW AND POOLED ANALYSIS

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Background/Purpose: Lupus Nephritis (LN) may result in end-stage kidney disease (ESKD) in up to one-third of the patients 10 years after diagnosis. Most randomized controlled trials (RCTs) have failed to demonstrate the superiority of biologic drugs over standard-of-care (SoC). The aim of this systematic review was to quantify the response to placebo (and SoC) in patients with active LN.

Methods: Systematic review (2020 PRISMA statement). PubMed database was searched (01/2000-09/2024) for phase II/III RCTs of biologics in LN. The primary end-point was complete renal response (CRR, proteinuria <0.5 g/day and serum creatinine <120% from baseline at 48-52 weeks. Secondary end-points were partial (PRR, 50% improvement in proteinuria and serum creatinine <120% from baseline at 48-52 weeks) and overall renal response (CRR + PRR). The expected and actual differential responses were also recorded. Descriptive statistics were used.

Results: A total of 10 RCTs (n=2318 in total) were included with 1006 patients treated with placebo and SoC. Baseline characteristics are shown in Table 1. CRR was achieved by 176/660 patients (26.7%), and PRR was achieved by 146/527 patients (27.7%) (Figure 1A). The expected differential response rate was 20%; the actual differential response rate was 7.5% (Figure 1B). Safety: infections 46.4%, serious infections 12%, malignancies 0.2% , deaths 2.88%.

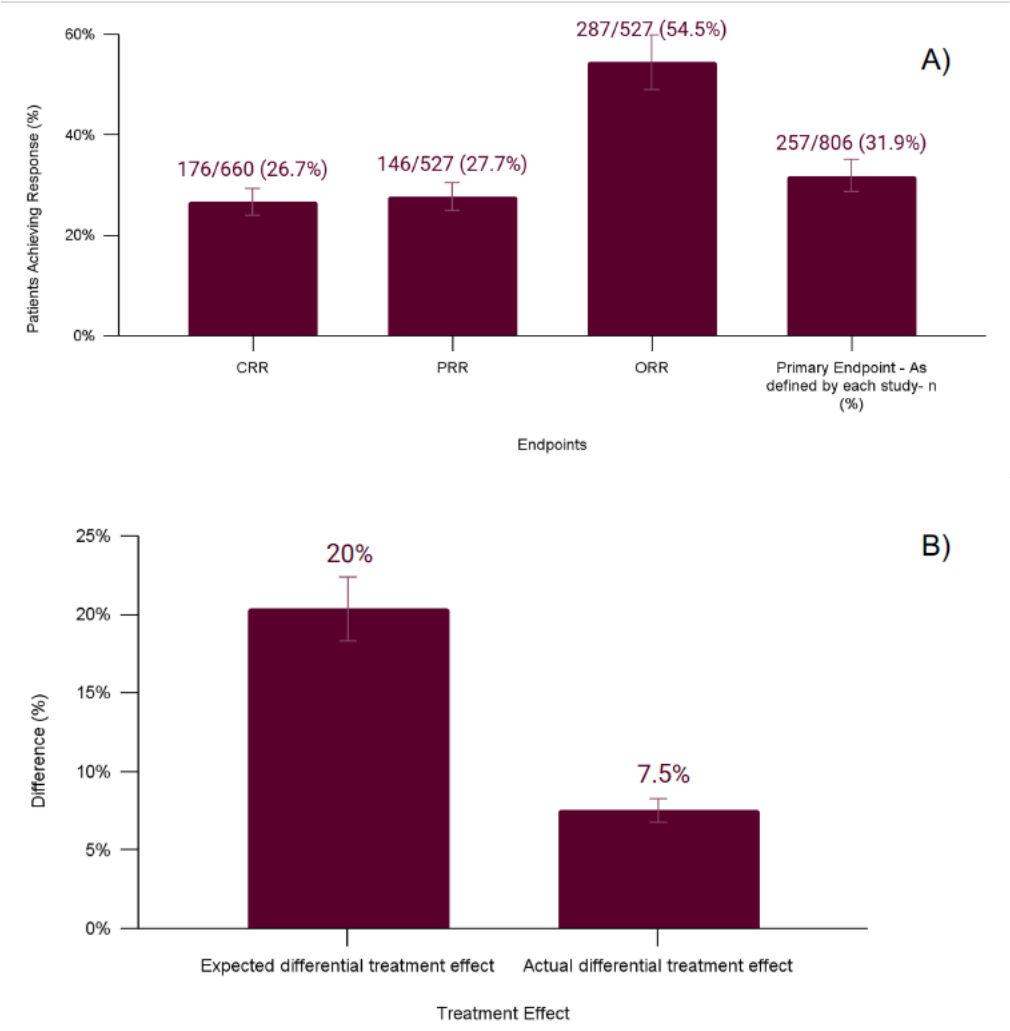
Table 1. Baseline characteristics of the placebo (+ SoC) treated patients

Variable	N	(%) or SD
Total patients - n	1006*	
Females - n (%)	867/1006	86.2%
Mean Age - years (+/- SD)	32.1	1.23
Mean Disease Duration - months (+/- SD)	29.0	20.8

Race		
White / Caucasians - n (%)	405/1006	40.3%
Asian - n (%)	326/1006	32.4%
Black / African-American - n (%)	117/1006	11.6%
Hispanic - n (%)	23/1006	2.3%
American Indian - n (%)	40/1006	4.0%
Other - n (%)	95/1006	9.4%
Renal and disease characteristics		
Class III - n (%)	256/980	26.1%
Class IV - n (%)	457/980	46.6%
Class V - n (%)	71/980	7.2%
Class III or IV + V - n (%)	196/980	20.0%
eGFR - mL/min per 1.73m2 (+/- SD)	90.5	14.3
Serum Creatinine - mg/dL (+/- SD)	0.93	0.20
UPCR - mg/mg (+/- SD)	3.73	0.54
Elevated dsDNA - n (%)	538/767	70.1%
Low C3 - n (%)	435/692	62.9%
Low C4 - n (%)	247/692	35.7%
SLEDAI-2K (+/- SD)	11.5	0.61
Therapeutic characteristics		
Treated with MMF - n (%)	800/955	83.8%
Treated with CYC - n (%)	155/955	16.2%
Prednisone (oral) - n (%)	955/955	100.0%
IV Pulse glucocorticoids - n (%)	609/664	91.7%
Antimalarials - n (%)	232/360	64.4%
ACEis/ARBs - n (%)	445/678	65.6%

eGFR: estimated glomerular filtration rate, UPCR: urine protein-to-creatinine ratio, MMF: mycophenolate mofetil, CYC: cyclophosphamide, ACEIs: angiotensin-converting enzyme inhibitors, ARBs: angiotensin receptor blockers * Some outcome data was not reported for 51 patients from the ocrelizumab trial.

Figure 1. A. Complete (CRR), partial (PRR), overall (ORR) renal response and percentage of patients achieving the primary endppoint of each study at 48-52 weeks. **B.** Expected and actual differential treatment effect.



Conclusions: Approximately 27% of the placebo (+SoC)-treated patients achieved complete renal response while more than half of them achieved an overall (CRR+PRR) renal response at 48 to 52 weeks in RCTs with biologics in LN. There was a significant discrepancy between the expected and actual differential treatment effect that raises significant points to consider for the design of future studies.

PV130 / #54

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

RISK FACTORS FOR DE NOVO LUPUS NEPHRITIS IN NON-RENAL SLE PATIENTS TREATED WITH AZATHIOPRINE

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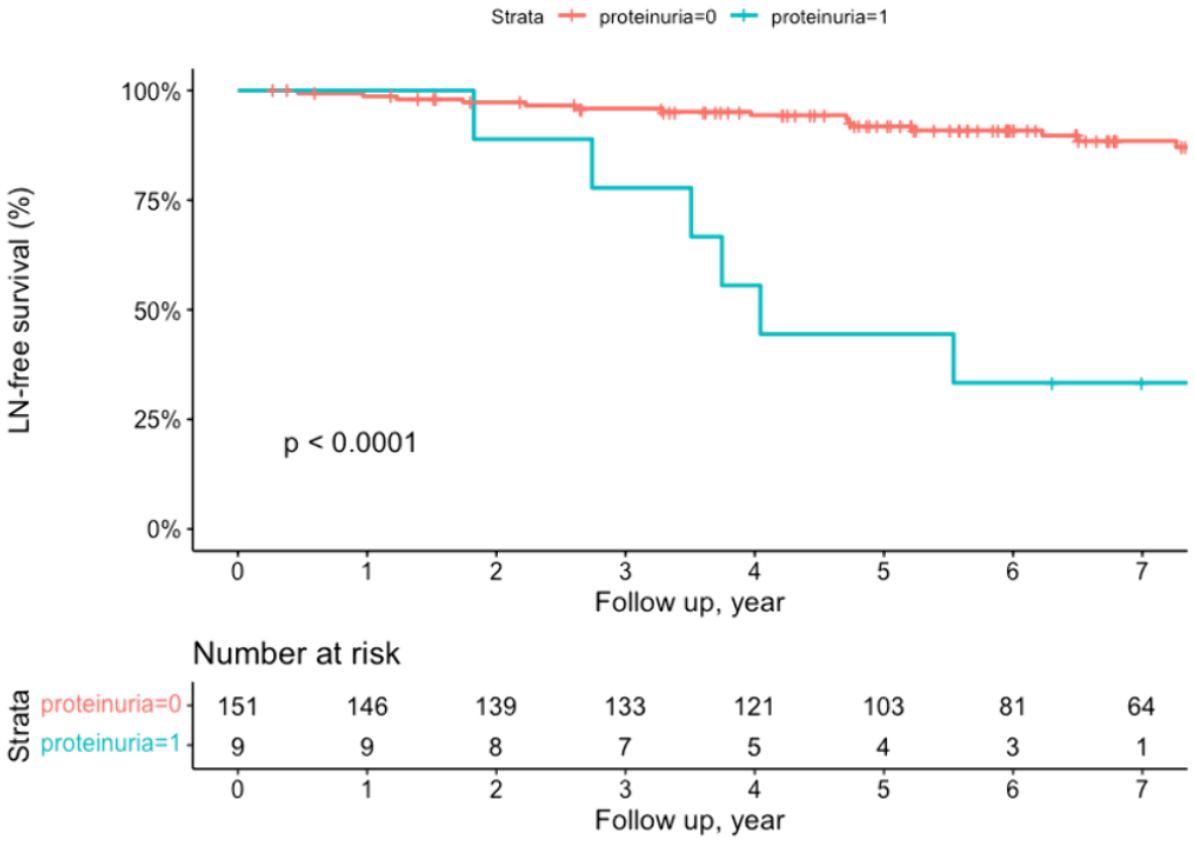
Background/Purpose: Lupus nephritis (LN) is one of the most common, potentially organ-threatening, and even fatal complications for patients living with systemic lupus erythematosus (SLE). The initial signs of lupus nephritis include persistent proteinuria > 0.5 g daily, microscopic hematuria with or without erythrocyte dysmorphism, cellular casts, and new-onset hypertension. The risk factors (e.g., active extra-renal disease, male sex, smoking, and history of renal diseases) for LN were identified. Azathioprine (AZA) had been widely used for non-renal SLE and is one of the standard-of-care options for maintenance therapy for lupus nephritis. However, lupus nephritis develops even in patients already on immunosuppression. In this study, we attempted to identify the baseline risk factors for new LN flares in SLE patients receiving AZA for non-renal SLE.

Methods: In this retrospective, multi-center study, we identified SLE patients treated with azathioprine for non-renal manifestations. Individuals with previous or active LN at the AZA initiation were excluded. The demographics, systemic lupus erythematosus disease activity index-2K (SLEDAI-2K), and transient proteinuria with UPCR > 0.5 g/g for less than 1 month were identified. The LN flares were defined as either persistent proteinuria with UPCR > 0.5 g/g for 2 consecutive visits for more than 1 month or LN diagnosed on renal biopsy. The prognostic values of baseline SLEDAI score, serology (positive anti-dsDNA and low complement levels), active disease by organ domains, and transient proteinuria were analyzed.

Results: From 2006 to January 2023, 160 eligible patients were included in the analysis. 88% were female and the median age at enrollment was 37 (29-48) years. 96.9% patients received hydroxychloroquine concomitantly, and all were taking glucocorticoids. The SLEDAI score was 7.5 (4.0-11.0), and 5.6% patients had transient proteinuria at the time of AZA initiation. The median follow-up time was 6.1 (4.4-9.3) years. Through the observation period, LN flare occurred in 16% patients. The median time to LN flare was 4.4 (2.6-6.4) years. The LN flared patients had higher baseline SLEDAI score (10.5 vs. 6.0, $p = 0.002$), mucocutaneous disease (69% vs. 43%, $p = 0.015$), and transient proteinuria (27% vs. 1.5%, $p < 0.001$). The transient proteinuria at

baseline was associated with decreased LN-free survival (Figure). On multivariable analyses, mucocutaneous (HR 2.88, p = 0.015), vasculitis (HR 6.81, p < 0.001), and transient proteinuria (HR 11.3, p < 0.001) were independent risk factors for LN flares. (Table)



Univariable and multivariable Cox regression analysis of baseline predictors for LN flare

Risk factors	**Univariable**			**Multivariable**		
	HR	95% CI	p-value	HR	95% CI	p-value
SLEDAI score	1.18	1.09-1.29	< 0.001			
Serological	2.67	0.62-11.5	0.13			
Mucocutaneous	3.22	1.39-7.46	0.004	2.88	1.23-6.73	0.015
Musculoskeletal	1.78	0.82-3.86	0.14			
Hematological	0.61	0.26-1.47	0.3			
Cardiopulmonary	1.35	0.32-5.77	0.7			

Univariable and multivariable Cox regression analysis of baseline predictors for LN flare

Risk factors	Univariable			Multivariable		
Vasculitis	4.30	1.46-12.7	0.025	6.83	2.18-21.3	< 0.001
NPSLE	0.34	0.05-2.51	0.2			
Transient proteinuria	10.3	4.14-25.4	< 0.001	11.3	4.34-29.3	< 0.001

Conclusions: In non-renal SLE patients treated with AZA, lupus nephritis flares were not uncommon. The baseline SLEDAI score, mucocutaneous disease, and vasculitis were associated with lupus nephritis development. The transient, low-level proteinuria was a strong predictor for lupus nephritis. Although low level proteinuria might not be leading to renal biopsy, close monitoring and prompt diagnostic workup should be considered even in patients under immunosuppression.

PV131 / #261

Poster Topic: *AS15 - Lupus Nephritis-Clinical*

SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF INDUCTION TREATMENTS FOR LUPUS NEPHRITIS

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Background/Purpose: This study aims to evaluate the comparative efficacy and safety of various initial treatments for lupus nephritis through a systematic review and network meta-analysis.

Methods: A comprehensive literature search was conducted across MEDLINE, EMBASE, Cochrane Library, and LILACS from inception to June 2024 in order to identify randomized controlled trials (RCTs) comparing initial treatments for lupus nephritis. Two reviewers independently performed data extraction and assessed the risk of bias. A frequentist random-effects network meta-analysis was conducted using the restricted maximum likelihood (REML) method to estimate heterogeneity. The certainty of evidence was evaluated using the GRADE approach.

Results: We included 38 RCTs encompassing 5,146 participants and 11 interventions. Mycophenolate mofetil was selected as the common comparator. The network meta-analysis revealed that voclosporin combined with Mycophenolate mofetil (RR 1.9 95% CI 1.47 to 2.47, RD 281.4, 95% CI 146.3 to 465.4; high certainty) and belimumab combined with Mycophenolate mofetil (RR 1.47, 95% CI 1.23 to 1.74, RD 145, 95% CI 72.7 to 230.9; high certainty) increased complete renal response compared to Mycophenolate mofetil alone. Tacrolimus combined with Mycophenolate mofetil (RR 1.24 95% CI 1.05 to 1.46, RD 113.7, 95% CI 25.2 to 217.7; low certainty) and Obinutuzumab combined with Mycophenolate mofetil (RR 1.57 95% CI 1.05 to 2.34, RD 270.4, 95% CI 22.7 to 640.5; low certainty) also showed potential benefits but with low certainty evidence. Cyclophosphamide was possibly associated with a small decrease in complete renal response compared to Mycophenolate mofetil (RR 0.90, 95% CI 0.77 to 1.04; low certainty). However, the effects of the assessed interventions on mortality and renal replacement therapy outcomes were highly uncertain.

Conclusions: Combination therapies, particularly voclosporin or belimumab with Mycophenolate mofetil, may provide enhanced outcomes for lupus nephritis initial treatment. Given the complexity of lupus nephritis, clinicians should weigh these findings alongside considerations such as drug availability, cost, and individual patient preferences to guide treatment decisions.

PV132 / #416

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

DISPARITIES IN OUTCOMES OF PATIENTS WITH LUPUS NEPHRITIS BASED ON AREA DEPRIVATION INDEX: A RETROSPECTIVE ANALYSIS

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Background/Purpose: Lupus nephritis (LN) is a significant complication of systemic lupus erythematosus, with varying histological classifications influencing treatment strategies and outcomes. Living in a disadvantaged neighborhood has been linked to several healthcare outcomes, including higher rates of diabetes and cardiovascular disease, increased utilization of health services, and earlier death. This study aims to compare clinical and laboratory outcomes at the time of biopsy and 12 months post-biopsy in patients with LN classified as class III, III/IV, IV, IV/V, and III/V based on area deprivation index (ADI).

Methods: A total of 95 patients were retrospectively identified who had undergone kidney biopsy from June 1st, 2016 until December 19th, 2023, at Houston Methodist Hospital. From these patients, those who did not have a follow-up visit or labs 12 months after biopsy were excluded. The remaining 62 were placed in 3 different categories by Area Deprivation Index (ADI), constructed from variables such as education, income, employment status, housing, and household characteristics to assess the level of neighborhood deprivation with higher numbers indicating more socioeconomic disparity. The categories were as follows; 1-39 (low), 40-69 (middle), 70-100 (high). The clinical characteristics were manually documented from the electronic medical record.

Results: Of the 62 patients, 25 (40.3%) patients were in the low, 24 (38.7%) in the middle, and 13 (21.0%) patients were in the high range. Demographic distribution and other characteristics are as described in table
1.

	Low ADI (1-39)	Middle ADI (40-69)	High ADI (70-100)
Asian	7 (28%)	2 (8.3%)	0 (0%)
Black	10 (40%)	13 (54.1%)	5 (38.4%)
Hispanic/Latino	2 (8%)	4 (16.6%)	4 (30.8%)
White	6 (24%)	5 (21%)	4 (30.8%)
Female	22 (88%)	18 (75%)	10 (76.9%)
Age (average)	40.4 (SD=13.0)	38.1 (SD=10.4)	36.5 (SD=16.4)
Obese BMI >30	6 (24%)	13 (54.2%)	7 (54.8%)
Active tobacco use	2 (8%)	3 (12.5%)	1 (7.7%)

Table 1: Demographic, anthropometric, and social history of patients.

Serologies	Low ADI (1-39)	Middle ADI (40-69)	High ADI (70-100)
Anti-smith	8 (32.0%)	7 (29.2%)	9 (69.2%)
RNP	8 (32.0%)	7 (29.2%)	6 (46.2%)
SSA	10 (40.0%)	6 (25.0%)	9 (69.2%)
SSB	2 (8.0%)	1 (4.2%)	3 (23.1%)
SSA/SSB	2 (8.0%)	1 (4.2%)	2 (15.4%)

Table 2: The number of patients in each ADI group with positive serologies. The serologies of the patients in each of the 3 ADI groups are presented in table 2. 4 (16.0%) patients in the high, 0 (100%) in the middle, and 2 (15.4%) met the laboratory criteria for antiphospholipid syndrome (positive lupus anticoagulant and/or moderate-high titer of anti-cardiolipin or anti-b2-glycoprotein antibody). The laboratory findings noted in each ADI group are discussed in table 3 looking at values at the time of biopsy and 12 months

after. Those in the higher ADI group, on average, had higher SLEDAI scores, higher creatinine, lower eGFR, and higher UPCR at the time of biopsy. These differences were noted at the 12-month mark after biopsy as well. Finally, it also appears that the middle ADI group has higher rates of obesity and smoking and perhaps, given this lifestyle, is experiencing worse outcomes, as their SLEDAI scores do not improve as much as others and eGFR and proteinuria worsen. They also are more likely to be on dialysis before and after biopsy.

	Month	C3	dsDNA	C4	WBC	Hgb	Platelets	Cr	eGFR	UPCR mg/mg	24 h protein	SLEDAI score	HD
	0	67.3 (SD=29.6)	14 (56%)	10.2 (SD=5.4)	6.8 (SD=3.3)	10.5 (SD=2.1)	242.3 (SD=93.8)	1.5 (SD=0.9)	59.5 (SD=27.2)	2.4 (SD=2.6)	5.7 (SD=6.2)	11.9 (SD=5.9)	0 (0.0%)
Low	12	98.6 (SD=37.2)	7 (28%)	22.5 (SD=17.5)	6.0 (SD=2.8)	10.7 (SD=1.6)	261.6 (SD=88.5)	1.6 (SD=1.1)	65.7 (SD=37.4)	1.6 (SD=2.0)	1.9 (SD=1.0)	5.0 (SD=3.8)	2 (8.0%)
	0	64.2 (SD=31.7)	10 (41.6%)	16.7 (SD=16.4)	5.9 (SD=4.4)	20.5 (SD=53.8)	191.1 (SD=75.7)	2.3 (SD=1.9)	42.2 (SD=27.8)	2.6 (SD=2.4)	1.3 (SD=0.9)	14.4 (SD=11.4)	5 (20.8%)
Mid	12	86.9 (SD=32.3)	6 (25%)	24.8 (SD=20.5)	5.5 (SD=2.5)	10.1 (SD=1.9)	234.6 (SD=79.7)	2.3 (SD=1.8)	51.9 (SD=35.3)	3.9 (SD=5.8)	3.7 (SD=3.0)	11.9 (SD=5.9)	7 (29.2%)
	0	74.8 (SD=27.7)	7 (53.8%)	17.9 (SD=12.8)	6.7 (SD=4.8)	12.5 (SD=1.4)	229.4 (SD=68.7)	2.2 (SD=1.2)	41.5 (SD=19.4)	3.3 (SD=3.0)	5.2 (SD=4.5)	16.3 (SD=8.1)	2 (15.4%)
High	12	98 (SD=30.1)	3 (23.1%)	23.5 (SD=10.4)	6.8 (SD=2.8)	9.9 (SD=1.7)	294.0 (SD=92.7)	2.2 (SD=3.1)	44.3 (SD=28.9)	1.9 (SD=1.6)		5.6 (SD=7.0)	4 (30.7%)

Table 3: The average laboratory findings comparing the 3 ADI groups at the time of biopsy and 12 months afterwards. (HD: hemodialysis, Cr: creatinine, Hgb: hemoglobin, WBC: white blood count, eGFR: estimated glomerular filtration rate)

Conclusions: This study highlights the crucial impact of socioeconomic factors, measured by the area deprivation index, on LN outcomes. Patients in disadvantaged areas face significant challenges, leading to worse initial presentations and results. Notably, middle-ADI individuals may need more lifestyle modifications, which could improve their proteinuria, eGFR, SLEDAI scores, and decrease the likelihood of requiring hemodialysis. These findings underscore the urgent need for targeted interventions that address socioeconomic disparities and promote lifestyle changes in LN patients.

PV133 / #80

Poster Topic: ***AS15 - Lupus Nephritis-Clinical***

VOCLOSPORIN WAS EFFECTIVE AND SAFE IN TREATING LUPUS NEPHRITIS, ALSO IN PATIENTS WHO HAD PREVIOUSLY FAILED OTHER IMMNOSUPPRESSANTS AND BIOLOGICS. A SINGLE CENTER REAL-WORLD EXPERIENCE.

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Background/Purpose: Voclosporin, a new calcineurin inhibitor, has demonstrated efficacy in clinical trials, but real-world data on its use are limited. Our aim was to evaluate the effectiveness of voclosporin in combination with MMF in reducing proteinuria and preserving renal function in patients with lupus nephritis (LN). In addition, to evaluate its safety in a real-world setting.

Methods: This retrospective analysis of perspectively collected data included patients with LN treated with voclosporin at a single center. Clinical and laboratory data, including 24-hour proteinuria, estimated glomerular filtration rate (eGFR), and prednisone dose, were collected at baseline and at 2, 4, 6, and 9 months of follow-up. Complete renal response (CRR) was defined as 24-hour proteinuria <0.5 g/day, stable or improved renal function (eGFR), and inactive urinary sediment.

Results: Eight patients were included: median age 44 years (IQR 28.7-48.7), mean disease duration 11.6±6.9 years, 62.5% Caucasians, 62.5% class IV LN, 37.5% combination of class IV and V LN. Most patients had previously failed MMF as induction therapy (87.5%), with some also failing belimumab (62.5%), rituximab (37.5%), or tacrolimus (Table 1). After voclosporin initiation, the mean 24-hour proteinuria decreased from 2.3±0.74 g at baseline to 1.0±0.72 g at 2 months, 0.64±0.52 g at 4 months, 0.47±0.36 g at 6 months, and 0.47±0.22 g at 9 months. A ≥50% reduction in proteinuria was observed in 71.5% of patients at 2 months, and 100% at 6 months. Proteinuria <0.5 g/24-hour was achieved as early as at month 2 in 71.4% of patients. CRR was achieved in 66% of patients at 6 months and in 75% at 9 months. Renal function remained stable with no significant changes in eGFR. Prednisone was tapered to a mean of 5 mg/day at 4 months and 2.5 mg/day at 6 months. No adverse events were reported, including no significant worsening of comorbidities, including pre-existent hypertension (3 cases), dyslipidemia (2 cases) or diabetes (1 case). Table 1.Characteristics of the 8 patients treated with voclosporin from November 2023 to October 2024.

Age	Sex	Class of LN	Clinical features	Previous therapies	Last therapy before VOC*	Duration of last flare	Baseline 24h prot & eGFR	24h prot at 2 mts	24h prot & eGFR at 4 mts	24h prot at 6 mts	24h prot & eGFR at 9 mts
44	F	IV	antiDNA+, C3 ↓, no active sediment	AZA, MMF, CYC, RTX, MMF+Bel	MMF 1g+TAC	48 months	2.80 g eGFR 77	1.80 g	1.60 g eGFR 80	0.89 g	0.78 g eGFR 78
51	M	IV	antiDNA+, C3 ↓, active sediment	MMF, MMF+TAC	CsA	1 months	1.41 g eGFR 101	0.22 g	0.20 g eGFR 100	0.13 g	0.51 g eGFR 100
21	M	IV	antiDNA+, C3/C4 ↓, active sediment	MMF, MMF+Bel	MMF 2g+RTX	10 months	2.50 g eGFR >90	0.89 g	0.68 g eGFR >90	0.32 g	0.25 g eGFR >90
29	M	IV/V	antiDNA+, C3/C4 ↓, no active sediment	MMF+Bel	MMF 2g+Bel	18 months	2.05 g eGFR>90	0.44 g	0.45 g eGFR>90	0.40 g	0.38 g eGFR>90
63	M	IV/V	antiDNA+, active sediment	Bel+MTX, MMF	MMF 3g	12 months	2.40 g eGFR 98	1.16 g	1.08 g eGFR 102	0.95 g	-
48	F	IV	antiDNA-, C3/C4 ↓, active sediment	-	-	New onset LN	3.60 g eGFR 84	2.2 g	0.341 g eGFR 82	-	-
28	M	IV/V	antiDNA+, no active sediment	AZA, MMF, ABA (trial), CYC, RTX MMF+Bel,	MMF 2g+RTX (II cycles)	24 months	1.4 g eGFR >90	0.6 g	0.18 g eGFR >90	0.15 g	-
32	F	IV	antiDNA-, GR	MMF	MMF 2g	6 months	1.8 g eGFR >90	-	-	-	-

*all patients were also on renin angiotensin system inhibitors and 7/8 were on hydroxychloroquine.

VOC, voclosporin, AZA: azathioprine, MMF: mycophenolate mofetil, CYC: cyclophosphamide, RTX, rituximab, Bel: belimumab, TAC: tacrolimuse, ABA: abatacept, CsA; cyslosporin A, GFR: for some patients, eGFR within the normal range was expressed as ">90 ml/min" by local lab.

Conclusions: Voclosporin in combination with MMF was effective in reducing proteinuria and preserving renal function in LN patients, even in those who have failed prior therapies. The treatment was well tolerated and allowed for significant corticosteroid tapering, supporting its use in clinical practice as a valuable option for managing lupus nephritis.

PV134 / #630

Poster Topic: *AS16 - Lupus Nephritis-Pathogenesis*

INTRACYTOPLASMIC TOLL- LIKE RECEPTORS (TLR) 7, 9 AND MYD88 IN PERIPHERICAL B CELL SUBSETS AS A PREDICTOR OF RENAL RESPONSE IN PATIENTS WITH LUPUS NEPHRITIS

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Background/Purpose: A gain of-function mutation within TLR7 was identified in a SLE murine model and increased the survival of B lymphocytes, age associated B cells (ABCs), extrafollicular B lymphocytes and autoantibodies production, mediated by MyD88. The aim of this study is to analyze the role of TLR7, 9 and MyD88 expression in diverse B cell subsets as renal response predictors in patients with lupus nephritis.

Methods: We included SLE patients who fulfilled the ACR/EULAR 2019 classification criteria and active proliferative LN (Class III or IV +/- V). A blood sample was taken at baseline and 6 months after induction treatment. Treatment with anti-CD20 drugs or IVIg were excluded. The outcome was the renal response. We measured the expression of TLR7, 9 and MyD88 in the B cell subsets: ABCs [$CD19^{pos}CD21^{neg/lo}$ $CD11c^{hi}$ $Tbet^{pos}$], antibody-secreting cells (ASC) [$CD19^{pos}$ $CD27^{hi}$ $CD38^{hi}$], classic memory cells (CMC) [$CD19^{pos}$ $CD27^{pos}$ IgD $^{pos/neg}$], double negative cells (DNC) [$CD27^{neg}$ IgD ^{neg}], naive cells (NC), non-classic memory cells (NCMC) [CD27 ^{neg}] and transitional cells (TrC) [CD21 $^{neg/lo}$]) from a peripheral blood sample, using a BD LSR Fortessa flow cytometer and FlowJo software. We quantified the absolute numbers and percentage of TLR7, TLR9, and MyD88, alongside determining the mean fluorescence intensity (MFI). Spearman correlation coefficient was used with quantitive variables. Wilcoxon signed-rank test was used to analized variables before and after treatment. A logistic regression was used to addres association between TLRs and MyD88 expresion and renal response.

Results: 66% of 30 patients reached renal response. These, presented a lower expression of TLR7 in NC (MFI, 573 (498-792) vs 759 (544-873), $p<0.05$) and expansion of TLR9+ NCMC (1.4% (0.7-2.5) vs 0.3% (0.3-0.4), $p<0.05$) (Table 1). At follow up, we observed an expansion of TLR9+ B cells (8.1% (2.6-15) vs 0.5% (0.2-0.6), $p<0.05$); TLR9+

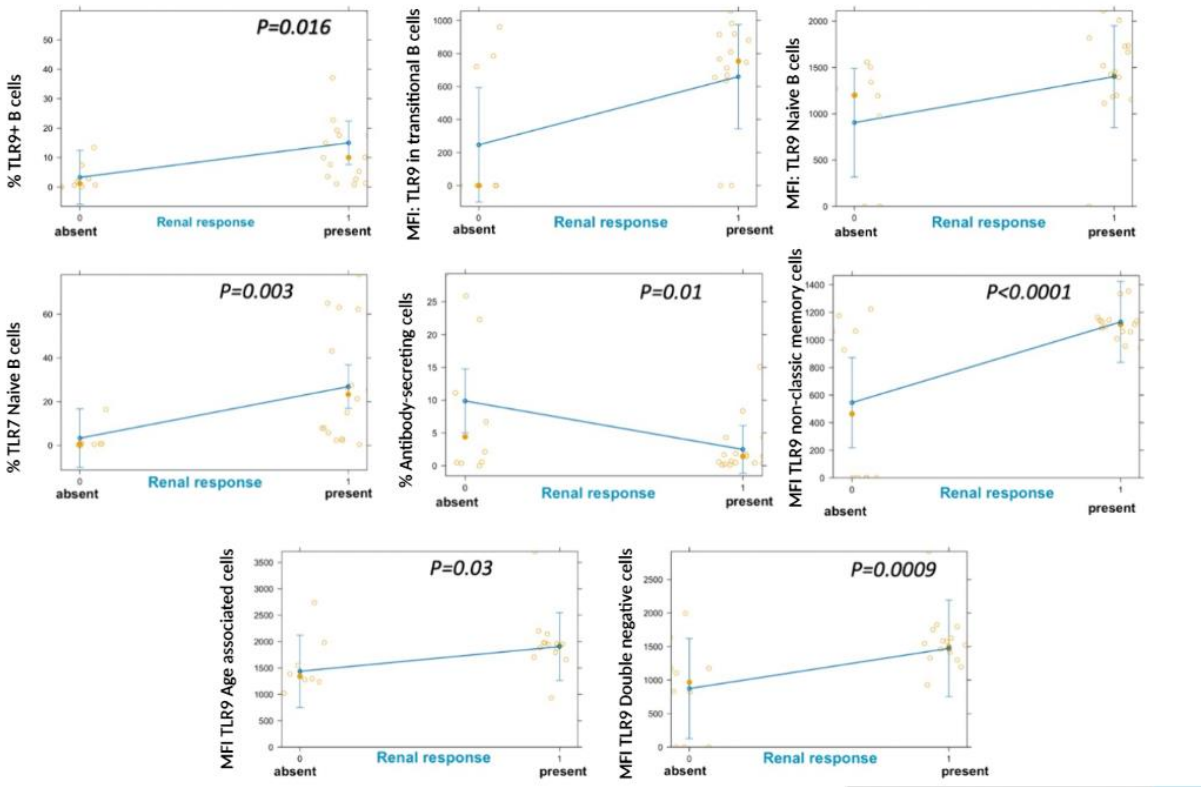
TrC (MFI, 747 (537-767) vs 0 ((0.0-0.0), p<0.05); TLR7+ TrC (23% (11.1-44.5) vs 0 %(0.0-0.2), p<0.05); TLR7+ NC (27.4 %(7.9-63) vs 0.3 %(0.0-0.4); TLR9+ NCMC (MFI, 1128 (1006-1135) vs 0 (0.0-0.0), p<0.05); classical TLR9+ B cells (1.9 (1.1-3.2) vs 0.07 (0.02-0.09), p<0.05), and a decreased TLR9+ ABCs (0.8 % (0.4-24.4) vs 13% (2.4-67), p<0.05) (Table 2). Table 1. Comparison of B cells at baseline in patients who reached renal response and those who did not.

	Absent Renal Response	**Renal response present**	
B Cells	**Median**	**Median**	***p***
TLR7+ naive B cells (MFI)	759 (544-873)	573 (498-792)	<0.05
TLR9+ non-classical memory B cells (%)	0.3 (0.3-0.4)	1.4 (0.7-2.5)	<0.05

Table 2: B cells at the end of follow-up in patients who reached renal response and those who did not.

	Absent Renal Response	**Renal response present**	
B Cells	**Median**	**Median**	***p***
TLR9+ B cells (%)	0.5 (0.2-0.6)	8.1 (2.6-15)	<0.05
TLR9+ transitional B cells (MFI)	0 (0.0-0-0)	747 (537-767)	<0.05
TLR7+ transitional B cells (%)	0 (0.0-0.2)	23 (11.1-44.5)	<0.05
TLR7+ naive B cells (%)	0.3 (0.0-0.4)	27.4 (7.9-63)	<0.05
TLR9+ non-classical memory B cells (cells/µl)	0 (0.0-0.0)	0.4 (0.1-1.4)	<0.05
TLR9+ non-classical memory B cells (MFI)	0 (0.0-0.0)	1128 (1006-1135)	<0.05
TLR9+ age associated B cells (%)	13 (2.4-67)	0.8 (0.4-24.4)	<0.05

Figure 1: Paired median analysis with time as an aleatory variable, in patients with and without renal response.



Conclusions: Our data suggest that renal response is associated with enhanced TLR9 expression in the effector humoral compartment, which might be implicated in the mechanisms of renal damage in lupus nephritis.

PV135 / #415

Poster Topic: *AS16 - Lupus Nephritis-Pathogenesis*

IDENTIFICATION OF FOXM1 AS A CANDIDATE DRIVER OF SLE AUTOIMMUNITY AND LUPUS NEPHRITIS

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Background/Purpose: Among the variable organ system manifestations experienced by patients with SLE, lupus nephritis (LN) is both common, affecting approximately 60% of patients, and severe. Patients with LN are characterized by enrichment in particular autoantibodies, including anti-double-stranded (ds)DNA and anti-Smith (Sm). We studied PBMC from our longitudinal SLE patient cohort and characterized gene transcripts that are correlated with levels of LN-associated autoantibodies. We focused on those transcripts that identify pathways and mechanisms that are particularly related to production of anti-dsDNA and/or anti-Sm autoantibodies compared to those associated with production of autoantibodies that are more generally characteristic of systemic autoimmunity, such as anti-Ro52. Understanding the mechanisms involved in development of pathogenic lupus autoantibodies could lead to identification of novel therapeutic targets.

Methods: Subjects included 80 SLE patients from our longitudinal SLE patient cohort at Hospital for Special Surgery. Samples were collected at 1 to 14 visits over a period of 3 (0-12) years, with an average of 4 time points per patient. Plasma levels of autoantibodies present in each patient sample were determined based on clinical assays and antigen array. RNA sequencing of patient PBMC was performed and the obtained data matrix of autoantibody levels and gene transcripts used to generate functionally annotated groups of co-expressed genes using the Weighted Gene Co-expression Analysis (WGCNA) algorithm. Comparison of autoantibody titers with gene expression was analyzed by linear mixed model, using either a per module or per gene approach. Transcripts associated with levels of pathogenic autoantibodies (anti-dsDNA and anti-Sm/RNP) were identified and their mechanisms of regulation assessed by literature review.

Results: Clusters of specific autoantibodies were identified based on degree of correlation between their titer and the level of expression of individual mRNA transcripts. Titers of LN-associated autoantibodies were highly associated with expression of cell cycle genes. Among those, the most significant correlations ($p < 10^{-5}$) were seen for *TK1, AURKB, KIFC1, KIF15, FOXM1, GINS2, NGAPG, CDC45, CDCA5, CCNA1,* and *CCNB1*. In contrast, the cluster of autoantibodies that are not associated with LN (e.g., anti-Ro52) did not show an association with cell cycle transcripts. Based on literature review of the identified cell cycle-related genes, *FOXM1*, encoding an

important transcription factor, is itself a key regulator of many of the cell cycle transcripts identified in this analysis.

Conclusions: Our data indicate that cell cycle-related gene transcripts are associated with plasma levels of pathogenic autoantibodies implicated in LN (anti-dsDNA and anti-Sm) in contrast to anti-Ro52 autoantibodies that represent a more general measure of systemic autoimmunity. Of those cell-cycle-related transcripts, *FOXM1* is not only highly associated with elevated levels of pathogenic lupus autoantibodies, but is also identified as a critical regulator of many of the other cell cycle-related genes associated with high level pathogenic autoantibodies. FOXM1is recognized as a critical regulator of malignant cells, is considered a therapeutic target in oncology, and pharmacologic inhibitors are in development for a number of malignancies. Characterization of the specific roles played by FOXM1 in the regulation of autoimmunity may provide the rationale for that transcription factor serving as a novel therapeutic target for LN.

PV136 / #489

Poster Topic: *AS16 - Lupus Nephritis-Pathogenesis*

RENAL (CD133+) PROGENITOR CELL POPULATION IS DECREASED IN LUPUS NEPHRITIS BIOPSIES.

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Background/Purpose: Lupus nephritis (LN) leads to end-stage renal disease in up to 10% of patients. While much attention has been paid to the immunological mechanisms underlying the disease, mechanisms of renal repair in the aftermath of flares are under-investigated. Renal progenitor cells (RPCs), which line the Bowman's capsule of glomeruli, are thought to play a key role in renal repair after kidney injury. We sought to analyze the abundance and distribution of these cells in lupus nephritis kidneys.

Methods: Paired renal biopsies from 13 patients, taken at diagnosis (baseline, T0) and one year of treatment (T12), were analyzed. Biopsies from four kidney transplants were used as controls. Serial 5µm FFPE sections were stained for: : **a)** Multiplex fluorescence immunohistochemistry (IHC) Panel 1: Hoechst (nuclei), CD133 (an RPC marker), podocin (podocytes) and CD31 (endothelial cells); **b)** Multiplex fluorescence IHC Panel 2: Hoechst (nuclei), CD68 (pan-macrophage), CD3 (pan-T cell) and CD8 ($CD8^+$ T cells); **c)** IHC for $p16^{INK4a}$ (a marker of cellular senescence), and **d)** PicroSirius Red (staining collagen I and III, reflecting fibrosis). Images were scanned, and semi-quantitative and quantitative analyses were performed using QuPath software v0.5.1. For each patient, pertinent clinical, biological and histological data were collected from medical files and pathological reports.

Results: At baseline, 11 patients were diagnosed with proliferative lupus nephritis (class III/IV), 1 patient with class II, and 1 with class V. The number of CD133 positive cells per glomerulus was significantly decreased amongst lupus patients as compared to controls, at both T0 and T12 (median 855 (IQR 687-1067) $CD133^+$ cells/mm^2 in controls, *vs.* 141 (IQR 0-326) in LN biopsies at T0 and 188 (IQR 0-421) in LN biopsies atT12, $p < 0.001$, **Fig. 1**). We did not observe any significant correlation between the number of glomerular $CD133^+$ cells and Activity Index or Chronicity Index. Surprisingly, the number of $CD133^+$ cells at baseline was lower amongst patients with good long-term outcome (estimated glomerular filtration rate (eGFR) 5 years after diagnosis),

showing an inverse correlation (**Fig 2.**). At baseline, we did not observe any significant correlation between the number of CD133⁺ cells and the number of senescent (p16⁺) cells; neither did we observe a correlation with the number of CD8⁺ or CD68⁺ cells infiltrating glomeruli or within a 30-µm radius around glomeruli. Taken together, we hypothesize that CD133⁺ cells undergo differentiation to repair glomeruli in the aftermath of an LN episode and lose the expression of this marker in the process. This could explain why patients with lower numbers of CD133⁺ cells have better outcomes. Further studies are required to confirm this finding and understand the (RPC-intrinsic and/or -extrinsic) mechanisms underlying differential RPC differentiation/repopulation capacity amongst individuals.

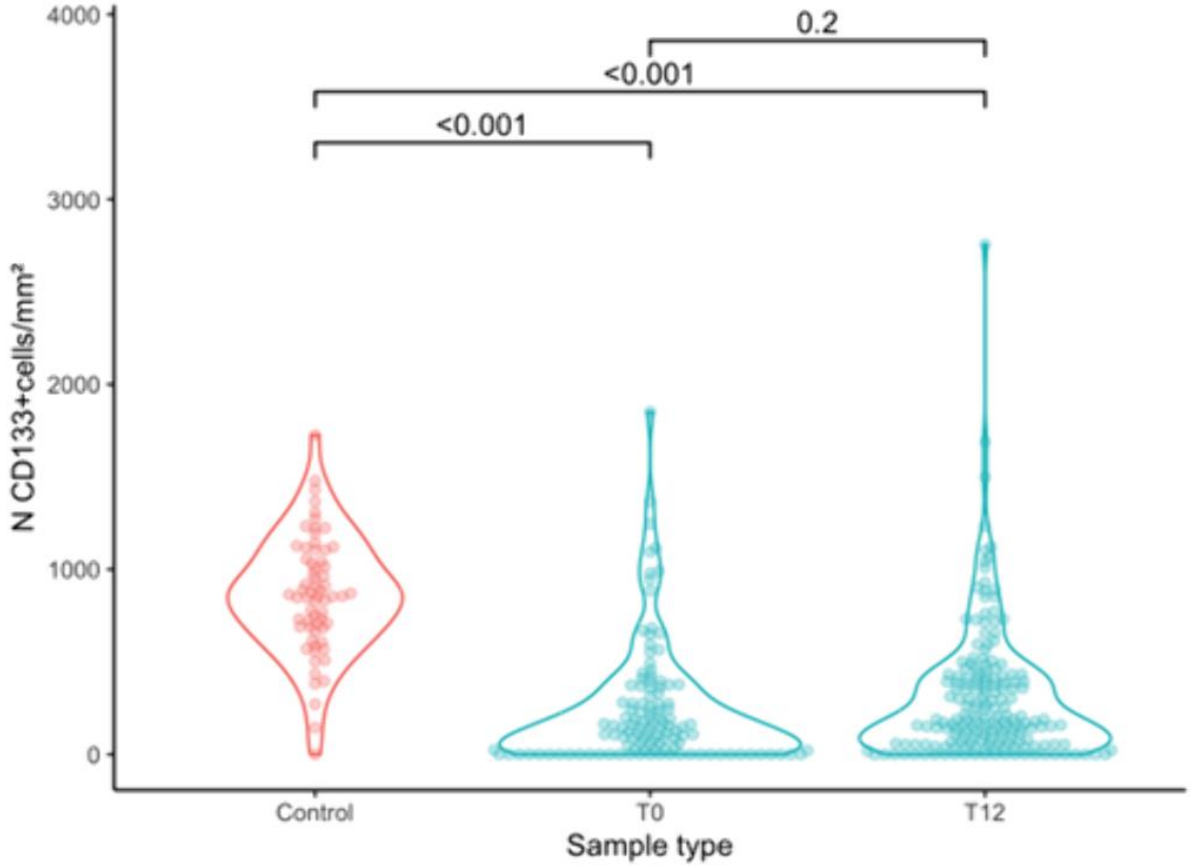

Fig 1: Number of CD133 positive cells in glomeruli, across all biopsies, grouped by sample type. Each dot represents a glomerulus. *p*-values: ANOVA with Tukey's correction for multiple comparisons.

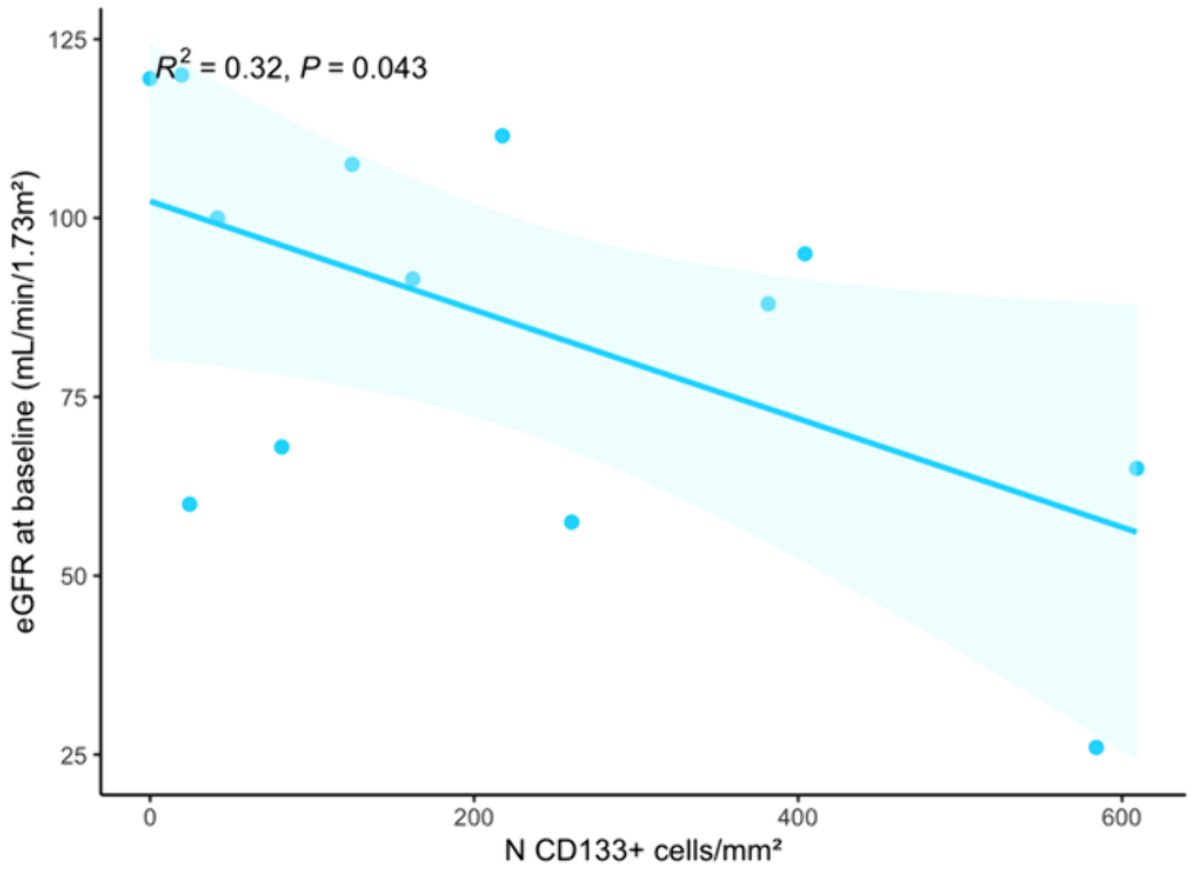

Fig 2: Estimated glomerular filtration rate (eGFR) versus the number of CD133 positive cells in glomeruli, in baseline (T0) LN biopsies. Each dot represents a patient. R^2 value and *p*-value: Pearson linear regression analysis.

Conclusions: CD133 staining is drastically decreased in biopsies from lupus nephritis patients as compared to controls. Nevertheless, it is inversely correlated with eGFR at five years, suggesting that loss of CD133 expression may reflect differentiation of RPCs to repair kidney, and thus be predictive of good outcome.

PV137 / #64

Poster Topic: *AS16 - Lupus Nephritis-Pathogenesis*

CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH LUPUS NEPHRITIS AND CONCOMITANT TMA

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Background/Purpose: Thrombotic microangiopathy (TMA) can be seen in up to 24% of patients with lupus nephritis and may be renally limited or have systemic manifestations. It may also occur in the setting of autoimmunity, with an overall poor prognosis. This study examines a cohort of patients with biopsy-proven lupus nephritis with concomitant TMA lesions on kidney biopsy, highlighting their clinical associations and outcomes.

Methods: We reviewed medical records of 255 patients with biopsy-proven lupus nephritis from June 2015 to December 2023 at Houston Methodist Hospital, identifying seven patients with concomitant TMA on renal biopsy. We manually extracted pathological and clinical characteristics of these patients from their electronic medical record.

Results: Three patients (43%) developed ESRD requiring hemodialysis without remission. The remaining had partial remission, with a mean creatinine of 1.2 ± 0.4 mg/dL, GFR 68 ± 15.7 mL/min, and UPCR 0.9 ± 0.6 mg/mg around 6 months of follow up. Induction therapy varied: mycophenolate (3), belimumab (1), cyclophosphamide (2), and rituximab (1). All patients received concurrent hydroxychloroquine and prednisone. Results are summarized below:

Patient	Sex	Age	Race	Tobacco Use	BMI
1	M	68	African-American	N	25-29.9
2	F	54	African-American	Y	18.5-24.9
3	F	37	African-American	Y	> 30
4	F	23	African-American	N	> 30
5	F	70	Hispanic	N	> 30
6	F	26	Hispanic	Y	18.5-24.9

7	F	44	White	N	> 30
Mean ± SD (if applicable)		46 ± 18.9			

Table 1. Cohort Demographic Characteristics

Patient	Lupus Nephritis Class	ANA	ANA Pattern	dsDNA	Smith	RNP	SSA	SSB	C3	C4	APLS
1	IV	1:320	Homogenous	1:2560	-	-	+	-	68	24	-
2	III	1:1280	Cytoplasmic	1:640	+	+	+	-	43	5	-
3	III	1:320	Nucleolar	1:160	+	+	-	-	39	4	-
4	V	1:320	Speckled	1:80	+	+	+	-	124	41	+
5	V	1:160	Speckled	undetectable	-	-	+	-	111	28	-
6	IV	1:320	Speckled	1:1280	+	+	+	-	24	6	-
7	III	1:160	Homogenous	1:320	+	+	+	-	101	9	+
Mean ± SD									73 ± 41	17 ± 15	

Table 2. Cohort Serologies

Patient	WBC	Hgb	Plts	Cr	GFR	ESRD on HD	AST	ALT	UPCR	UA protein	UA RBC
1	3.8	10.5	208	1.32	59	No	27	13	0.61	3	0-5
2	4.3	9.2	244	1.1	61	No	20	17	3.6	3	>10
3	1.3	7.8	41	1.4	56	No	1987	274	2.8	2	>10
4	3.8	8.6	226	7.7	8	Yes	14	8	4.7	3	0-5

5	13	6.7	311	4.2	23	Yes	24	22	11.4	3	0-5
6	1.8	6.1	46	3.5	18	Yes	554	100	15	3	>10
7	10	9.5	174	1.4	47	No	12	8	0.4	2	0-5
Mean ± SD	5.4 ± 4.3	8.3 ± 1.6	179 ± 111	2.9 ± 2.6	38.9 ± 23.7		377 ± 788	63 ± 105	5.5 ± 5.6		

Table 3. Pertinent Labs

Conclusions: In this study, there was a higher prevalence of African Americans, obesity, and tobacco use in patients with lupus nephritis and TMA. Only 29% of our cohort had antiphospholipid syndrome, illustrating that not all TMA is associated with APLS. Importantly, 43% of our cohort progressed to ESRD. Vigilant monitoring and larger studies should be done to better characterize TMA diagnosis on biopsy as a significant risk factor for poor outcomes.

PV138 / #549

Poster Topic: *AS17 - Miscellaneous*

MENOPAUSE SYMPTOM SEVERITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune condition with a predominance in females. Pregnancy complications are well studied in SLE, but the effects and treatment of menopause in SLE is not well known. It has been established that due to medications and the condition itself, menopause can occur earlier in SLE and confers an increased risk of osteoporosis and cardiovascular disease compared to the general populations. Type 2 SLE symptoms which include fatigue, reduced cognition, anxiety, depression, and generalized pain can overlap with menopausal symptoms. This can impact functioning and quality of life significantly without inciting a change in SLE therapy because typical medical evaluations focus on Type 1 inflammatory SLE symptoms. There is a lack of information regarding how menopause in SLE may affect the severity and prevalence of Type 2 symptoms. We conducted a survey study of menopause in our SLE cohort and its impact on disease outcomes and functioning.

Methods: A cross-sectional survey study of patients with 2019 EULAR/ACR SLE and menopause was performed at the Ottawa Hospital. Patients within menopause age range between 40-65 years were recruited. Participation involved completion of a three-page survey relate to menopause symptoms adapted from the Menopause Specific Quality of Life Questionnaire. We collected data related to patient reported demographics, social habits, co-morbidities, menopause (natural, surgical, or premature), treatments for menopause and menopause symptoms. Menopause symptoms severity was rated on a scale of 0-6, with 6 being extremely bothersome to everyday life. Control participants included those within the same age range without known diagnosis of SLE or other autoimmune disease. Descriptives statistics were applied.

Results: We have identified 195 patients for recruitment from our SLE cohort. Preliminary results show 55% of participants are Caucasian, 10% are Black and the remainder comprise of Hispanic, Asian and First Nations women. Pre-menopausal responses accounted for 10% and remained were menopausal at the time of the survey. Vasomotor symptoms, poor memory, fatigue, and aches were the most reported symptoms, overlapping with Type 2 lupus symptoms. Many participants (56%) reported insufficient information and support for their menopausal symptoms.

Conclusions: At this preliminary stage, we report lupus patients experiencing menopause symptoms that are like type 2 lupus symptoms and can be difficult to manage. We are continuing to collect more survey data to better understand the symptom severity in comparison to non-SLE participants. Identifying gaps in the care of SLE women with menopause will help promote more awareness and advocacy for understanding and addressing these important issues.

PV139 / #320

Poster Topic: *AS17 - Miscellaneous*

COVID-19 IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTER EXPERIENCE

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Background/Purpose: The COVID-19 pandemic has posed significant challenges to peoples' life worldwide. Patients with systemic lupus erythematosus (SLE) are particularly susceptible to infections. Emerging evidence suggests that the prevalence of COVID-19 may be higher among patients with rheumatic conditions. Various factors, including co-morbidities, disease state, and treatment regimens, can influence outcomes. However, the specific impact of COVID-19 on lupus patients is not yet fully understood. More evidence-based knowledge is necessary to plan effective strategies for managing these patients in the future. This study aimed to investigate the effects of COVID-19 on patients with SLE.

Methods: This observational study was conducted at the Green Life Center for Rheumatic Care and Research from June 2021 to May 2022. Participants included previously diagnosed SLE patients who attended follow-up or new appointments and had a confirmed history of COVID-19 infection based on positive RT-PCR results for SARS-CoV-2 from oral or nasopharyngeal swabs. Patients with suspected but unconfirmed infections, as well as those with overlap syndromes or mixed connective tissue disease (MCTD), were excluded. The sample size was of 94. Data were colected through patient interviews and medical record reviews. The severity of COVID-19 was assessed according to national guideline: mild was defined as symptomatic, meets case definition, and no evidence of pneumonia or hypoxia; moderate was defined as clinical signs of pneumonia with saturation above 90% in room air; and severe was defined as presence of signs of pneumonia with either respiratory rate above 30 breaths per minute and or saturation less than 90% in room air. Data were collected on a preformed data sheet and analyzed using SPSS.

Results: Among the 94 patients, 89 (94.7%) were female and 5 were male, with a mean age of 36.7 ± 12.2 years. The majority (44%) of patients were over the age of 40. Severity assessments indicated that 66% had mild disease, while 12.8% had severe disease. The most common comorbidities reported were hypertension (42%), hypothyroidism (35.1%), and asthma (29.8%). Of the 76 available HRCT chest reports, 25 (32.8%) showed lung involvement. Eighteen (19.1%) patients had a history of hospitalization,

with a mean duration of 9.1 days. Treatment data indicated that most patients (96.9%) received antibiotics, while 25.5% required oxygen, 17.2% received low molecular weight heparin (LMWH), 33% were administered rivaroxaban, 38% received dexamethasone, 18% received intravenous remdesivir, and 2 patients were treated with intravenous tocilizumab. Five patients required high dependency unit (HDU) or intensive care unit (ICU) support, and 2 required mechanical ventilation. The majority of patients (86.1%) were on immunosuppressants (33% on methotrexate, 10.6% on azathioprine, and 24.5% on mycophenolate mofetil), and 81.9% were taking hydroxychloroquine. During their illness, 31.9% of patients were on steroids, with a mean dose of 8.9 mg/day. Regression analysis revealed that both mycophenolate mofetil and steroids were associated with a higher risk of developing severe disease (odds ratios of 3.2, p-value 0.005, and 2.7, p-value 0.04, respectively). Methotrexate and hydroxychloroquine were associated with a lower probability of severe disease (odds ratios of 0.96, p-value 0.04, and 0.73, p-value 0.5, respectively).

Conclusions: Most lupus patients experienced mild to moderate COVID-19 infections. This study had found the widespread use of antibiotics during the pandemic. Immunosuppressive medications were associated with severity of infection. Mycophenolate mofetil and steroid were associated with a higher risk of severe infection, while methotrexate and hydroxychloroquine were linked to a lower risk.

PV140 / #234

Poster Topic: *AS17 - Miscellaneous*

LUPUS RESEARCH ALLIANCE 2024-2028 RESEARCH STRATEGIC PLAN: ACCELERATING PRECISION MEDICINE FOR PEOPLE LIVING WITH LUPUS

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Background/Purpose: Lupus is a systemic autoimmune disease characterized by complicated etiopathogenesis, heterogeneous clinical manifestations and a range of immunological abnormalities that affects millions of people worldwide. At present, therapy for lupus is mostly empiric and involves largely non-specific anti-inflammatory and immunosuppressive agents. The Lupus Research Alliance (LRA), the world's largest private funder of lupus research, has invested over US$270M in more than 600 individual research programs since 1999. Recently, the LRA successfully completed its previous 5-year research strategic plan, resulting in the establishment of robust research governing bodies, a tripling of the number of grant programs, and the establishment of critical translational and clinical research infrastructure to include a Public-Private Partnership with the FDA, Lupus ABC, a lupus registry, biorepository, and data exchange platform, Lupus Nexus, and has significantly increased the number of clinical studies the organization supports through the clinical affiliate, Lupus Therapeutics. To build upon this success, the LRA set out to create a new five-year Research Strategic Plan as part of an organization-wide goal to directly impact individuals living with lupus by enabling research that advances safer and accessible treatment options.

Methods: More than 30 interviews with lupus patients and US and international lupus/related fields researchers were conducted, as well as a survey of the research and clinical landscape and a detailed analysis of the clinical trial landscape using clinicaltrials.gov and other sources. Additionally, an in-depth evaluation of LRA's research portfolio and broader funding landscape analyses were performed to inform the evolution of LRA's grant programs and ensure they continue to synergize with external research funding. A planning committee of academic and industry experts, and patients advised the development of the strategy by analyzing the data and engaging in discussions about emerging gaps and opportunities.

Results: With recent developments in understanding lupus pathogenesis and heterogeneity, impactful technological advancements, and the emergence of engineered cell therapy as a novel treatment paradigm for lupus, the LRA is uniquely positioned to address critical gaps and opportunities to accelerate precision medicine for people living with lupus. The clinical trial landscape analysis highlighted that while the number of lupus clinical trials has increased, there is a high failure rate for primary outcomes, demonstrating the need for better trial design and population characterization, as well as mechanistic understanding of therapies entering trials and for diagnostics/prognostics to stratify patients and quantify outcomes. Importantly, the analysis showed that the LRA clinical affiliate, Lupus Therapeutics, participated in ~25-30% of all lupus trials. The new strategic plan was built on its unique capabilities and the LRA's robust infrastructure and research programs and includes *three* 5-year research goals, each with corresponding objectives and intended patient impact: 1) Improve understanding of patient heterogeneity as a basis for individual therapeutic choices; 2) Increase the number of molecular stratification, prognostic/diagnostic tools, and biomarkers; 3) Accelerate development of treatments that reprogram the immune system. The new Plan calls for the LRA to become an effective driver of clinical development, for substantive changes to LRA's funding portfolio to focus on the new priorities, and the establishment of new partnerships and patient-centric research initiatives.

Conclusions: By implementing this plan, the LRA envisions a future where patients are promptly diagnosed, clinically and molecularly profiled, and offered safer and more effective personalized treatments and possible cures.

PV141 / #368

Poster Topic: *AS17 - Miscellaneous*

REAL-WORLD APPLICATION OF THE SLE RISK PROBABILITY INDEX TO TRIAGE ANA POSITIVE PATIENTS: A PRAGMATIC RETROSPECTIVE SINGLE-CENTER STUDY.

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Background/Purpose: Antinuclear antibodies (ANA) testing is crucial for identifying patients with systemic lupus erythematosus (SLE). However, its specificity is suboptimal and may result in unnecessary referrals to Rheumatology. Triage tools that enable early differentiation between SLE and non-SLE among ANA-positive patients could expedite initial assessment and improve patient outcomes [1], making them particularly valuable in lupus referral centers. The SLE Risk Probability Index (SLERPI) is a simple-to-use, machine-based model utilizing 8 clinical and 6 laboratory variables, designed to assist SLE diagnosis, with potential clinical utility for this purpose [2].

Methods: We retrospectively reviewed consecutive referrals that were received between January 1st and October 31st, 2024 to rule out SLE. Referrals for patients younger than 16 years old or without documented positive ANA (1:80 or greater by immunofluorescence) or with a prior diagnosis of connective tissue disease were excluded. A single reviewer analyzed each consultation request from the referring clinicians and scored SLERPI items individually, using only the information included in the referral. Based on this scoring, the total SLERPI score was classified as positive or negative, using a cut-off of >7 points, as previously described. Patients were classified as either non-SLE or diagnosed with SLE based on clinical documentation from their charts. Additional collected data included initial triage priority (Urgent, Semi-Urgent, Routine) assigned by the referral center, and a retrospective triage reassessment by the principal reviewer. Descriptive statistics were used.

Results: Fifty referrals meeting the selection criteria were identified. Of these, 44 were from general practitioners and 6 from specialists, with 90% showing positive ANA by immunofluorescence at titers ≥1/160. Initial triage classified 20% of cases as Semi-Urgent and 80% as Routine. On average, 8.7 out of 14 SLERPI items were undocumented by the referring provider. Only four items—Arthritis, Platelet levels, Leukocyte levels, and Proteinuria—were documented in ≥50% of referrals, while 8 out of 14 items were documented in ≤20% of referrals. Among the 50 charts reviewed, 5 had a positive SLERPI score (>7), while 45 were negative. Four patients were diagnosed with SLE, and 46 were deemed non-SLE. The preliminary analysis demonstrated a positive predictive value of 60% for a SLERPI score >7 to identify SLE patients, with a high negative predictive value of 98%, for an 8% SLE prevalence (Figure 1). SLERPI score >7

showed a positive likelihood ratio of 17.3 and a negative likelihood ratio of 0.26 for SLE identification. A SLERPI score >7 would have reclassified 6 non-SLE patients as Routine and prioritized one SLE case as Semi Urgent (Figure 2). The SLERPI score's negative likelihood ratio was 0.13 for identifying patients ultimately classified as Routine, including those initially marked as Routine who remained so after review and those reclassified from Semi-Urgent to Routine.

Conclusions: SLERPI shows potential as an effective triage tool for distinguishing SLE from non-SLE among ANA-positive patients. With a high negative predictive value of 98% for SLE diagnosis and a negative likelihood ratio of 0.13, the SLERPI score could help prioritize referrals. This may, in turn, accelerate early rheumatology assessment in newly diagnosed SLE patients, thus improving outcomes. This approach might also allow for more efficient resource allocation in lupus referral centers. References: [1.] Adamichou C. Ann Rheum Dis 2021;80(6):758-766 [2.] Floris A. Arthritis Care Res 2020;72:1794-9.

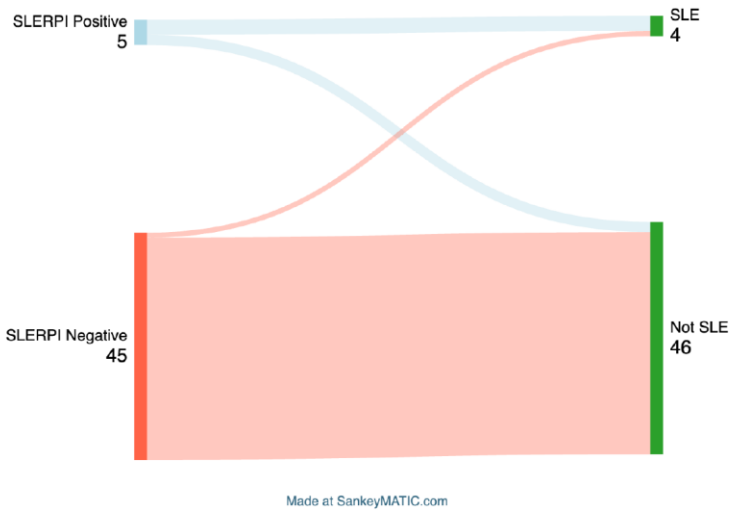

Figure 1

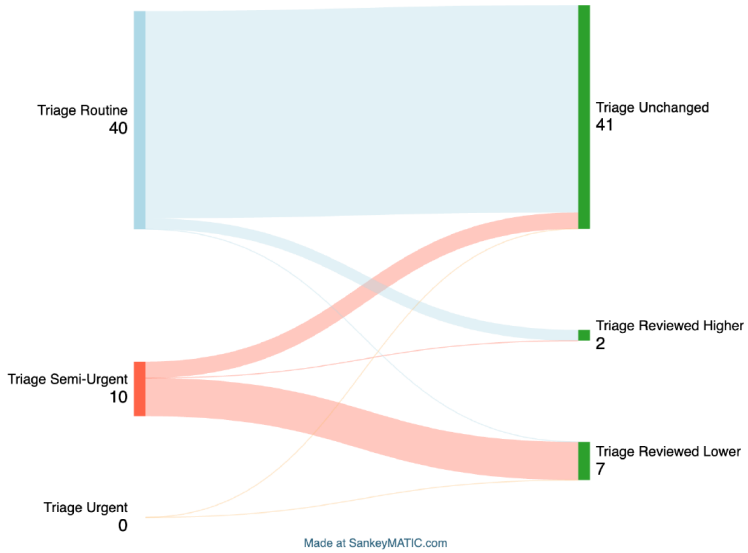

Figure 2

PV142 / #812

Poster Topic: *AS17 – Miscellaneous*
Late-Breaking Abstract

HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)/MACROPHAGE ACTIVATION SYNDROME (MAS) IN SYSTEMIC LUPUS ERYTHEMATOSUS - PREVALENCE, DRIVERS, TREATMENT AND PROGNOSIS OF A SINGLE-CENTRE MULTIDISCIPLINARY HLH/MAS TEAM

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Background/Purpose: Haemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS) can, though rarely, be the first presentation of systemic lupus erythematosus (SLE). It may also develop during the course of SLE, often triggered by disease flares, infections, medications, or concomitant neoplasms, especially lymphoma. While the mortality rate of HLH/MAS episodes in SLE is lower than in other conditions driving to HLH/MAS, it remains higher than that of non-HLH SLE-related hospital admissions. Aim: To describe the experience of a single tertiary centre experience with both SLE and HLH/MAS cohorts, focusing on the demographics, drivers, treatment, and prognosis of HLH/MAS complicating SLE.

Methods: HLH/MAS episodes were identified from our retrospective SLE cohort (1985-2023). Subsequent review of demographics, drivers, treatment and outcomes of SLE patients in our HLH/MAS cohort, which includes retrospective cohort (1-1-2004 to 31-12-2018) and a prospective cohort following the establishment of a multidisciplinary team (MDT) (1-1-2019 to 31-12-2023).

Results: HLH/MAS complicating SLE occurred in 9 patients out of the 974 SLE patients (1985-2023, all cases since 2004), representing a 0.92% prevalence. These 9 patients experienced had 11 HLH/MAS episodes, accounting for a subset of our HLH/MAS cohort of 54 patients with 60 episodes. All patients were female, with ages ranging from 19 to 44 years old at the time of their first HLH/MAS episode. In 5 patients (55.5%), HLH/MAS was the initial presentation of SLE. Concomitant triggers included infections in 7 episodes (bacterial, 1 post-COVID, 1 post-CMV) and lupus flares in 4 episodes (2 neuropsychiatric, 1 lupus nephritis, 1 fever and lymphadenopathy). Treatment options for HLH/MAS included glucocorticoids (various dosages of methylprednisolone

boluses, followed by prednisolone) and IVIG, which were administered to all patients. Additional therapies included short cycles of high-dose intravenous anakinra, cyclophosphamide, rituximab, ruxolitinib, and baricitinib. One patient died (11.1%) due to multi-organ dysfunction and hemorrhage within the first 48h of treatment. Compared to other HLH/MAS drivers, SLE had better prognosis (lymphoproliferative HLH-related mortality: 58,8% (10/17 patients); solid tumor HLH-related mortality: 40% (2/5 patients); HIV infection HLH-related mortality: 42,9% (3/7 patients); Chronic Active Epstein-Barr virus infection HLH-related mortality: 100% (2/2 patients)). Only 2 patients with SLE experienced HLH/MAS episodes following the establishment of the HLH/MAS MDT.

Conclusions: Our findings align with the limited published data on HLH/MAS in SLE. It highlights that although HLH/MAS-related mortality in SLE is lower than in other HLH/MAS drivers, it remains significantly higher than that of non-HLH/MAS severe lupus flares.

PV143 / #581

Poster Topic: ***AS17 - Miscellaneous***

PROTEIN SUBUNIT AND MRNA COVID-19 VACCINES: COMPARATIVE STUDY ON INDUCED-IMMUNOGENICITY IN RITUXIMAB-TREATED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, RHEUMATOID ARTHRITIS AND VASCULITIS

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Background/Purpose: Treatment with rituximab for systemic autoimmune rheumatic diseases (SARD) increases morbidity and mortality following COVID-19 infection [1], and reduces antibody responses to vaccination. We evaluated humoral responses following fourth or fifth doses of either a protein subunit (PSV) or messenger RNA (mRNA) vaccines.

Methods: We recruited adults with SARDs on rituximab post-third or fourth mRNA COVID-19 vaccine in an open label, non-randomized, comparative trial. Participants chose to receive either a fourth dose of mRNA (Spikevax®) or PSV (Nuvaxovid™) vaccines. Patients who already received a fourth dose of mRNA vaccine were offered PSV as their fifth dose. Humoral vaccine-responses were determined pre, 28 days and 6 months post-vaccination. Plasma and sera were evaluated for anti-receptor binding domain (anti-RBD) by ELISA, and for neutralizing antibodies to Wuhan pseudotyped lentiviruses. We used descriptive statistics for demographics and ANOVA for immunogenicity.

Results: We studied 86 participants with rheumatoid arthritis (39%), ANCA vasculitis (32%), idiopathic inflammatory myositis (9%), systemic lupus erythematosus (8%), systemic sclerosis (7%), and undifferentiated SARDs (4%). Mean (SD) age was 57.3 (15.3); 73% were female; 91% White; 23% were on prednisone, 21% on antimalarials, and 42% on other immunosuppressors. Of those receiving a fourth dose (N=49) more chose Spikevax® (n=35) than Nuvaxovid™ (N=14); 37 participants chose Nuvaxovid™ for their fifth dose. An increase of anti-RBD response at 28 days post-vaccination was present in those receiving a fourth dose mRNA vaccine, but not in those receiving fourth dose PSV (Figure 1). In those receiving fifth dose PSV, anti-RBD titers decreased at six months when compared to those at 28 days, while anti-RBD remained high in fourth dose mRNA recipients. The fourth dose mRNA recipients had higher neutralization titers against the Wuhan strain at 28 days compared to their pre-vaccination titers; this was not observed after the fourth dose of PSV. For all groups, the neutralizing response significantly decreased at 6 months post-vaccination compared to day 28.

Conclusions: In SARDs patients on rituximab, both fourth and fifth dose PSV vaccine recipients had decreased anti-RBD titers at 6 months, while post fourth dose mRNA recipients increased their anti-RBD up to 6 months post-vaccination. Overall, humoral response in mRNA vaccine recipients seemed superior to those receiving PSV. This emphasizes the importance of thorough evaluation of new COVID-19 vaccines in the immunocompromised.

References: [1] Strangfeld A. Ann Rheum Dis 2021; 80: 930-942

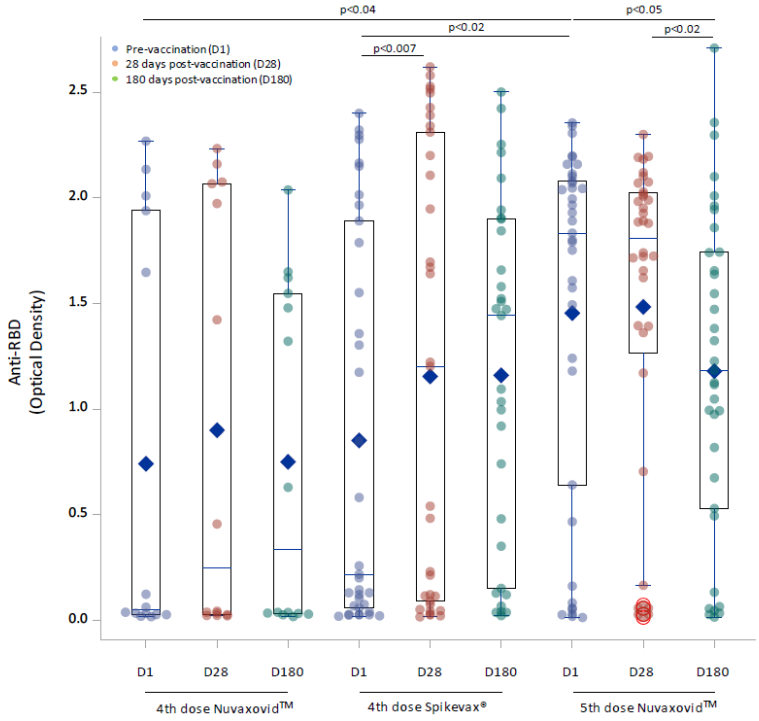

Figure 1 Anti-RBD antibody levels pre-vaccination (day 1) and at 28 days and 180 days post-vaccination. The line and the diamond inside the box indicate the median and the mean, respectively. Outliners are displayed by circle red (◯).

PV144 / #585

Poster Topic: *AS17 - Miscellaneous*

COVID-19 BOOSTER VACCINATION, EITHER MRNA OR PROTEIN SUBUNIT VACCINES, APPEARS SAFE IN RITUXIMAB-TREATED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, RHEUMATOID ARTHRITIS AND VASCULITIS

Paul R Fortin[1], Nathalie Amiable[2], Inés Colmegna[3], François Harel[4], Anne-Sophie Julien[4], Mehdi Benlarbi[5], Mathieu Dubé[5], Sonia Léger-Thériault[3], Alexandra Godbout[2], Gloria Delgado[5], Mélina Duchesne[5], Rose Cloutier[5], Josée Perreault[6], Annie Gravel[2], Lison Fournier[2], Giuliana Alfonso[3], Josiane Bourré-Tessier[7], Marie Hudson[8], Nicolas Richard[9], Jean-Paul Makhzoum[10], Arielle Mendel[11], Sasha Bernatsky[12], Marc Dionne[2], Michael Libman[3], Gaston De Serres[2], Mélanie Dieudé[5], Louis Flamand[2], Daniel Kaufmann[5], Andrés Finzi[5], Renée Bazin[6]
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Background/Purpose: People living with systemic autoimmune rheumatic diseases (SARD) on B-cell depletion agents have impaired immunogenicity and increased vulnerability to severe COVID-19. We assessed the 7-day solicited reactogenicity and safety of booster doses following COVID-19 vaccine primary series.

Methods: We recruited adults with SARDs on rituximab post-third or fourth dose of a messenger RNA (mRNA) COVID-19 vaccine in an open label, non-randomized, comparative trial. Participants chose to receive either a fourth dose of mRNA Spikevax® or Nuvaxovid™, a protein subunit vaccine (PSV). Patients who had already received a fourth dose of mRNA vaccine were offered the PSV as their fifth dose. From study entry, up to 180 days post-booster, subjects self-reported solicited 7-days reactogenicity, and unsolicited adverse events, adverse events of special interest (AESI) (defined as medically confirmed flares of the underlying SARD), new COVID-19 infections, and serious adverse events (SAEs) (requiring hospitalization). We used descriptive statistics for demographics and Chi square tests to report reactogenicity and adverse events.

Results: We recruited 86 participants with rheumatoid arthritis (39%), ANCA vasculitis (32%), idiopathic inflammatory myositis (9%), systemic lupus erythematosus (8%), systemic sclerosis (7%), and undifferentiated SARDs (4%). Mean (SD) age was 57.3 (15.3); 73% were female; 91% White; 23% were on prednisone, 21% on antimalarials, and 42% on other immunosuppressors. The most significant reactogenicity manifestations were fever, erythrema, swelling and pain. The proportion of side effects for all types of AEs were similar comparing the fourth-dose mRNA versus the fourth-dose PSV, and the fourth-dose PSV versus the fifth-dose PSV. Fever was only present in the fourth-dose mRNA group; erythema and swelling were reported more often in fifth-dose PSV vs fourth-dose mRNA; and pain significantly more in fourth-dose mRNA versus 5th-dose PSV. Disease flares (N=3, occurring at 14, 92, and 131 days) are presented in Table 1, along with COVID-19 and other infections (N=6). Including infections, there were nine SAEs experienced by eight participants (Table 1). There were no deaths.

Table 1. Adverse Events of Special Interest and Serious Adverse Events.

Adverse Event of Special Interest			
Trajectory	**Days from last vaccine to AESI**	**SARD diagnosis**	**Description**
AS	14*	Behcet's disease	Severe flare of Behcet's. Elevated CRP to 140. Extreme fatigue and occasional dizziness. Prednisone dose increased.
	92	MCTD	Severe increase pain in joints. Mycophenolate prescribed.
BN	131	Idiopathic Inflammatory Myositis - Anti-synthetase syndrome	Severe stiffness and arthritis. Hydroxychloroquine prescribed.
Serious Adverse Event (all required hospitalization)			
Trajectory	**Days from last vaccine to SAE**	**SARD diagnosis**	**Description**
AS	Before booster dose	Lupus	Moderate COVID-19 infection
	1 – 44* 2 – 99*	Behçet's	1 – Severe organized pneumonia due to Behçet's flare or post COVID infection. Injection of tixagevimab/cilgavimab (Evusheld™) and infusion of aCD20. 2 – Severe organizing pneumonia and Behçet's flare. Severe dyspnea with impaired saturation. Oxygen, antibiotics, prednisone and aCD20. Pulmonary biopsy with pneumothorax complication. Chest tube and transfer to intensive care unit with oxygen high flow.
	177	ANCA vasculitis	Severe pneumonia and COPD exacerbation.
AN	179	Systemic sclerosis	Intussusception. Surgery was performed without complications.
BN	15	RA	Severe COVID-19 infection with pulmonary embolism and pseudogout flare.
	53	IgG4-related disease	Severe COVID-19 infection with pneumonia.
	108	ANCA vasculitis	Severe bleeding from stoma anastomosis.
	181	RA	Severe COVID-19 infection with pneumonia, bronchitis, and respiratory distress.

Abbreviations: **AESI**= Adverse Event of Special Interest; **SARD**= Systemic Autoimmune Rheumatic Disease; **MCTD**= Mixed Connective Tissue Disease; **CRP**= C Reactive Protein; **SAE**= Serious Adverse Event; **aCD20**= Anti-CD20 therapy; **COPD**= Chronic Obstructive Pulmonary Disease; **RA**= Rheumatoid arthritis.h
*This patient had three events, one AESI at day 14, and two SAEs at day 44 and day 99.

Conclusions: Three of 86 patients experienced a disease flare and nine others required hospitalization, most for COVID-19/other infections. A fourth or fifth booster dose of either an mRNA or a PSV vaccine were not clearly associated with unexpected vaccine reactions in rituximab-treated SARD patients. Revaccination of patients on rituximab with either mRNA or PSV vaccines appears safe.

PV145 / #693

Poster Topic: *AS17 - Miscellaneous*

OPTIMIZING SYSTEMIC LUPUS ERYTHEMATOSUS CARE WITH ARTIFICIAL INTELLIGENCE: A SYSTEMATIC REVIEW OF CLINICAL APPLICATIONS

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Background/Purpose: Artificial Intelligence (AI) is revolutionizing healthcare, offering innovative solutions for early diagnosis, clinical and molecular phenotyping, prognosis prediction, and patient care optimization in different diseases, including Systemic Lupus Erythematosus (SLE). Machine Learning (ML) is a subset of AI that enables systems to learn from data and improve performance over time without being explicitly programmed. This study aims to analyze the state of the art on clinical applications of AI tools in patients with SLE.

Methods: A systematic literature review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement guidelines. The search was completed through MEDLINE, Scopus, and the Cochrane Library databases in November 2024. The search strategy employed various combinations of MeSH terms and keywords, including: "Artificial Intelligence," "Machine Learning," "Deep Learning," "Artificial Neural Networks," "Natural Language Processing," "Large Language Model," and "Systemic Lupus Erythematosus." Studies were included if they met the following criteria: (1) abstract available, (2) contained original data, (3) included adult patients with SLE, and (4) incorporated AI-based methodologies or tools in their study design or analysis.

Results: Out of 1.022 articles identified in scientific databases, 60 fulfilled the eligibility criteria and were included in the analysis (Fig.1). These selected articles included a total of 61.273 SLE patients, in which aspects such as lupus nephritis (LN, n=16), diagnosis (n=7), biomarkers (n=6), extra-renal SLE (n=6), pregnancy (n=4), disease activity (n=3), Electronic Health Records (EHRs) analysis (n=3), flares (n=2), among others, were evaluated. Most studies were published between 2023 and 2024, with China and the USA being the most represented countries (Fig.2). ML was employed in the majority of the selected studies, accounting for 75% (45 out of 60) of the total, followed by Deep Learning (n=5), Artificial Neural Networks (n=4), Natural Language Processing (NLP, n=4), and Large Language Models (specifically ChatGPT) in 2 studies. AI, employing NLP algorithms, demonstrates the capacity to extract clinically relevant data from EHRs, thereby enhancing the identification and comprehensive clinical characterization of SLE patients. A total of 37.800 SLE patients were evaluated using ML techniques. Extreme Gradient Boosting (XGBoost), Random Forest, Logistic Regression, and Support Vector Machines were the most frequently utilized models. These models

were applied to multiple aspects of the disease, focusing on LN, including biomarkers identification and prediction of proliferative lupus nephritis diagnosis, renal flares, coinfection, complete remission, and treatment response. In the context of SLE diagnosis, ML models effectively identified patterns in clinical data, predicting lupus probability and classifying patients into different diagnostic certainty levels. In the majority of cases, the performance of ML models was comparable or superior to traditional statistical models, as evaluated by area under the curve (AUC: range 0.63—0.98), accuracy (63.6—99.9%), precision (50.0—97.8%), sensitivity (35.0—99.3%), specificity (56.6—100%), and F1-Score (0.14—0.99, typically greater than 0.80). This review identifies data heterogeneity and publication bias as significant challenges that can impact the reliability and generalizability of these findings. **Figure 1.** Flowchart of Systematic Literature Review.

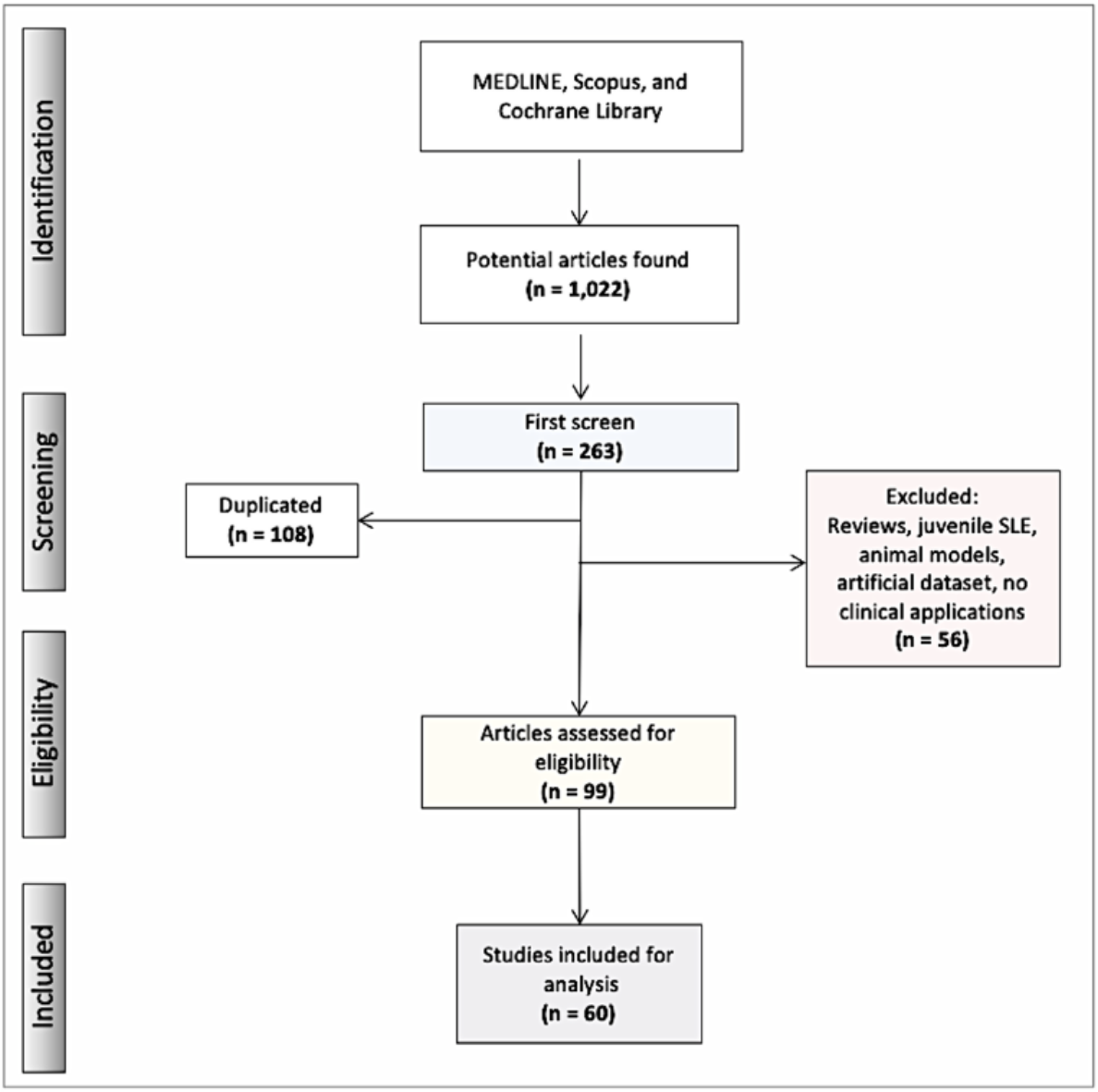

Figure 2. Heat Map of Selected Articles on AI Applications in Systemic Lupus Erythematosus.

AI	SLE									
	EHR	Biomarkers	Diagnosis	Flares	Activity	LN	Extra-renal	Pregnancy	Others*	TOTAL
Machine Learning	1	6	7	2	3	9	5	2	10	45
Deep Learning	0	0	0	0	0	3	1	0	1	5
Artificial Neural Networks	0	0	0	0	0	2	0	2	0	4
Natural Language Processing	2	0	0	0	0	1	0	0	1	4
Large Language Model	0	0	0	0	0	1	0	0	1	2
TOTAL	3	6	7	2	3	16	6	4	13	60
Number of patients	1.118	3.802	3.719	6.251	7.097	9.600	3.915	1.054	24.717	61.273

Country	China	USA	Italy	Japan	Iran	Taiwan	Others**	Multicenter		
	24	12	5	2	2	2	8	5		60
Year of publication	2002	...	2017	2018	2019	2021	2022	2023	2024	
	1		3	2	2	11	11	14	16	60

Heat map illustrating the number of selected articles across various AI methodologies and their applications in SLE patients. Each cell represents the count of articles corresponding to specific categories. The lower section of the figure depicts the distribution of selected articles across countries and publication years.
AI: Artificial Intelligence; EHR: Electronic Health Record; LN: Lupus Nephritis; SLE: Systemic Lupus Erythematosus.
*Prediction and cost of lupus hospitalization/readmission; Early identification of macrophage activation syndrome (MAS); Prediction of sirolimus effect on SLE activity, hypothyroidism, and chronic damage; Differentiation between flares and infections; Prevalence and incremental costs of SLE; Pharmacovigilance; Anxiety; Herpes infection; ChatGPT4's proficiency in addressing patients' questions on SLE.
**Australia (1), Singapore (1), Oman (1), Spain (1), Poland (1), Greece (1), Colombia (1), South Korea (1).

Conclusions: This systematic review highlights the role of AI, especially ML, in advancing the clinical management of SLE. The results demonstrate that ML models significantly enhance diagnostic accuracy and patient care, often surpassing traditional statistical methods. Understanding the limitations of AI tools is crucial before their implementation in clinical practice.

PV145a / #751

Poster Topic: *AS17 – Miscellaneous*
Late-Breaking Abstract

RHUPUS SYNDROME: DESCRIPTION OF CLINICAL MANIFESTATIONS, ANALYTICAL FINDINGS, AND THERAPEUTIC APPROACH IN A SERIES OF 10 CASES

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Background/Purpose: Rhupus is a rare syndrome that combines characteristics of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Its prevalence is estimated to be 0.09%. It is characterized by erosive polyarthritis along with typical SLE symptoms and specific autoantibodies. The debate continues as to whether Rhupus is a true overlap of RA and SLE or represents a form of SLE with erosive joint involvement. In order to provide a better understanding of the topic, the objective of this study is to describe the demographic variables, analytical data, clinical manifestations, and therapeutic approaches in patients diagnosed with Rhupus.

Methods: A cross-sectional, monocentric study was conducted on patients diagnosed with Rhupus between January 2019 and December 2024. All patients met the ACR/EULAR 2010 criteria for RA and ACR/EULAR 2019 criteria for SLE. Demographic variables, analytical data (autoantibodies, cytopenias, acute phase reactants, and complement consumption), clinical manifestations, and the different treatments received during their evolution, including synthetic and biologic DMARDs, were collected

Results: Ten patients were included, 90% women, with a median age of 62 years. All received treatment with at least three DMARDs. The most commonly used synthetic DMARDs were methotrexate and hydroxychloroquine. Seven patients received biologic DMARDs, with rituximab being the most commonly used. One patient was treated with certolizumab due to fertility desires. Six patients received JAK inhibitors (4 with baricitinib and 2 with upadacitinib) (Table 1).
All patients tested positive for antinuclear antibodies (ANA), 90% for anti-citrullinated peptide (anti-CCP), 80% for rheumatoid factor (RF), and 60% for anti-double-stranded DNA (anti-dsDNA). Other antibodies present can be seen in Table 2. The most frequent analytical alterations were elevated acute phase reactants (100%), lymphopenia (40%), and complement consumption (30%).
Regarding clinical manifestations, arthritis was present in 100% of patients, 70% of

which was erosive. Fatigue and morning stiffness affected 60%. Thirty percent showed typical SLE skin lesions such as malar rash, photosensitivity, and subacute cutaneous lupus. Other manifestations, such as alopecia and dry syndrome, were present in 30%. Less frequently, aphthosis, rheumatoid nodules, pericarditis, pericardial effusion, pleural effusion, and Raynaud's phenomenon were observed (Table 2).

TABLE 1. DEMOGRAPHIC CHARACTERISTICS AND TREATMENTS	
Age (years), median (IQR)	62 (42-71)
Gender, females (%)	90%
Years since diagnosis, median (IQR)	15 (2-32)
Patients treated with synthetic DMARDs, n (%)	10 (100%)
Methotrexate, n (%)	10 (100%)
Hydroxychloroquine, n (%)	8 (80%)
Leflunomide, n (%)	5 (50%)
Sulfasalazine, n (%)	3 (30%)
Patients treated with JAK inhibitors, n (%)	6 (60%)
Baricitinib, n (%)	4 (40%)
Upadacitinib, n (%)	2 (20%)
Patients treated with immunomodulators, n (%)	2 (20%)
Cyclosporine, n (%)	1 (10%)
Azathioprine, n (%)	1 (10%)
Patients treated with biologics, n (%)	7 (70%)
Rituximab, n (%)	3 (30%)
Abatacept, n (%)	2 (20%)
Tocilizumab, n (%)	1 (10%)
Certolizumab, n (%)	1 (10%)

TABLE 2. ANALYTICAL DATA AND CLINICAL MANIFESTATIONS			
ANALYTICAL DATA		**CLINICAL MANIFESTATIONS**	
Autoimmunity		**Articular**	
ANA positive, n (%)	10 (100%)	**Arthralgia, n(%)**	10 (100%)
Anti-CPP positive, n (%)	9 (90%)	**Arthritis, n(%)**	10 (100%)
Rheumatoid factor positivo, n (%)	8 (80%)	**Erosive arthritis, n(%)**	7 (70%)
Anti-dsDNA elevated, n(%)	6 (60%)	**Cutaneous manifestations**	
Lupus anticoagulant positive, n (%)	2 (20%)	**Photosensitivity n(%)**	2 (20%)
Beta2-glycoprotein positive, n (%)	2 (20%)	**Malas rash, n(%)**	1 (10%)
Anticardiolipin positive, n (%)	1 (10%)	**Subacute cutaneous lupus, n(%)**	1 (10%)
Anti-centromere positive, n (%)	1 (10%)	**Serositis**	
Anti-Ro52 positive, n (%)	1 (10%)	**Pericarditis, n(%)**	1 (10%)
Anti-Ro60 positive, n (%)	1 (10%)	**Pleural effusion, n(%)**	1 (10%)
Hematological alterations		**Pericardial effusion, n(%)**	1 (10%)
Elevated acude phase reactants, n (%)	10 (100%)	**Others**	
Lymphopenia, n(%)	4 (40%)	**Raynaud's phenomenon, n(%)**	1 (10%)
Complement consumption, n(%)	3 (30%)	**Splenomegaly, n(%)**	1 (10%)
Neutropenia, n(%)	2 (20%)	**Fatigue, n(%)**	8 (80%)
		Morning stiffness, n(%)	6 (60%)
		Xerophtalmia, n(%)	3 (30%)
		Xerostomia, n(%)	3 (30%)
		Alopecia, n(%)	3 (30%)
		Aphtosis, n(%)	1 (10%)
		Rheumatoid nodules, n(%)	1 (10%)

Conclusions: All patients presented with difficult-to-manage symptoms, requiring treatment with at least three DMARDs. The most frequently used treatments were methotrexate, hydroxychloroquine, JAK inhibitors (tofacitinib and upadacitinib), and rituximab. The most common analytical findings were elevated acute phase reactants, lymphopenia, and complement consumption. All patients had positive ANA, 90% had positive anti-CCP, 80% had RF, and 60% had anti-dsDNA. Arthritis was the most

frequent manifestation (100% of patients), with 70% of cases being erosive. Other typical SLE manifestations were present, with the most frequent being skin lesions in 30% of patients.

PV146 / #705

Poster Topic: *AS17 - Miscellaneous*

DEVELOPMENT, VALIDATION AND PERFORMANCE OF A PATIENT KNOWLEDGE ASSESSMENT TOOL FOR ASSESSING THE IMMEDIATE AND SHORT-TERM IMPACT OF AN INFORMATION COURSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Long-term outcomes in rheumatic diseases can be improved by improving patients' knowledge, beliefs and perception about their disease which can help them in coping with the disease better. However, there is a lack of tools/instruments in Systemic Lupus Erythematosus (SLE) to 1. objectively assess patients' knowledge in various domains & 2. To assess the impact of a patient education program. The aim of the study was to develop, validate and assess the performance of a self-prepared questionnaire for assessing patients' knowledge about their disease and to use this tool to assess the impact of an information course in improving the above-mentioned elements among patients.

Methods: A self-prepared questionnaire (Hindi/English) containing 23 multiple choice or true-false type questions with single correct answer assessing patients' knowledge about SLE in 3 domains (a. etiology, disease process, signs & symptoms b. drug therapy & monitoring c. role of investigations in disease diagnosis and monitoring) was prepared. All questions had an item-level content validity index (I-CVI) of at least 0.9. The scale-level content validity index based on the universal agreement method (S-CVI/UA) was 0.8 for the whole questionnaire as assessed by 6 experts. All questions had an option of 'I don't know' which would prevent patients from guessing the answer from the available options. Each question was given a score of 1 if answered correctly. The questionnaire was applied 3 times: at baseline, immediately after an information course to see the immediate impact and after 6 months to see the retention of the information. Information on demographic features and socio-economic status was also collected. Frequency data were compared using McNemar test for paired nominal data & kappa statistics for ordinal data. Student's paired t-test was used for comparison of mean scores to see the impact. A p-value<0.5 was considered significant.

Results: At baseline, the questionnaire was applied to 56 patients with SLE (F:M=54:2; median age 29(16-53) years) and the median(range) score was 10(2-19) (Table–1). Among them, 39 patients attended the information course. The option 'I don't know' was exercised 509 times (39.51%) before the information course which reduced to 169 (18.84%) times after the course and 108 (13.04%) times at 6 months. After the information course, median score increased from 10(2-19) to 17(0-23) (p<0.001) which was irrespective of the socio-economic classes and education status of the patients. A

total of 13 questions recorded a higher number of correct responses as compared to baseline after the course and at 6 months and this increase was significant for all 13 questions (Table–1). Upon re-administering the questionnaire after 6 months, 36 patients out of 39 responded. The median score 16(0-23) of the questionnaire (n=37) remained significantly higher ($p<0.001$) as compared to baseline score with 8 out of 23 questions achieving statistical significance (Table–2).

Conclusions: Indian patients with SLE have a poor knowledge base about their disease which one may strive to improve by implementing short information courses. The information course was found to be effective across the socio-economic classes and educational status. The provided information was retained at 6th month of follow up months without any reinforcement course.

Table – 1 Question-wise assessment of responses before and after the information course and the statistical significance of the change

S. No.	Question	Pre-Test Performance (n=56)			Post-Test Performance (n=39)			Statistical Significance (p<0.05)* Y/N
		Correct (%)	Incorrect (%)	I don't know (%)	Correct (%)	Incorrect (%)	I don't know (%)	
1.	Etiology of disease	44.64	5.36	50	66.67	12.83	20.5	N
2.	Hereditary nature	44.64	10.76	44.6	64.10	15.4	20.5	N
3.	Dietary restrictions in SLE	50.00	21.4	28.6	64.10	20.5	15.4	Y
4.	Possibility of cure	55.36	14.24	30.4	69.23	12.87	17.9	Y
5.	Extra-articular manifestations	60.71	24.99	14.3	71.79	10.31	17.9	Y
6.	Possibility of pregnancy	42.86	16.04	41.1	74.36	5.14	20.5	N
7.	Breastfeeding in SLE	60.71	13.69	60.7	66.67	7.73	25.6	N
8.	Prevention of flare	67.86	3.54	28.6	87.18	5.12	7.7	N
9.	Blood tests (CBC, LFT, RFT)	7.14	78.56	14.3	41.03	56.37	2.6	N
10.	Repeat ANA test	21.43	37.47	41.1	64.10	23.1	12.8	N
11.	Reason for doing urine test	25.00	57.1	17.9	43.59	51.31	5.1	Y
12.	Identification of steroids	58.93	10.67	30.4	69.23	15.37	15.4	Y
13.	Identification of DMARDs	46.43	12.47	41.1	69.23	2.57	28.2	Y
14.	Drugs during pregnancy & breastfeeding	8.93	8.97	82.1	33.33	23.07	43.6	Y
15.	Hydroxychloroquine in pregnancy	23.21	10.69	66.1	38.46	20.54	41.0	Y
16.	Duration of treatment in SLE	76.79	1.81	21.4	92.31	0.0	7.7	N
17.	Cure by using alternative medicine	37.50	19.6	42.9	66.67	15.43	17.9	Y
18.	Steroid adverse effects 1	10.71	28.59	60.7	35.90	30.8	33.3	N
19.	Steroid adverse effects 2	48.21	5.39	46.4	69.23	7.67	23.1	Y
20.	Forgetting to take medicines	66.07	10.73	23.2	82.05	10.25	7.7	Y
21.	Onset of DMARDs action	46.43	30.37	23.2	71.79	17.91	10.3	Y
22.	Lupus Nephritis	33.93	17.87	48.2	69.23	15.37	15.4	Y
23.	Renal Biopsy	25.00	23.2	51.8	66.67	10.23	23.1	N

*change with respect to the correct responses before and after the information course (Assessed by McNemar test)

Table – 2 Question-wise assessment of responses before the information course and after 4 months with the statistical significance of the change

S. No.	Question	Pre-Test Performance (n=56)			6 months responses (n=36)			Statistical Significance (p<0.05)* Y/N
		Correct (%)	Incorrect (%)	I don't know (%)	Correct (%)	Incorrect (%)	I don't know (%)	
1.	Etiology of disease	44.64	5.36	50	72.22	16.68	11.1	N
2.	Hereditary nature	44.64	10.76	44.6	83.33	11.07	5.6	N
3.	Dietary restrictions in SLE	50.00	21.4	28.6	77.78	11.12	11.1	N
4.	Possibility of cure	55.36	14.24	30.4	80.56	11.14	8.3	Y
5.	Extra-articular manifestations	60.71	24.99	14.3	75.00	19.4	5.6	Y
6.	Possibility of pregnancy	42.86	16.04	41.1	88.89	11.11	0	N
7.	Breastfeeding in SLE	60.71	13.69	60.7	50.00	33.3	16.7	N
8.	Prevention of flare	67.86	3.54	28.6	91.67	5.53	2.8	N
9.	Blood tests (CBC, LFT, RFT)	7.14	78.56	14.3	27.78	72.22	0.0	N
10.	Repeat ANA test	21.43	37.47	41.1	61.11	30.59	8.3	N
11.	Reason for doing urine test	25.00	57.1	17.9	38.89	61.11	0.0	N
12.	Identification of steroids	58.93	10.67	30.4	77.78	11.12	11.1	Y
13.	Identification of DMARDs	46.43	12.47	41.1	69.44	8.36	22.2	Y
14.	Drugs during pregnancy & breastfeeding	8.93	8.97	82.1	33.33	22.27	44.4	N
15.	Hydroxychloroquine in pregnancy	23.21	10.69	66.1	38.89	16.71	44.4	Y
16.	Duration of treatment in SLE	76.79	1.81	21.4	97.22	2.78	0.0	N
17.	Cure by using alternative medicine	37.50	19.6	42.9	72.22	22.18	5.6	N
18.	Steroid adverse effects 1	10.71	28.59	60.7	22.22	44.48	33.3	Y
19.	Steroid adverse effects 2	48.21	5.39	46.4	72.22	5.58	22.2	Y
20.	Forgetting to take medicines	66.07	10.73	23.2	94.44	2.76	2.8	N
21.	Onset of DMARDs action	46.43	30.37	23.2	75.00	19.4	5.6	N
22.	Lupus Nephritis	33.93	17.87	48.2	69.44	11.16	19.4	Y
23.	Renal Biopsy	25.00	23.2	51.8	58.33	22.27	19.4	N

*change with respect to the correct responses at 6 months compared to the correct responses before the information course

(Assessed by McNemar test)

PV147 / #399

Poster Topic: *AS17 - Miscellaneous*

COMPARING CHILDHOOD-ONSET VERSUS ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS YOUNG ADULTS' LIVED EMPLOYMENT EXPERIENCES

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Background/Purpose: Young adulthood (18 to 30 years), is an important life stage with many transitions. Young adults with Systemic Lupus Erythematosus (SLE) must navigate this period while living with a devastating illness, however young adults with childhood-onset SLE (cSLE) have a longer time to adapt to SLE compared to those with adult-onset SLE (aSLE). As such, the lived experiences of young adults with cSLE may differ from their aSLE counterparts. We aimed to compare the lived employment (school and work) experiences of young adults with cSLE and aSLE.

Methods: Participants were recruited from 3 rheumatology clinics in Canada for individual semi-structured, English language qualitative interviews. Participants completed a pre-interview questionnaire (socio-demographics, SLE history and work characteristics). Semi-structured interviews were conducted by video/phone , transcribed verbatim, double-coded and analyzed using thematic analysis.

Results: 34 SLE patients: 47% cSLE and 53% aSLE, were interviewed. Majority were females (27/34, 73.5%), the rest were males or non-binary. Median ages were 21 (cSLE) and 28 years (aSLE). 15 were working, 13 were students, and 6 were unemployed, in between school and work, at the time of the interview . 59% of cSLE and 76% of aSLE participants were working. Major organ involvements were present in 56% (similar in cSLE and aSLE). There were 4 main themes and 10 sub-themes, with some divergence between cSLE and aSLE: *Decreased productivity (subthemes: physical tasks, cognitive performance):* Both groups described decreased productivity. In physical tasks, aSLE participants reported difficulties due to joint pain while the cSLE group attributed fatigue. In cognitive performance, the aSLE group tended to be forgetful, while cSLE patients described concentration difficulties. *Interference with employment (subthemes: changing career path, losing/quitting job or school, medical appointments):* The subthemes diverged as the cSLE group reported both positive and negative effects of SLE which both guided and hindered their career *choices*, while the aSLE group adapted their careers to SLE. Medical appointments were deemed

disruptive as both groups had to miss entire work/school days. *Social relations (subthemes: questions from peers and colleagues, interference with social relations, and social support needs):* The aSLE group reported feeling judged by peers and colleagues about their disease after disclosure, while the cSLE group chose not to talk about their illness. Some in the aSLE group reported that SLE did not impact their social relations but most of cSLE felt negative impacts. Those with aSLE actively sought peer advice, while the cSLE group additionally obtained physical accommodations (e.g. writing class notes.) *Flexibility (subthemes-:remote or hybrid, accommodations):* Flexibility was reported as an important factor for positive employment experience in both groups. The cSLE group valued social interactions more than the flexibility of remote work, while aSLE valued the latter. Both groups needed accommodations, to allow flexibility to perform their employment tasks.

Conclusions: Young adults with aSLE and cSLE face similar challenges during employment but the cSLE patients' lived experiences were different compared to aSLE patients. This observation may reflect differences in age, life stage, and type of employment (school vs. work) between the 2 groups. Physicians can help advocate for SLE young adults to have flexibility in their school/ work tasks. Late cSLE teens and early post-diagnosis aSLE patients could be offered personalized counselling, considering their ages/ life-stage, taught skills to disclose and obtain accommodations, to help them be successful in their academic and employment trajectories.

PV148 / #463

Poster Topic: *AS17 - Miscellaneous*

SURVIVAL AND OUTCOMES OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH PULMONARY HYPERTENSION - A PROSPECTIVE OBSERVATIONAL COHORT STUDY

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Background/Purpose: Pulmonary hypertension (PH) is a severe manifestation in patients with systemic Lupus erythematous (SLE). Many treatment approaches have been suggested for SLE PH. These treatments include vasodilatory drugs, steroids, immunosuppressive agents. There are many observational studies, case series, case reports & one RCT supporting the beneficial effect of cyclophosphamide in PH. However, response to other immunosuppressive agents has not been studied. This prospective observational study was planned to record survival at 24 months and treatment response in SLE PH patients diagnosed by echocardiography to different immunosuppressive agents and vasodilators at 12 months.

Methods: Patients aged >18yrs with a diagnosis of SLE based on 2019 ACR/EULAR criteria & with clinical suspicion of PH are screened for PH by resting Doppler echocardiography. 22 patients with SLE-PH based on Systolic pulmonary artery pressure (SPAP) of >30 mmHg were recruited from among inpatient and outpatients of Clinical Immunology and Rheumatology department of Christian Medical College, Vellore from January 2021 till 2023 August. Patients with overlap connective tissue disease and pregnant females are excluded from the study. The clinical profile, antinuclear antibody, antiphospholipid antibodies (APLA), anti ribonucleoprotein (RNP)antibody, anti ds DNA antibody levels and complement levels are documented at baseline. Follow up echo at 6,12 & 24 months were noted. They were given either IV or oral steroids followed by second line immunosuppression with either cyclophosphamide, or mycophenolate or rituximab or azathioprine and also vasodilatory therapy for PH based on clinician's decision. Patients were assessed at 12 months to monitor treatment response in the form of improvement in clinical features, lab parameters & echocardiographic parameters. Patient's response to treatment was documented in the following manner: Clinical improvement in - Shortness of breath – NYHA class, improvement in Resting doppler echocardiography parameters - decrease of SPAP by > 15 mmhg or > 20 % improvement from baseline or TRVmax < 2.8m/sec. The survival at 12 and 24 months is documented.

Results: The study included 22 patients of SLE-PH. 95.4 % (21/22) were women. At diagnosis of PH 13.64 % (3/22), did not report suggestive symptoms. SLE & PH was simultaneously diagnosed in 18.18% (4/22) patients. The mean age at diagnosis of pulmonary hypertension was 34.7 years (range 19-57 years). PH based on PASP values

was severe in 45.4%, moderate in 40.9% and mild in 13.63% . 45.4% cases were in NYHA functional class III/1V & 54.5% in NYHA function class I/II. 18 patients had follow up PASP values at 12 months, 61.1% (n=11) were treatment responders, 38.9% (n=7, 1 died) non responders. The mean decrease in PASP value in responder group was 22.84mmHg and non responder group was 0.78mmhg. No significant difference was noted in baseline characteristics, treatment modalities between the groups. One year survival was 95.4% (n=21) and 2 year survival was 80% (n=12/15).

Conclusions: SLE patients with PH have a high 1 and 2 year mortality in our cohort of patients. Anti U1RNP antibodies are in a high percentage of our SLE patients with PH . A higher percentage of patients had their PH responding to immunosuppression and vasodilatory therapy.

PV149 / #422

Poster Topic: ***AS17 - Miscellaneous***

COVID-19 IS ASSOCIATED WITH LUPUS FLARE AND PERSISTENT DISEASE ACTIVITY: LONGITUDINAL DATA FROM THE REUMACOV-BRAZIL REGISTER

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Background/Purpose: Background: The study aimed to evaluate flares in systemic lupus erythematosus (SLE) patients over a period of six months after COVID-19.

Methods: Methods: a multicenter, observational, and prospective cohort study. SLE adult patients with COVID-19 (case group) were compared to SLE patients without

COVID-19 (control group). Assessments were performed at baseline (V0), immediately after COVID-19 (V1), and three and six months after infection (V2 and V3). Disease activity was evaluated by patient global assessment (PGA) and the modified SLE Disease Activity Index 2000 (SLEDAI-2K). A flare was defined as increase in SLEDAI-2K score greater than three and persistent disease activity was measured by SLEDAI-2K greater than three over two consecutive visits.

Results: Results: 715 patients were included, 363 in the case group and 352 in the control group. The case group had a higher mean age (SD) compared with the control group [41 years (12.38) versus 38.8 years (12.07), p=0.017]. There were no differences between groups at baseline regarding sex, comorbidities, treatment, or disease activity scores. The control group showed a significant reduction in PGA [0.24 (95% CI: -0.39 to -0.09), p=0.001] and SLEDAI-2K [0.85 (95% CI: 0.76 to 0.96) p=0.010] throughout the visits while in the case group the scores remained stable. The frequency of new SLE manifestations was higher in the case group compared with patients in the control group at V2 [20 (9.4%) versus 5 (3.0%), p=0.012] and V3 [22 (9.6%) versus 4 (2.8%), p=0.012]. In the case group, eleven severe disease manifestations (nephritis, neurological, vasculitis, pneumonitis, and myositis) were described at V2 and eight at V3, while in the case group there was only one severe disease manifestation (nephritis). Patients with COVID-19 were 3.7 (95% CI: 1.2 to 10.9) times more likely to have new SLE disease manifestations compared to patients without COVID-19. Case group presented more frequent flares or persistent disease activicty [74 (18.5%) versus 33 (10.5%), p=0.001]. COVID-19 at any time in the study was linked to a higher chance of a flare and persistent disease activity [OR=1.70 (95% CI: 1.06 to 2.74), p=0.029].

Conclusions: Conclusions: COVID-19 was associated with new SLE disease manifestations and worse outcomes (flares and persistent disease activity) in SLE patients. **Acknowledgments:** We thank the researchers involved in the centers participating in ReumaCoV-Brasil, the Brazilian Society of Rheumatology and the Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq.

PV150 / #420

Poster Topic: *AS17 - Miscellaneous*

SAFETY PROFILE OF VACCINES AGAINST SARS-COV-2 IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM PROSPECTIVE MULTICENTRIC STUDY - SAFER STUDY

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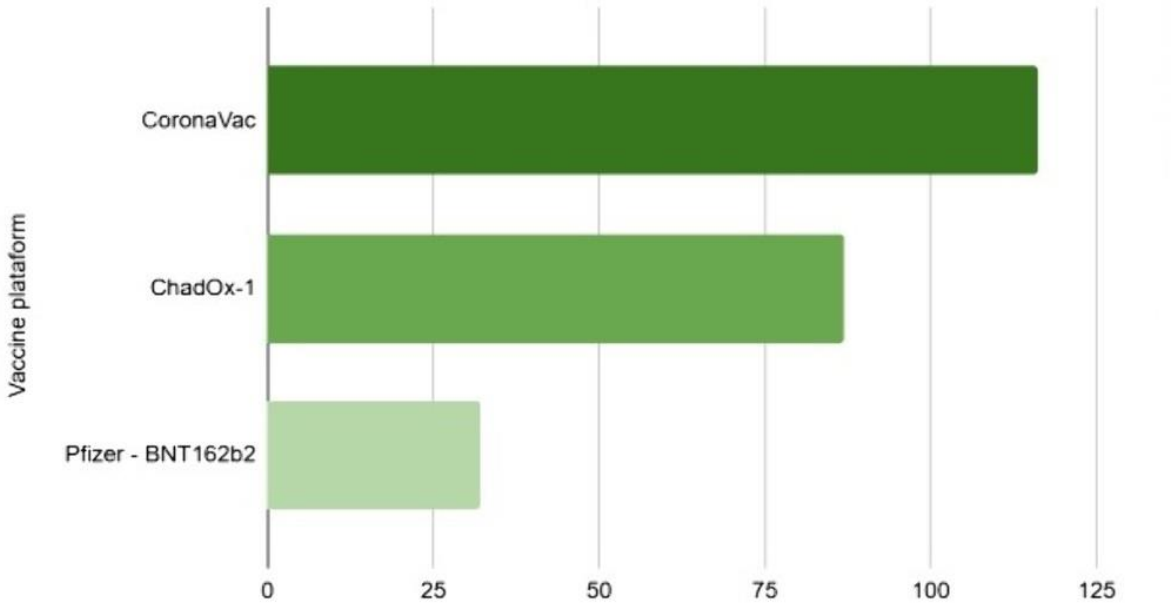
Background/Purpose: Systemic lupus erythematosus (SLE) patients are at greater risk of different infections when compared to the general population, due to abnormalities in the immunological response. Vaccination is the most effective measure for preventing infectious diseases, however, there is still low vaccination

coverage due to its acceptance, mainly due to fear of adverse events related to immunization. The objective of this study was to evaluate the safety of vaccines against SAR-CoV-2 available in the Brazilian Public Health system.

Methods: Data from the multicenter study - SAFER "Study of safety, effectiveness and duration of immunity after vaccination against SARS-CoV-2 in patients with immune-mediated inflammatory disease", a Brazilian, observational, prospective, phase IV cohort study were evaluated. Patients diagnosed with SLE who met the ACR/EULAR 2019 classification criteria and who received a complete vaccination schedule (2 doses + booster) against SARS-CoV-2, as recommended by the Brazilian National Immunization Plan, were included. All patients underwent clinical and laboratory evaluation before and after the vaccine dose associated with scheduled telephone monitoring and diary recording to monitor adverse events that could be related to the vaccine received.

Results: A total of 235 individuals with SLE with a complete vaccination schedule (initial scheme with 2 doses of CoronaVac, ChadOx-1 or Pfizer plus booster Pfizer) were included. Around 90% of participants were female with an average age of 38 years. The majority of patients without other significant comorbidities and a median time since disease diagnosis was 10 years. Based on SLEDAI-2K, the majority of patients were in remission or low disease activity (72.4%). Arthritis (15.74%), alopecia (14.04%), proteinuria (11.91%), consumption of complements (10.64%), anti-dsDNA antibody positivity (9.79%) and skin rash (9.36%) were the manifestations most frequently scored. Regarding the degree of immunosuppression, 135 (58.1%) were with a high degree of immunosuppression and 70 (30.1%) without immunosuppression. Of these participants, 116 patients received 2 doses of CoronaVac followed by 1 dose of BNT162b2 (PfizerBioNTech), 87 received 2 doses of ChadOx-1 (AstraZeneca) followed by 1 dose of BNT162b2 (PfizerBioNTech) and 32 received 3 doses of BNT162b2 (PfizerBioNTech). [Figure 1] The most common adverse events after receiving the vaccine were local hypersensibility, headache, musculoskeletal pain, these events being more frequent in both 3 doses received, but less commonly observed in patients in the group who received CoronaVac in the first and second doses when compared to those who received an initial regimen with Chadox-1 and Pfizer ($p < 0.05$) [table 1]. Evaluating the risk of flare of disease activity after vaccination, measured by SLEDAI-2K, a total of 136 patients were evaluated in relation to disease activity after the second dose and 69 after the third dose. No increase in disease activity was observed between groups. [table 2]

Figure 1: Vaccine scheme according initial doses (1st and 2nd dose)



Adverse events	Total N=235 (%)	02 CoronaVac doses + booster Pfizer dose N=116 (%)	02 ChadOx-1 doses + booster Pfizer dose N=87 (%)	03 Pfizer doses N=32 (%)	*P*
After 1st dose					
local hypersensibility	138(59.7)	49 (43.7)	65 (74.7)	24 (75.0)	***<0.001***
headache	111(48.0)	43 (38.3)	53 (60.9)	15 (46.8)	***0.007***
musculoskeletal pain	85(36.8)	30 (26.7)	43 (49.4)	12 (37.5)	***0.005***
After 2nd dose					
local hypersensibility	100(45.0)	34 (31.7)	48 (57.8)	18 (56.2)	***<0.001***
headache	72(32.4)	31 (28.9)	31 (37.3)	10 (31.2)	***0.47***
musculoskeletal pain	59(26.5)	24 (22.4)	27 (32.5)	8 (25.0)	***0.29***
After 3rd dose - booster Pfizer					
local hypersensibility	112/184 (60.8)	52/81 (64.2)	44/72 (61.1)	16/31 (51.6)	***0.47***
headache	75/184 (40.7)	34/81 (41.9)	32/72 (44.4)	9/31 (29.0)	***0.33***
musculoskeletal pain	56/184 (30.4)	21/81 (25.9)	28/72 (38.8)	7/31 (22.5)	***0.13***

Disease activity	Inclusion N =136 (%)	After 2nd dose	P	Inclusion N =69 (%)	After 3rd dose	P
Remission	52 (38.2)	67 (49.2)	***0.022***	30 (43.4)	34 (49.2)	***0.433***
Low activity	46 (33.8)	41 (30.1)	***0.513***	26 (37.6)	16 (23.1)	***0.059***
Moderate to high activity	38 (27.9)	28 (20.5)	***0.077***	13 (18.8)	19 (27.5)	***0.109***

Disease activity score (SLEDAI- 2K; categorized into remission (SLEDAI-2K = 0), low activity (SLEDAI-2K 1-5) and moderate to high activity (SLEDAI 2K ≥ 6)). The P value refers to the comparison of 4 weeks after the first dose vs. 4 weeks after the second dose versus baseline.

Conclusions: This study reveals the safety profile of vaccines against SARS-CoV-2 in patients with SLE and a complete vaccination schedule. Outcome that demonstrates adverse events mainly related to symptoms at the site of vaccine application and systemic symptoms not serious commonly observed in vaccines against other agents. Most importantly, no worsening of disease activity after a complete vaccination schedule regardless of the vaccine platform.

PV151 / #17

Poster Topic: *AS17 - Miscellaneous*

CLUSTER ANALYSIS IN MALE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is a disease with greater severity in male patients due to greater renal and neuropsychiatric involvement; as well as greater positivity for anti-DNA, anti-Sm, anti-Ro/SSA, anti-U1RNP, anti-cardiolipin antibodies, decreased complement C3, and SLEDAI.1 This greater severity is related to testosterone levels and its action in regulating the immune system, where IL6, TNF alpha and IL1b levels are negatively regulated by this hormone. The main objective was to explore although a cluster analysis, the groupability of male patients with SLE according to their Euclidean distances.

Methods: Cross-sectional retrospective study in the rheumatology department of the San Rafael Clinic University Hospital from Bogotá (Colombia). The chi square test (X^2) was used to evaluate the association between qualitative variables, with a p value <0.05 considered significant. To evaluate the correlation between the quantitative variables, the Pearson correlation coefficient (r) was carried out, a simple linear regression model was used to estimate the value of the beta coefficient and the R^2. For the multivariate analysisA cluster analysis was performed with distance measurement by the Euclidean method, and different link methods were explored.

Results: 162 patients were included, which 32 (19.7%) were men, with a significantly older age compared to women (43±16.9 versus 35.5±26 years, p = 0.032), as well as a higher SLEDAI (11.5±12.5 versus 8±12 p = 0.047) and shorter duration of the disease in months (12±0.5 versus 24±72, p= 0.008). Regarding clinical manifestations, men were 80% less likely to have acute/subacute cutaneous lupus (15.6% versus 52.3% OR: 0.20 95% CI 0.05 – 0.58 p=0.001) and oral ulcers/ nasal ulcers (15.6% versus 42.3% OR: 0.25 95% CI 0.07 – 0.72 p= 0.009), although thrombocytopenia was more prevalent (46.8% versus 26.9% OR: 2.38 95% CI 0.99 – 5.69 p= 0.048). A hierarchical cluster model was performed; the matrix of Euclidean distances was created and the groupability of the data was evaluated based on the Hopkins test with a value of 0.74.This grouping was performed using the Ward method: cluster 1 composed of 28 patients and cluster 2 of 4; in the cluster 1, the patients were older (43±16.2 versus 31.5±18.4 p=0.23) and had greater disease activity by SLEDAI (13.5±14 versus 10±5.3 p=0.62).They had a shorter time of evolution (12±23 versus 105±37.1 p= 0.001). The positivity of antiphospholipid antibodies occurred more frequently in cluster 2, corresponding to the youngest age group.

Conclusions: The severity of the disease differs according to sex, with greater inflammatory expression in older male patients.

PV152 / #774

Poster Topic: *AS17 – Miscellaneous*
Late-Breaking Abstract

SARS-COV-2 MRNA VACCINE IMMUNOGENICITY IN SLE

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Background/Purpose: The ACR recommends SARS-CoV-2 vaccination for all patients with rheumatic diseases, but the impact of immune suppressing medications on SARS-CoV-2 immunogenicity remains poorly understood. This study sought to answer how SLE patients, on a variety of medications, responded to the two-dose primary SARS-CoV-2 mRNA vaccine. We also evaluated the degree to which additional vaccine doses and natural infection impacted the development of SARS-CoV-2 anti-spike antibodies.

Methods: Using biobanked serum from before and following vaccination, we investigated anti-spike antibody development in 87 adult SLE patients and 16 adult healthy controls who had each received two doses of a SARS-CoV-2 mRNA vaccine 14-180 days prior a clinic visit. ELISA was used to assess the amount of vaccination strain (D614G) anti-spike antibodies being produced, reported as area under the curve (AUC); AUC <2 was considered a non-responder, 2-6 blunted response, and >6 full response. The dates of primary vaccine doses and subsequent vaccine doses were determined based on the state immunization registry. Dates of COVID infection were documented by patient recall and confirmed by chart review. Medication hold strategies were determined by chart review.

Results: As seen in Table 1, healthy controls had a higher AUC (mean 7.95, median 7.72, range 5.88-10.60) compared to the 87 SLE patients (mean 6.23, median 7.09, range 0.34-11.5; p=0.0002). The responses of 23 SLE patients who were receiving no immunosuppressive medications (mean 7.36, median 7.96, range 0.34-10.5) were not different, as a group, from those of healthy controls (p=0.3). Among SLE patients, neither disease activity nor prednisone dose (0-60 mg; p=0.8) were associated with AUC. Compared to healthy controls (p=0.0008) or SLE patients not taking immunosuppressants (p=0.008), SLE patients treated with rituximab (n=3, mean 4.90, range 3.75-5.70) or mycophenolate (n=20, mean 5.01, median 5.68, range 0.50-10.34) had significantly reduced antibody production. Of the 6 MMF primary non-responders (Table 2), 1 experienced COVID infection and 3 received additional vaccine doses over the subsequent year. While the patient experiencing natural infection demonstrated a robust anti-spike response (7.97) following infection, 2 of the 3 primary MMF non-responders did not mount an antibody response, even following 3rd, 4th, or 5th doses (AUCs all <1). One primary MMF non-responder, however, demonstrated a robust

response following her 3rd vaccine dose, which was administered with instructions to hold the next 7 doses (3.5-days) of MMF; this patient's AUC rose to 9.74 following her 3rd primary dose.

	Healthy Controls (n=16)	All SLE (n=87)	Only HCQ (n=23)	MMF (n=20)	MTX (n=10)	AZA (n=10)	All Belim (n=11)	Belim, no DMARD (n=2)	RTX (n=3)
Mean pred dose (mg)	0	1.22	0.40	1.25	0.7	3.00	6.59	2.50	5.83
Days since 2nd vaccine	71	77	70	88	79	74	67	65	103
AUC Mean	7.95	6.23	7.36	5.01	5.89	6.67	5.55	5.36	4.90
AUC Median	7.72	7.09	7.96	5.68	7.28	6.94	6.10	n/a	n/a
AUC Range	5.9-10.6	0.3-11.5	0.3-10.5	0.5-10.3	0.4-11.5	3.1-9.7	0.6-9.2	4.62-6.10	3.7-5.7
AUC StDev	1.22	2.90	2.29	3.18	3.95	2.15	2.79	1.05	1.02
p-value (HCQ=ref)	0.3	0.08	n/a	**0.008**	0.19	0.42	0.05	0.24	0.08
p-value (HC=ref)	n/a	**.0002**	0.30	**0.0008**	0.10	0.10	0.02	0.01	**0.0008**

Table 1. Amount of vaccination strain SARS-CoV-2 anti-spike antibody produced by health controls and by SLE patients who had each received two doses of a SARS-CoV-2 mRNA vaccine described as area under the curve (AUC). HCQ=hydroxychloroquine; MMF=mycophenolate or mycophenolic acid; MTX=methotrexate; AZA=azathioprine; Belim=belimumab; RTX=rituximab; pred=prednisone. A Bonferroni correction for multiple comparisons suggests a p-value of ≤0.006 as the cutoff for statistical significance (significant p-values are bolded).

Patient	AUC s/p dose 2	AUC s/p dose 3	AUC s/p dose 4	AUC s/p dose 5	AUC s/p infection
1	0.45	0.54			
2	0.64	9.74 (MFF held)			
3	0.66	0.71	0.74	0.87	
4	0.77				7.97 (50 days)

Table 2. Of the 6 primary MMF non-responders, 4 received subsequent vaccine doses (n=3) or documented infection (n=1). Among those who received additional vaccine doses, 2 remained non-responders while the 3rd developed a robust response in the setting of MMF being (7 held doses immediately following vaccination).

Conclusions: We herein demonstrate that treatment with rituximab and mycophenolate significantly blunts the humoral immunogenicity of SARS-CoV-2 mRNA vaccines. Primary MMF non-responders can go on to develop a robust humoral response following natural COVID infection and may be more likely to respond to mount a humoral response to subsequent SARS-CoV-2 immunization if MMF doses are held around the time of vaccine administration. These findings suggest that holding a small

number of MMF doses during the days immediately following vaccination could be a practical and safe strategy for enhancing vaccine immunogenicity.

PV153 / #118

Poster Topic: *AS17 - Miscellaneous*

LUPUS NEXUS: DEVELOPING A LUPUS REGISTRY, BIOREPOSITORY AND DATA EXCHANGE PLATFORM TO ACCELERATE PRECISION MEDICINE IN LUPUS

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Background/Purpose: Systemic lupus erythematosus remains a disease of high unmet medical need. Protean manifestations and the lack of clear understanding of etiology, pathogenesis, and disease subgroups hinder the development and application of targeted therapeutic approaches. Community-wide access to a longitudinal, highly curated, centralized patient dataset with linked biospecimens and molecular data is critical to enable advances in this area. To address this unmet need, the Lupus Research Alliance created the Lupus Nexus (LNx), a lupus registry, biorepository and data exchange platform.

Methods: To ensure that the design of LNx reflected the needs of the research and patient communities, LNx was developed with guidance from over 100 individuals representing clinicians and scientists from academia and industry, governmental and non-profit groups, and patients with lupus. A Steering Committee was formed to provide leadership, oversight and direction to the design, implementation and governance of LNx including the oversight of eight Working Groups (WGs) (Table 1) charged with developing individual components of the program. Members of the WG included experts in clinician- and patient-reported outcomes, registries, biorepositories, bioinformatics, biospecimen analyses, and lived lupus experience. Many of these individuals have transitioned to roles on active Advisory Boards to continue to provide guidance on LNx operations. The LNx has three main components: a registry, a biorepository, and a data exchange platform. The registry and biorepository are first being established through the Lupus Landmark Study (LLS), a prospective, longitudinal observational study that began in 2023. The LLS will enroll up to 3,500 people living with lupus into 4 cohorts-new onset, extra-renal flare, active lupus nephritis, prevalent- and will follow them over 5 years. Participants are recruited from 24 sites across the LRA Lupus Clinical Investigators Network. The registry includes medical information (full medical, familial autoimmune, serological, medications, vaccination history), clinician-

reported outcomes (SLEDAI-Flare Index, SLICC/ACR Damage Index, neuropsychiatric SLE, SLEDAI-2K, PGA-VAS), and patient-reported outcomes (sociodemographic, health habits, SLAQ, PROMIS, Lupus Erythematosus Quality of Life). The biorepository includes genomic DNA, RNA, plasma, serum, PBMC[AK1] , urine, saliva, stool and tissue. The data exchange platform is a federated Trusted Research Environment (TRE) that aggregates datasets and provides a high-performance infrastructure with portals for researcher and patient communities. The researcher portal allows for biospecimen search and data mining using native analytical tools, while the patient community portal allows individuals to view their study data with supportive interpretative services and to connect with other patients. Raw data from biospecimen analyses will be deposited in the TRE, amassing a deep and comprehensive dataset over time.

Table 1. Steering Committee and Working Group overview

Committee	Number of members	Composition
Steering Committee	11-14	36% academic, 36% industry, 28% government/non-profit/patient advocate
Working Groups		
Registry	15	80% academic, 20% industry
Biorepository	12	58% academic, 42% industry
Technology Oversight	9	22% academic, 78% industry
Patient Recruitment, Diversity and Engagement	9	100% patient advocate
Return of Research Results to Study Participants	11	63% academic, 10% industry, 27% patient advocate
Biospecimen Analyses	11	73% academic, 27% industry
Access and Publication	11	73% academic, 9% industry, 18% non-profit
NPSLE Assessment	5	80% academic, 20% industry

Results: As of 11/04/24, there are 174 participants enrolled into the registry (Table 2). Actual enrollment in the 4 cohorts is 10% new onset, 18% active lupus nephritis, 25% extra-renal flare, and 46% prevalent cases, with 35% Black patients, 20% Hispanic/Latino patients, and 12% Asian/Pacific Islander patients. Over 2200 unique samples (subject x timepoint x sample type) have been collected and plans are underway for specific biomarker analyses to stimulate broader community utilization.

Table 2. Recruitment demographics

Recruitment by Sex/Gender			
	Actual %	Target %	Difference %
Female	83	90	-7
Male	13	10	3
Transgender	1	n/a	n/a
Unknown	3	n/a	n/a
Recruitment by Cohort			
Extra-Renal	25	≥26	-1
Ln-Active	18	≥27	-9
New-Onset	10	≥17	-7
Prevalent	46	≤25	21
Cohort assignment in adjudication	1	n/a	n/a
Recruitment by Race			
Black	35	≥31	4
American Indian/Alaska Native	1	≥3	-2
Asian/Pacific Islander	12	≥6	6
White	35	≤60	-25
Other	3	n/a	n/a
Unknown	13	n/a	n/a
Recruitment by Ethnicity			
Hispanic or Latino	20	≥20	0
Not Hispanic or Latino	67	n/a	n/a
Unknown	13	n/a	n/a

Conclusions: LNx is a unique resource for researchers and patients that will help accelerate precision medicine for lupus (www.lupusnexus.org). The LRA acknowledges the many experts that have contributed to its creation, especially those individuals living with lupus and their care partners.

PV154 / #267

Poster Topic: *AS17 - Miscellaneous*

LONG-TERM OUTCOMES OF POSTNATAL IMMUNOSUPPRESSIVE THERAPY IN CHILDREN WITH CARDIAC NEONATAL LUPUS ERYTHEMATOSUS

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Background/Purpose: Neonatal lupus erythematosus (NLE) is a passively acquired autoimmune condition. The antibody-mediated neonatal heart disease of NLE is associated with a high risk of mortality and adverse health outcomes. Prenatal treatment can slow progression from incomplete to complete heart block and improve neonatal survival. However, the impacts of postnatal immunosuppressant treatment have not been described. This study aimed to describe the outcomes of children with antibody-mediated cardiac NLE treated with postnatal therapy.

Methods: We reviewed patients consented from the NLE clinic in a tertiary pediatric center, born between January 1, 1997 – June 10, 2024. We identified patients with cardiac manifestations who received postnatal immunosuppressants. The protocol typically included one dose of intravenous immunoglobulin (IVIG) 2g/kg, pulse corticosteroid of 30 mg/kg/day for 3 days, followed by 2mg/kg/day for 4 weeks with tapering guided by troponin levels. We reviewed medical records with long-term outcomes supplemented by patient/parent questionnaires. We report the prevalence of features and outcomes using summary statistics.

Results: We reviewed 33 patients with cardiac manifestations of NLE and postnatal therapy. Of the total cohort, 28 (85%) mothers received prenatal immunosuppressive therapy with dexamethasone, IVIG and/or a beta agonist. The median duration of follow-up was 6.04 years (IQR: 2.47 – 11.36 years). The majority (70%) of patients presented with heart block at birth (first-degree/second-degree atrioventricular block [n=7], complete heart block [n=16]). The remaining 10 patients had extranodal manifestations of cardiac inflammation, including echogenic endocardium and valvular regurgitation. All the patients received corticosteroids, 17 with pulse and 28 received IVIG. Of the 7

patients with first or second-degree block at birth, 4 progressed to complete heart block within an average of 11 months. One patient with first degree block had complete reversal to normal sinus rhythm. Of the 18 (70%) patients that required a permanent pacemaker, 83% were paced within the first year of life. Of all patients that developed complete heart block in their lifetime, two never required pacing (age at last follow-up 17.38 and 19.25 years). None of the patients required a heart transplant. Three patients developed device-associated or sternal wound infections an average of 1.1 months after birth. Mortality in the cohort was 9% with cause of death attributed to circulatory shock due to sepsis and an unrelated genetic syndrome.

Conclusions: We report on the outcomes of a large series of children with cardiac NLE who received postnatal immunosuppressive therapy. The vast majority of patients had good outcomes. The 9% mortality is improved upon historical reports ranging from 13-30%. Postnatal immunosuppressive therapy may be responsible for improved cardiovascular outcomes in children with antibody-mediated neonatal heart disease.

PV155 / #552

Poster Topic: *AS17 - Miscellaneous*

IDENTIFYING STEREOTYPES AMONGST EARLY TRAINEES FOR PATIENTS SYSTEMIC LUPUS ERYTHEMATOSUS

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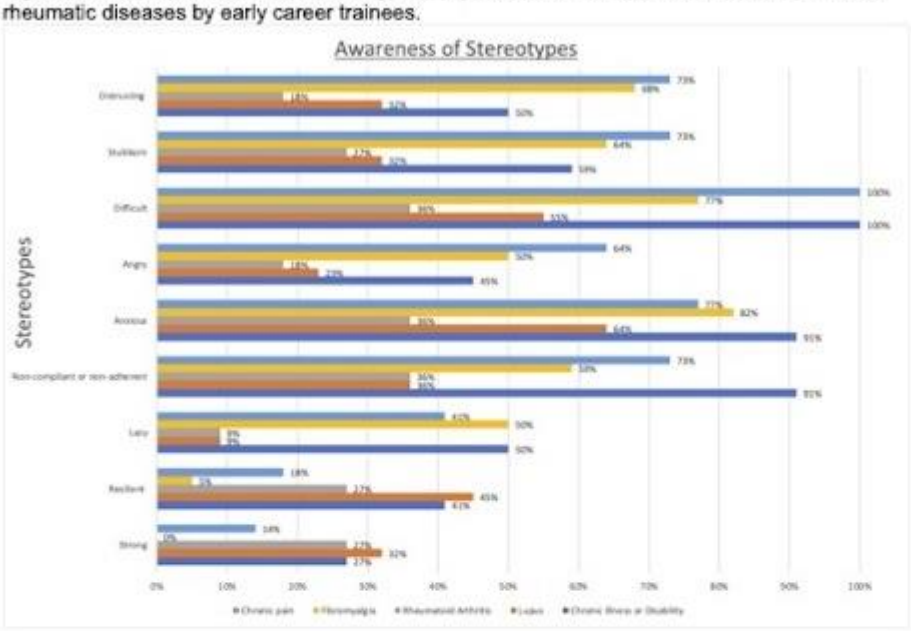
Background/Purpose: Stereotyping and bias are common in medical care, especially for patients with chronic health conditions or from marginalized backgrounds. While there is extensive research on bias in conditions like fibromyalgia and chronic pain, less is known about how these biases impact patients with autoimmune rheumatic diseases, such as systemic lupus erythematosus (SLE). These patients often face significant health disparities and may encounter bias that contributes to delayed diagnosis and treatment. The primary objective of this study was to document stereotypes of patients with SLE in early career trainees.

Methods: Between April and May 2024, Internal Medicine Residents at university teaching hospital were invited via email to participate in a voluntary, anonymous survey on trainee bias, stereotyping, and knowledge of common rheumatic diseases. After consenting, participants answered questions assessing their awareness of stereotypes commonly heard about patients with SLE, rheumatoid arthritis, fibromyalgia, and chronic pain. Respondents were also presented with four clinical vignettes, validated by rheumatologists, to assess their management of patients with suspected SLE. The vignettes tested diagnostic accuracy, treatment choices, and management of complications. Participants provided demographic information, including training year, post-training plans, and whether they identified as having a chronic illness or disability. Only respondents who completed the entire survey were included in the analysis.

Results:

Figure 1. Awareness of common stereotypes for patients with chronic illness and autoimmune rheumatic diseases by early career trainees.



A total of 75 internal medicine residents were sent the survey, with 22 completing the survey in its entirety (29% response rate). Respondents demonstrated varying levels of awareness regarding stereotypes associated with chronic illnesses (Figure 1). For SLE, participants largely were aware of positive stereotypes, with resilience (45%) as a commonly heard stereotype and 32% as strong, though 36% identified a stereotype of non-compliance and 64% recognized anxiety as a stereotype in patients with lupus. For

rheumatoid arthritis, respondents recognized a mix of stereotypes, with 27% associating strength or resilience with patients, while 36% indicated a stereotype of non-compliance and only 9% referenced laziness. Respondents frequently associated fibromyalgia with non-compliance (59%) and laziness (50%), with limited awareness of resilience (5%) or strength (0%). Chronic pain was similarly linked to non-compliance (73%) and laziness (41%), with some awareness of resilience (18%) and strength (14%). For general chronic illness or disability, non-compliance (91%) and laziness (50%) were common stereotypes, though awareness of resilience (41%) and strength (27%) was also noted. For all disease states respondents indicated that females experience more distressing symptoms than male patients. In knowledge-based questions aimed at assessing the residents as primary care physicians perspective, 59% of respondents correctly identified appropriate timing for referring a patient to rheumatology, 32% referred a patient with a severe lupus flare to the emergency department for urgent evaluation, 82% accurately determined when to order an ANA, and 82% correctly recognized when to treat and monitor the patient in the primary care office.

Conclusions: Early-career trainees are aware of stereotypes commonly held by clinicians about chronic illnesses. Negative stereotypes, such as non-compliance and laziness, are particularly prevalent for fibromyalgia and chronic pain, whereas lupus and rheumatoid arthritis are more often associated with positive traits like resilience and strength. By identifying these biases, the research underscores the need for targeted interventions to reduce disparities and support equitable care for patients with autoimmune rheumatic diseases.

PV156 / #327

Poster Topic: *AS17 - Miscellaneous*

AUTOIMMUNE DISEASE PREVALENCE IN PEOPLE LIVING WITH HIV AT CIPTO MANGUNKUSUMO GENERAL HOSPITAL: A COHORT STUDY

Suzy Maria[1,2], Evy Yunihastuti[1,2], Megandhita Sharasti[1], Alvina Widhani[1,2], Bramantya Wicaksana[1,2], Sukamto Koesnoe[2], Anshari Hasibuan[1,2], Monika Herliana[1]
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Background/Purpose: Infection is one of the risk factors for developing autoimmune diseases (AD). Apart from Cytomegalovirus and Epstein-Barr virus infections which are often associated with AD pathogenesis, Human Immunodeficiency Virus (HIV) infections which have become epidemics may also play a role in triggering the occurrence of AD. Moreover, after HIV infection can be controlled with antiretroviral therapy (ART) which increases life expectancy for people living with HIV (PLHIV), the recovery of the immune system may have an impact on the emergence of AD manifestations. This research aimed to examine the prevalence and profile of AD in PLHIV.

Methods: It is a retrospective cohort study in the HIV and Infectious Diseases Integrated Service Installation, Dr. Cipto Mangunkusumo General Hospital from January 2012 to June 2024. We included all HIV patients aged 18 years old and above who were diagnosed with systemic or organ-specific AD. All data were collected from electronic and paper-based medical records. We collected the diagnosis based on ICD-10 written in the medical records.

Results: Of the 4235 HIV patients included in the cohort, only 61 patients (1.3%) were confirmed to have AD. As many as 55.6% were women and the mean age was 36.0 years. Only a few patients have co-infection with hepatitis B or Hepatitis C. Demographic characteristics are shown in table 1 **Table 1.** Demography characteristics of the study

Characteristics

CD4 count when diagnosed with autoimmune disease

< 200 cells/mm3

200-350 cells/mm3

>350

No data

Viral load when diagnosed with autoimmune disease

< 40 copies/ml

≥ 40 copies/ml

No data

The interval of ART initiation to the diagnosis of autoimmune disease
Median (min-max) = 24.0 months (0–180)

<3 months

3 months-1 year

1-5 years

>5 years

Manifested before ART initiation

Coinfection

Hepatitis B Virus

Hepatitis C Virus

The most common AD were Graves disease (n=14), systemic lupus erythematosus (n=9), psoriasis vulgaris (n=7), axial spondyloarthritis (n=5), and antiphospholipid syndrome (n=4). Seven patients were presented with two ADs. Systemic AD were diagnosed more after >5 years following ART initiation (12 patients) and before ART initiation (11 patients), while organ-specific AD were diagnosed more in 1-5 years following ART initiation (12 patients) and before ART initiation (8 patients) (figure 1a and 1b).

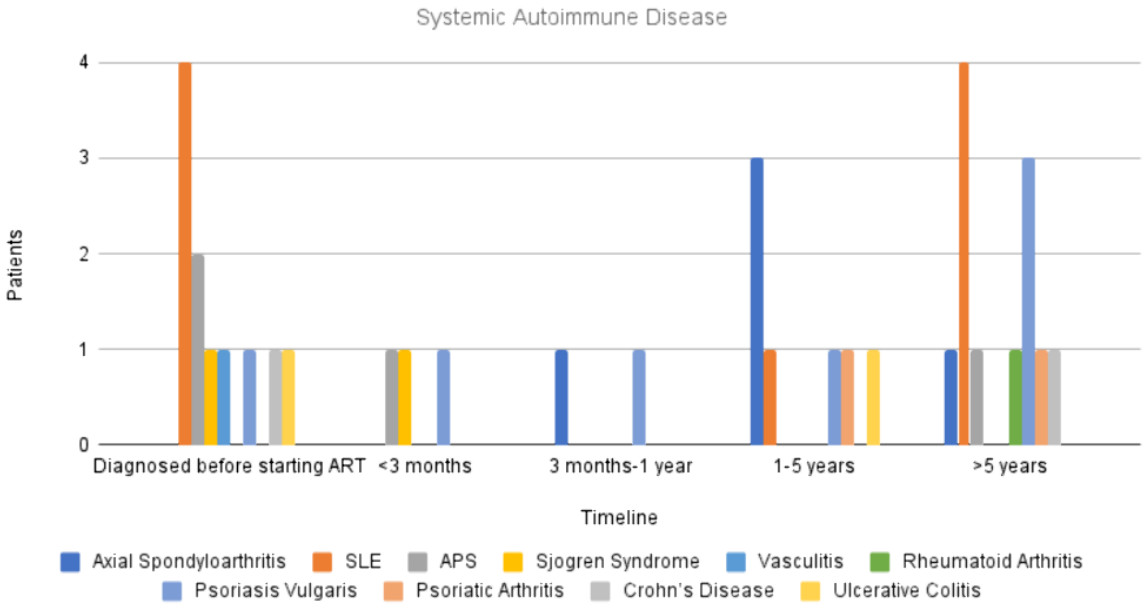

Figure 1a. Systemic AD: Diagnosis Interval from ART Initiation

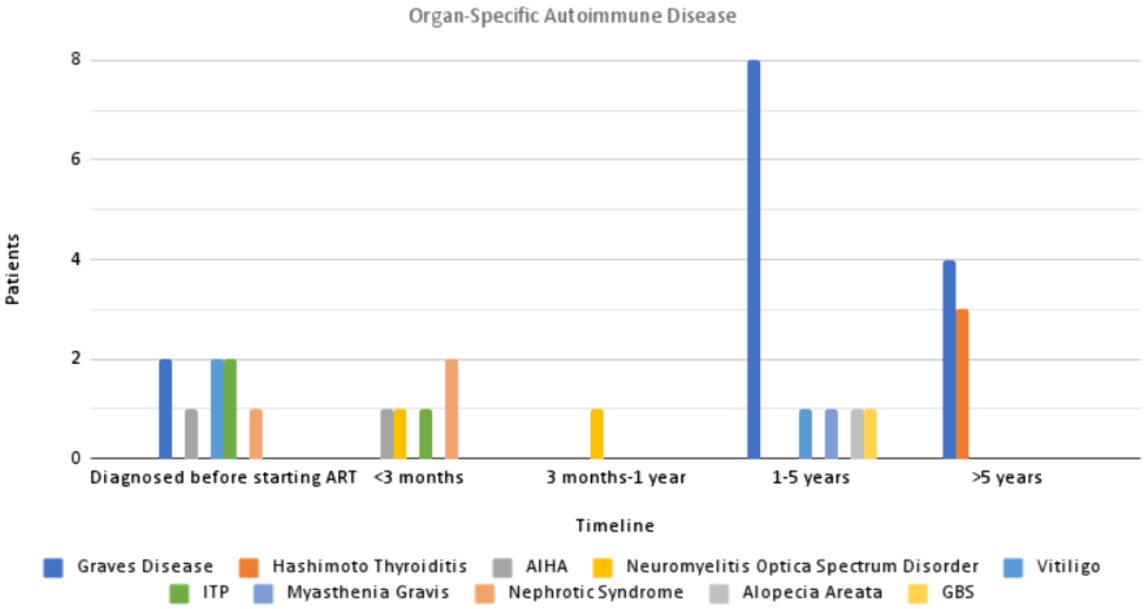

Figure 1b. Organ-Specific AD: Diagnosis Interval from ART Initiation SLE: Systemic lupus Erythematosus, APS: Antiphospholipid Syndrome, AIHA: Autoimmune Hemolytic Anemia, ITP: Idiopathic Thrombocytopenic Purpura, GBS: Guillain-Barré syndrome Six female patients and one male patient were presented with two AD. These female patients were diagnosed with 1) APS and crohn's disease, 2) psoriasis vulgaris and psoriatic arthritis, 3) psoriatic arthritis and rheumatoid arthritis, 4) Graves disease and Sjogren's syndrome, 5) AIHA and SLE, and 6) APS and SLE. Besides, one male patient was diagnosed with Graves disease and ITP.

Conclusions: AD in PLHIV in this cohort was rare. Graves' disease was the most common organ-specific AD and was most commonly diagnosed at >1 year following ART initiation. SLE was the most common systemic AD and was most commonly diagnosed at >5 years following ART initiation and before ART initiation. Multiple AD was found in a small percentage of patients.

PV157 / #280

Poster Topic: ***AS18 - Paediatric SLE***

LONG-TERM OUTCOMES OF PATIENTS WITH PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (PSLE) TREATED WITH COMBINATION RITUXIMAB AND CYCLOPHOSPHAMIDE: A SINGLE CENTER COHORT AND REVIEW OF LITERATURE

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Background/Purpose: Patients with pSLE with life/organ threatening manifestations are treated with a protocol of rituximab and cyclophosphamide at our institution as previously described. [1] However, the few published reports of the systematic administration of rituximab and cyclophosphamide in pSLE lacked representation of Black patients and/or evaluation of long-term damage indices beyond 1-2 years. We aimed to evaluate long-term Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores, exposure to steroids, and Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Indices of patients with pSLE treated with a systematic administration of rituximab and cyclophosphamide.

Methods: Retrospective review of medical records between 2013-2023 of patients diagnosed with severe SLE at ≤ 18 years old and treated with rituximab and cyclophosphamide for life/organ threatening manifestations with at least 1 year of follow-up were found (Table 1). Case records were analyzed for clinical symptoms, physical exam findings, and laboratory and imaging results associated with SLE. Descriptive statistics were calculated with continuous variables as means and categorical variables as percentages. A PubMed search for articles published after 2000 was performed using search terms “cyclophosphamide and rituximab” AND “systemic lupus erythematosus” AND “pediatric patients OR children OR adolescents” to compare prior studies with our cohort.

Results: Eleven patients met eligibility criteria. Nine of the eleven patients completed sixty months of follow up. The most common symptoms and clinical manifestations of disease included anemia in eight patients (73% of cohort), mucocutaneous findings of malar or discoid rash as seen in seven patients (64% of cohort), and proteinuria and renal disease ultimately diagnosed as Class III-V lupus nephritis in eight patients (73% of cohort) prior to initiation of the Rituximab and Cyclophosphamide protocol. The most severe manifestations included altered mental status due to lupus cerebritis, wet gangrene of the lower extremity requiring trans-metatarsal amputation, and lupus pneumonitis leading to ARDS and multi-system organ failure requiring ECMO. Mean prednisone dose and mean SLEDAI scores decreased significantly over follow-up periods, and we achieved low disease activity in all our patients as defined by SLEDAI score < 4 and prednisone dose < 7.5 mg/day in all our patients (Figure 1). There was no

statistically significant difference between SLICC/ACR damage indices over time. No difference in outcomes between races was seen. Our literature review resulted in seven studies, which varied from case reports (n = 1) to small cohorts (n = 17). We compared our results to those seen in the studies whose population included more than 10 patients (Table 1). Our cohort had a more diverse population, including multiple Black patients, compared to previous studies [1] and included longer-term mean outcomes than earlier studies (51 months versus 10 months, respectively). [2] Despite some variability in dosing, all studies reported improvement of disease activity and relatively low incidence of infections.

Figure 1a. Mean Prednisone Doses Over Time

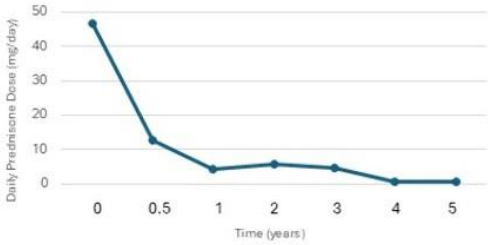


Figure 1b. Mean SLEDAI Scores

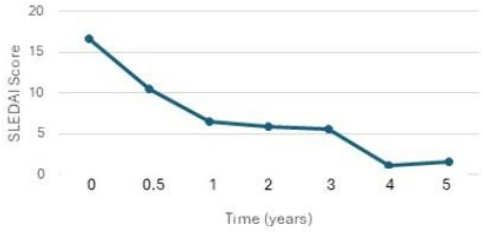
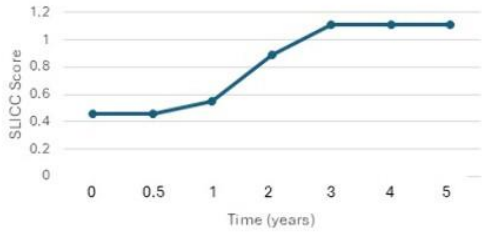


Figure 1c. Mean SLICC Scores



Cohort by Author, Year	Stony Brook Children's Hospital Cohort between 2013-2023	Lehman et al., 2014 [1]	Ale'ed et al., 2013 [2]
Number of included patients (n)	11	12	16
Mean age (years) [range]	12.5 years [5-18 years]	12.5 years at diagnosis [10-28 years at start of protocol]	8.1 years [5-11.5 years]
Sex (female: male)	8:3	9:3	13:3
Race (n)	Black/African-American (6) Caucasian (2) Hispanic (2) Asian (1)	Caucasian Hispanic Asian	Middle Eastern
pSLE life/organ threatening manifestation	Stage III-V Lupus Nephritis (n = 10) Neuropsychiatric lupus (seizures, n = 1 and lupus cerebritis, n = 1) Multisystem organ failure due to lupus pneumonitis (n = 1) Peripheral vascular disease resulting in wet gangrene and trans-metatarsal amputation (n = 1)	Diffuse Proliferative Glomerulonephritis (DPGN)	Nephritis Refractory arthritis Thrombocytopenia Severe mucocutaneous lesions CNS involvement
Treatments prior to combination rituximab and cyclophosphamide	Mycophenolate mofetil (n = 3) Mycophenolic acid (n = 1) Azathioprine (n=1) Hydroxychloroquine (n = 1)	Mycophenolate mofetil or Cyclophosphamide (alone)	Azathioprine, Mycophenolate mofetil, Cyclophosphamide, Cyclosporine or Methotrexate
Rituximab and cyclophosphamide dosing/timing	All patients: Day 0, 14 and Months 6, 18: Rituximab 750 mg/m² (max 1 gram) Day 1, 15 and Months 6, 18: Cyclophosphamide 750 mg/m² Patients with active DPGN: Cyclophosphamide 750 mg/m² at 6, 10, 14, and 18 weeks	All patients: Day 0, 14 and Months 6, 18: Rituximab 750 mg/m² (max 1 gram) Day 1, 15 and Months 6, 18: Cyclophosphamide 750 mg/m² Patients with active DPGN: Cyclophosphamide 750 mg/m² at 6, 10, 14, and 18 weeks	All patients: Day 1, 15: Rituximab 375 mg/m² Day 2, 16: Cyclophosphamide 500 mg/m² 1 cycle: 12 patients 2 cycles: 2 patients 4 cycles: 2 patients
Long-term clinical outcomes	Mean SLEDAI score decreased from 16.6 to 1.6 (p < 0.001) (n = 9). Mean prednisone dose decreased to < 10 mg/day (n = 11) Off all immunosuppressive medications after protocol completion (n = 6) Successful term pregnancy (n = 1) Required dialysis (n = 1) Required dialysis and ultimately deceased donor renal transplant (n = 1)	Mean SLEDAI score decreased from 10.10 ± 5.9 to 1.0 ± 1.8 at 1 year (p < 0.005) and 0 at 5 years (p < 0.005) Mean daily prednisone dose decreased from 29.7 ± 24 mg/day to 12.7 ± 4.1 mg/day at 1 year (p < 0.05) and 7.0 ± 2.5 at 5 years (p < 0.005) Mean C3 increased from 55.5 ± 27mg/mL to 113 ± 32 mg/mL at 1 year (p<0.001) and 107.5 ± 36 at 5 years (p<0.001)	Mean SLEDAI score decreased from 15.31 ± 8.55 to 6.56 ± 4.98 6 months post-treatment (p = 0.0002) Mean daily corticosteroid dose decreased from 0.3 ± 0.19 mg/kg/day to 0.14 ± 0.11 mg/kg/day (p = 0.005) Mean C3 increased from 0.69 ± 0.36 to 1.03 ± 0.42 (p = 0.003) Mean C4 increased from 0.11 ± 0.07 to 0.17 ± 0.12 (p = 0.01)
Mean follow up period [range]	51 months [12-60 months]	60 months [60 months]	10 months [6-42 months]
Adverse Effects	Anaphylaxis to Rituximab (n = 2) Delayed cyclophosphamide due to cytopenia (n = 3)	Febrile neutropenia (n = 2)	Haemophilus influenzae bacteremia with concurrent ankle osteomyelitis (n = 1) Severe soft tissue fungal infection (n = 1) Pancreatitis (n = 1) Infusion-related reaction (n = 2)

Conclusions: Our racially diverse cohort shows the efficacy of systematic administration of rituximab and cyclophosphamide in decreasing disease activity scores and decreasing overall exposure to steroids in pSLE. Long-term organ damage was not seen 5 years after treatment in our cohort, further emphasizing disease control with early aggressive therapy. This protocol was well-tolerated. Larger, prospective randomized clinical trials are needed for further validation. **References:** [1] Lehman, T.J., et al. Pediatr Rheumatol Online J 2014;12:3. [2] Ale'ed, A., et al. Rheumatol Int 2014; 34:529-33.

PV158 / #289

Poster Topic: ***AS18 - Paediatric SLE***

ELUCIDATING COGNITIVE IMPAIRMENT IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Samara Sepresse[1], Taís Mazzola[1], Ana Carolina Capelli Alencar[1], Mariana Da Silva Lucino[1], Bruna De Aquino[1], Franciele De Lima[1], Jaqueline De Amorim[1], Paulo Julio[1], Danilo Pereira[1], Renan Frittoli[1], Roberto Marini[1], Leticia Rittner[1], Diedre Camargo[1], Timothy Niewold[2], Zahi Touma[3], Simone Appenzeller[1]
[1]University of Campinas, Campinas, Brazil, [2]Hospital of Special Surgery, Campinas, United States of America, [3]University of Toronto, Toronto, Canada

Background/Purpose: Childhood-onset systemic lupus erytthematosus (cSLE) is characterized by a more severe disease and a high frequency of neuropsychiatric manifesttaions. Especially cognitive impairment (CI) is observed in around 40% of cSLE patients and associated with worse outcome in adult life. Here, we aimed to pursue the associations among serum cytokines, anti-P antibodies, the NMDA receptor antibodies, magnetic ressonance imaging findings in cSLE patients with or without CI.

Methods: We did a cross-sectional study including consecutive cSLE patients with well characterized clinical and laboratory data. We evaluated CI through Pediatric-Automated Neuropsychological Assessment Metrics (Ped-ANAM). All included subjects had MRI performed with a 3T Philips Achieva (Best, The Netherlands). Sagittal T1-weighted images (3-dimensional acquisitions obtained in the sagittal T1-weighted gradient echo plane with 1 mm thickness, an angle of excitation of 35, a repetition time of 22 ms, a time to echo of 9 ms, a matrix of 240 × 240 pixels, a field of view of 230 × 250 cm, 1 × 1 pixel). MRI were analyzed using FreeSurfer and volBrain softwares. The concentration of cytokines was determined by Luminex immunoassay (MILLIPLEX map Human High Sensitivity T Cell Panel, Millipore, USA) according to the manufacturer's protocol. The limit of detection was 0.48pg/mL for IFN-gamma, 1.12pg/mL for IL-4, 0.11pg/mL for IL-6, 0.56pg/mL for IL-10, 0.15pg/mL for IL-12 (p70) and 0.16pg/mL for TNF. When the concentration was undetectable, it was attributed the half of these values for statistical purposes. The concentration of NMDA NR-2 subunit receptor was determined by Enzyme-Linked Immunosorbent Assay (ELISA, Mybiosource, CA, USA) according to the manufacturer's protocol, with the limit of detection of 0.09ng/mL. The presence of anti-P was determined by Enzyme-Linked Immunosorbent Assay (ELISA, Quanta Lite™ Ribosome P, Ivona, CA, USA) according to the manufacturer's protocol, and samples were classified as negative or positive. The Statistical Package for the Social Sciences software (IBM SPSS, version 22) was used for analysis.

Results: Eighty-five cSLE patients were included. There was no significant difference regarding the dosages of cytokines, NR-2 and anti–P in patients with or without CI.

Patients with CI had impaired scores on eight subtests and three indexes from Ped-ANAM. Also, the volumes of Central (p=0.035) and Mid Anterior (p=0.016) Corpus Callosum were significantly lower in the group with CI (p=0.045). NR-2 concentration correlated inversely with SLEDAI scores (p=0.021) and with the Cornu Ammonis 1 (CA1) volume (p=0.029). IL-4 correlated inversely with the Ped-ANAM scores (p=0.033), IL-10 correlated inversely with Total CA2 CA3 (p=0.012) and right CA2 CA3 volumes (p=0.014) and directly with Left Caudate volume (p=0.026). Also, IL-6 correlated inversely with Right CA2 CA3 volume (p=0.047).

Conclusions: Simple reaction time and procedural reaction time were the cognitive domains more often affected in cSLE patients with CI. We observed a significant reduction of corpus callosum and hippocampal subfields in cSLE associated with the presence of NR2 and inversevly with IL6, sugessting that autoantibodies and cytokines may be associated with structural brain abnormalities and CI in cSLE.

PV159 / #51

Poster Topic: ***AS18 - Paediatric SLE***

PERFORMANCE OF VALIDATED CARDIOVASCULAR RISK SCORES IN A GLOBAL (UK/US) COHORT OF YOUNG PEOPLE WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS STRATIFIED BASED ON CROSS-VALIDATED METABOLOMIC SIGNATURES

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Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) is associated with increased cardiovascular disease risk (CVD-risk) starting early in life. As a consequence, 4% of children and young people (CYP) with cSLE recruited to a large UK study experienced at least one CVD-event 2 years post diagnosis, at a median age of 16 years. The APPLE trial, a large interventional clinical trial in cSLE, evaluated the efficacy of atorvastatin in decreasing atherosclerosis progression in CYP aged 10-18 years, using serial carotid intima-media thickness (CIMT) measurements. Although the trial did not meet the primary endpoint, it provided the opportunity to discover a novel serum metabolomic signature associated with a high rate of atherosclerosis progression.

Methods: We explored the comparative performance of four age-appropriate and validated CVD-risk scores in a global cSLE (UK/US) cohort. Demographic data, CVD-risk factors and cSLE characteristics were collected cross-sectionally from two cSLE cohorts: a retrospective UCL (University College London) cohort (N=109, UK) and a prospective APPLE trial cohort (N=121) cohort, both stratified based on the metabolomic signature of high CIMT progression, we previously identified in the APPLE trial. QRISK-3, Framingham (FRS), Atherosclerotic Cardiovascular Disease (ASCVD) scores (validated for age 20-25) and the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) score (validated from age ≥14) were calculated and assessed for performance against cross-validated metabolomic signatures of CIMT progression. We used descriptive statistics, area under the curve (AUC), and linear regression analyses.

Results:

LE patient cohorts stratified sed on cross-validated etabolomic signatures of CIMT ogression	The UCL cohort (N=109) was stratified as: 29.2% low 48.3% moderate, and 22.5% high CVD-risk N (%)	The APPLE cohort (N=12 was stratified as: 28.5% low, 42.4% moderate, an 29.1% high CVD-risk N (%
RISK-3 SCORE (N)	109	119
ry low QRISK-3 risk <5%	92 (84.4%)	98 (82.3%)
w QRISK-3 risk = 5-9.9%	8 (7.3%)	16 (13.4%)
derate QRISK-3 risk = 10-19.9%	2 (1.8%)	3 (2.5%)
gh QRISK-3 risk >20%	7 (6.4%)	2 (1.7%)
S SCORE (N)	80	119
ry low FRS <5%	80 (100%)	119 (100%)
w FRS = 5-9.9%	0	0
derate FRS =10-19.9%	0	0
gh FRS >20%	0	0
CVD SCORE (N)	62	80
w ASCVD risk <5%	60 (96.8%)	73 (91.1%)
derate ASCVD risk = 5-7.4%	1 (1.6%)	3 (3.8%)
gh ASCVD risk = 7.5-20%	1 (1.6%)	4 (5.0%)
AY SCORE (N)	78	116
ry low PDAY score <2 points	6 (7.7%)	84 (72.4%)
w PDAY score = 2-5 points	21 (26.9%)	22 (19.0%)
derate PDAY score = 6-10 points	17 (21.8%)	6 (5.2%)
gh PDAY score>10 points	34 (43.6%)	4 (3.5%)

All scores had very low performance against CVD-risk metabolomic stratification. The PDAY-score performed best, with 67% specificity, but 50% sensitivity, in correctly classifying CYP with high CVD-risk, and only in the slightly older UCL cohort. Linear regression analysis found that age/disease activity were the strongest determinants of

PDAY-score (one year increase in age/one point increase in median SLEDAI-2K score over the disease course were associated with 1.13/0.41 points increase in PDAY-score, respectively, when corrected for sex/disease duration/damage/lipid levels/steroids).

Conclusions: In conclusion, in this large study, CVD-risk scores, even if validated for ages ≥14, do not adequately capture CVD-risk in adolescents with cSLE (APPLE trial cohort). PDAY-score performed moderately well for young adults only (UCL cohort), highlighting the need for better CVD-risk stratification tools. Future research is warranted for optimised CVD-risk identification/management in cSLE.

PV160 / #31

Poster Topic: ***AS18 - Paediatric SLE***

PROSPECTIVE IMPLEMENTATION OF T2T STRATEGIES IN ADOLESCENTS AND YOUNG ADULTS WITH CHILDHOOD ONSET SYSTEMIC LUPUS ERYTHEMATOSUS LED TO IMPROVED DISEASE CONTROL AND MINIMISED DAMAGE ACCRUAL

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Background/Purpose: Treat-to-target (T2T) strategies aim to facilitate tight disease control. No previous studies evaluated prospectively the feasibility and impact of active implementation of T2T strategy at every routine clinical appointment in adolescents and young adults (AYA) with childhood-onset SLE (cSLE).

Methods: AYA with cSLE were recruited for T2T implementation from a large tertiary centre over a period of 6 months, and followed up at least twice over a prospective period of 12 months. The study had the following design: 1. The first phase of the study was a 6-month cross-sectional evaluation of the feasibility to implement and systematically document routine outcome measures in AYA with cSLE. At the end of this phase, only AYA with cSLE and complete data collection including disease activity evaluation as well as treatment target assessment and documentation, were included. 2. The second phase of the study was a 12-month prospective evaluation of disease control against the agreed cSLE target between the baseline assessment and the final timepoint (last routine clinic appointment during the 12-month study follow-up period). In support of our project design robustness, a preliminary sample size calculation was undertaken, which showed that we needed to include at least 115 individuals to be able to detect with 90% confidence and 80% power, a 10% improvement in the proportion of AYA with cSLE achieving LLDAS after 12 months of active T2T strategy implementation.

Results: During Oct 2022-April 2023, 135/162 (83.3%) AYA with cSLE had disease scores evaluated at their routine appointment to enable inclusion in the study and 122/135 (91.2%) had their disease assessed, and a suitable treatment target agreed and documented at each routine clinical appointment over the following 12 months. T2T strategy led to improved disease: more AYA with cSLE achieved clinical remission off steroids (4.1% vs. 10.7%, P=0.048), or minimum childhood-lupus low disease activity (cLLDAS) (81.9% vs. 91.8%, P=0.022) (Table). Achieving minimum cLLDAS for longer than 3 months was associated with reduced damage accrual (HR=1.7; 95%CI=1.1-2.5; P<0.0001) and a trend in flare risk improvement (HR=1.6, 95% CI=0.98-1.4; P=0.06) after 12 months.

Table: Assessment of disease states at the time point of agreeing a treatment target (baseline) and after 12 months routine follow-up

Treatment target achievement at baseline vs. 12 months (median 3 routine follow-ups/AYA)	N=122 At baseline 100/122 in target	N=122 At last assessment 112/122 in target	P value
Complete remission off steroid treatment	13 (10.6%)	17 (13.9%)	0.43
Complete remission on steroid treatment	34 (27.8%)	32 (26.2%)	0.77
Clinical remission off steroid treatment	5 (4.1%)	13 (10.7%)	0.048
Clinical remission on steroid treatment	29 (23.8%)	39 (31.9%)	0.158
cLLDAS	19 (15.5%)	11 (9%)	0.121
Not on target because of moderate flare	5 (4.1%)	2 (1.6%)	0.24
Not on target because of severe flare	5 (4.1%)	5 (4.1%)	0.99
Not on target despite no significant clinical activity recently	12 (9.8%)	3 (2.5%)	0.017
AYA with cSLE in target (minimum cLLDAS)	100 (81.9%)	112 (91.8%)	0.022

We found a positive correlation between the damage (pedSDI) score and cumulative steroid dose (median dose = 615 mg) over the 12-month prospective evaluation (ro=0.37, p=0.04).

Conclusions: This is the first large prospective study in AYA with cSLE which showed that T2T strategy implementation was achievable in routine practice and led to an improved proportion of AYA 'in target'. Spending at least 3/12 months in cLLDAS led to less damage accumulation over 12-month follow-up.

PV161 / #509

Poster Topic: ***AS18 - Paediatric SLE***

INVESTIGATING THE GENETICS OF DEPRESSION IN A MULTI-ANCESTRAL COHORT OF CHILDREN AND ADOLESCENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Patients with childhood-onset systemic lupus erythematosus (cSLE) have a higher prevalence of depression compared to healthy peers. Patients with cSLE also have a 10% greater risk of major depressive disorder (MDD) compared to those with adult-onset SLE (39% vs. 29%). Genetics plays a role in mood disorders and SLE susceptibility. Genome-wide association studies (GWAS) have identified >100 genetic risk variants for each of depression and SLE. The cumulative effects of these variants can be combined into polygenic risk scores (PRS). Our study aims to test the association between genetic risk variants for (1) SLE and (2) MDD with depression, in a multi-ancestral cohort of children and adolescents with SLE.

Methods: We included patients followed in a tertiary care Lupus clinic from January 1, 2000, to December 31, 2023. All patients met ≥4 American College of Rheumatology (ACR) and/or Systemic Lupus International Collaborative Clinics (SLICC) criteria for SLE with data prospectively collected in a dedicated lupus database. Patients were genotyped on an Illumina multiethnic array, with un-genotyped single nucleotide polymorphisms (SNPs) imputed using TopMed as a referent. Ancestry was genetically inferred using principal components (PCs) and ADMIXTURE. We calculated weighted, additive PRSs for: 1) SLE (HLA and non-HLA) and 2) MDD using risk SNPs from the largest GWAS to date. We identified patients with depression as those with a depression diagnosis and/or persistent depressive symptoms over a course of at least two months

prior to or following SLE diagnosis. We tested the association between each PRS and depression in univariate and multivariable-adjusted logistic regression models, adjusted for sex and 5 PCs (P<0.017). We additionally carried out a sensitivity analysis focusing only on patients with a clinical depression diagnosis.

Results: Our study included 491 patients, 84% were female, with a median age of SLE diagnosis of 14 years (IQR: 11-15). There were 64 (13%) patients with a depression diagnosis, 130 (26%) with a depression diagnosis and/or persistent depressive symptoms. The majority of patients were of European (29%) and East Asian (27%) ancestry (Table 1). We did not observe a significant association between PRSs for either SLE (HLA and non-HLA) or MDD and depression (Table 2). Regarding SLE clinical features, the most common was arthritis (68%), followed by lupus nephritis (39%) and neuropsychiatric SLE (NPSLE; 25%). NPSLE was significantly associated with depression in univariate and multivariable adjusted models (OR 2.37, 95% CI 1.51-3.73; *P*=0.0002). Sensitivity analyses demonstrated similar associations between the PRSs and clinical depression.

Conclusions: In a multi-ancestral cohort of children and adolescents with SLE, we did not observe a significant association between genetic loci for SLE and MDD and depression. This may be due to the limited generalizability of European SLE and MDD risk loci to a multi-ancestral population. Our cohort is comparable to prior studies of mood in cSLE as we found a significant association between NPSLE and depression. Future work will examine
anxiety.

Table 1: Demographic characteristics and clinical and laboratory features of cohort (n=491)

Variable	Total n=491	Depression n=130	No Depression n=361
Female sex (n (%))	412 (84)	114 (88)	298 (83)
Age at SLE diagnosis, years (median (IQR))	14 (11-15)	14 (12-16)	14 (11-16)
Genetically Inferred Ancestry (n (%))			
European	144 (29)	42 (32)	102 (28)
East Asian	134 (27)	31 (24)	103 (29)
African	54 (11)	19 (15)	35 (10)
South Asian	51 (10)	10 (8)	41 (11)
Admixed*	108 (22)	28 (22)	80 (22)
Clinical Features (n (%))			
Arthritis	332 (68)	93 (72)	239 (66)
Lupus Nephritis	193 (39)	51 (39)	142 (39)
Neuropsychiatric (NPSLE)	123 (25)	47 (36)	76 (21)
Serositis	68 (14)	22 (17)	46 (13)
Hematologic			
Leukopenia	296 (60)	73 (56)	223 (62)
Thrombocytopenia	132 (27)	39 (30)	93 (26)
Coombs Positive Hemolytic Anemia	168 (34)	54 (42)	114 (32)
Mucocutaneous			
Oral Nasal Ulcers	170 (35)	39 (30)	131 (36)
Malar Rash	376 (77)	99 (76)	277 (77)
Laboratory Features (n (%))			
SLE-specific Antibodies			
Anti-dsDNA antibody	326 (66)	84 (65)	242 (67)
Anti-Smith antibody	165 (34)	44 (34)	121 (34)
Antiphospholipid Antibodies			
Anti-Cardiolipin	171 (35)	42 (32)	129 (36)
Lupus Anticoagulant	72 (15)	22 (17)	50 (14)

Categorical variables are represented by n (%) and continuous variables are represented by median (IQR). The depression category included patients with a diagnosis and/or persistent depressive symptoms. * The admixed category represents patients who had <80% single ancestral proportion and patients of American ancestry (n=19).

Table 2: Univariate and multivariable logistic regression results (n=491)

	Depression Diagnosis and Symptoms		Depression Diagnosis	
	Univariate OR (95% CI) p-value	Multivariable OR (95% CI) p-value	Univariate OR (95% CI) p-value	Multivariable OR (95% CI) p-value
HLA SLE PRS	0.63 (0.38-1.02)	0.53 (0.31-0.87)	0.59 (0.30-1.13)	0.52 (0.26-0.99)
	0.06	0.03	0.12	0.05
Non-HLA SLE PRS	1.03 (0.84-1.25)	0.99 (0.80-1.22)	0.98 (0.85-1.27)	0.87 (0.65-1.16)
	0.80	0.02	0.85	0.36
MDD PRS	1.65 (0.64-4.27)	1.83 (0.54-6.27)	0.30 (0.08-1.10)	0.88 (0.18-4.48)
	0.30	0.33	0.07	0.88

Multivariable logistic regressions were adjusted for sex and 5 PCs. SLE: systemic lupus erythematosus, HLA: human leukocyte antigens, MDD: major depressive disorder; PRS: polygenic risk score.

PV162 / #428

Poster Topic: ***AS18 - Paediatric SLE***

COMPARING PERFORMANCE-BASED MEASURES AND SELF-REPORTED QUESTIONNAIRES FOR ASSESSMENT OF EXECUTIVE FUNCTION FOR YOUTH WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Executive dysfunction is common in childhood-onset systemic lupus erythematosus (cSLE). Comprehensive neuropsychological assessments use both performance-based measures and standardized questionnaires, capturing different cognitive constructs. However, comprehensive assessments are time-consuming, resource-intensive, and often inaccessible. Standardized questionnaires measuring self-rated daily executive function (EF), are brief and easy to administer, with potential clinical utility to identify patients needing comprehensive assessment. The study aimed to examine associations between performance-based measures and self-rating of daily EF in youth with cSLE.

Methods: This cross-sectional study analyzed prospectively collected data from cSLE patients (meeting ACR 1997 or SLICC classification criteria) aged 11-17 years recruited from an outpatient Lupus Clinic from January 2020–December 2023, and age and sex-matched healthy controls. Participants completed the Behaviour Rating Inventory of Executive Function 2nd Edition Self-Report Form (BRIEF-2-SR) assessing daily EF measured by the General Executive Composite (GEC), Behavior Regulation Index (BRI), Cognitive Regulation Index (CRI), and Emotion Regulation Index (ERI). The Delis-Kaplan Executive Function System (D-KEFS) Color-Word Interference Test (CWIT), a performance-based measure, assessed information processing speed (Colour Naming, Word Reading), cognitive inhibition and flexibility (Inhibition, Inhibition/Switching). Correlations were calculated between the BRIEF-2-SR summary scores (GEC, BRI, CRI, and ERI) and scaled scores for performance in the four tasks of the D-KEFS CWIT. Mann-Whitney U tests were used to examine group differences in scores.

Results: There was a total of 58 cSLE participants (84% female; mean age=15.3y ± SD 1.7) and 47 controls (83% female; mean age=14.9y ± SD 1.9) (Table1). For cSLE

participants, worse performance-based scores for cognitive inhibition and flexibility showed statistically significantly correlations with worse self-rated daily EF scores for the GEC, BRI, and ERI (Figure 1). For controls, worse scores for cognitive inhibition and flexibility correlated with worse self-rated daily EF scores for GEC and CRI (Figure 1). Performance-based processing speed scores were not significantly associated with the BRIEF-2 scores in either group. No significant differences were found between cSLE and controls across BRIEF-2-SR indices. On the D-KEFS, cSLE participants displayed significantly poorer performance on Color Naming ($U = 1027$, $p = 0.022$), Inhibition ($U = 1027$, $p = 0.021$), and Inhibition/Switching ($U = 1049$, $p = 0.030$) compared to controls.

Table 1. Demographics and Disease Characteristics		
Demographics	cSLE (n=58)	Healthy Controls (n=47)
Age, mean (SD) years	14.9 (1.9)	15.3 (1.6)
Female, n (%)	49 (84.5)	39 (83.0)
Low-income Families, n (%)	17(29.3)	4 (8.5)
Race / ethnicity, n (%)		
Black/African-American	7 (12.1)	4 (8.5)
Asian	29 (50)	8 (17)
American Indian/Alaska Native	1 (1.7)	-
White	14 (24.1)	30 (63.8)
Other	7 (12.1)	5 (10.6)
Disease Characteristics		
Disease duration in years, median (IQR)	2.0 (1.0 -3.7)	-
SLEDAI, median (IQR)	2 (2-4.2)	-
Active disease (SLEDAI-2K>4), n (%)	14 (24.1)	-
Disease damage (SLICC Damage Index>0), n (%)	5 (8.6)	-

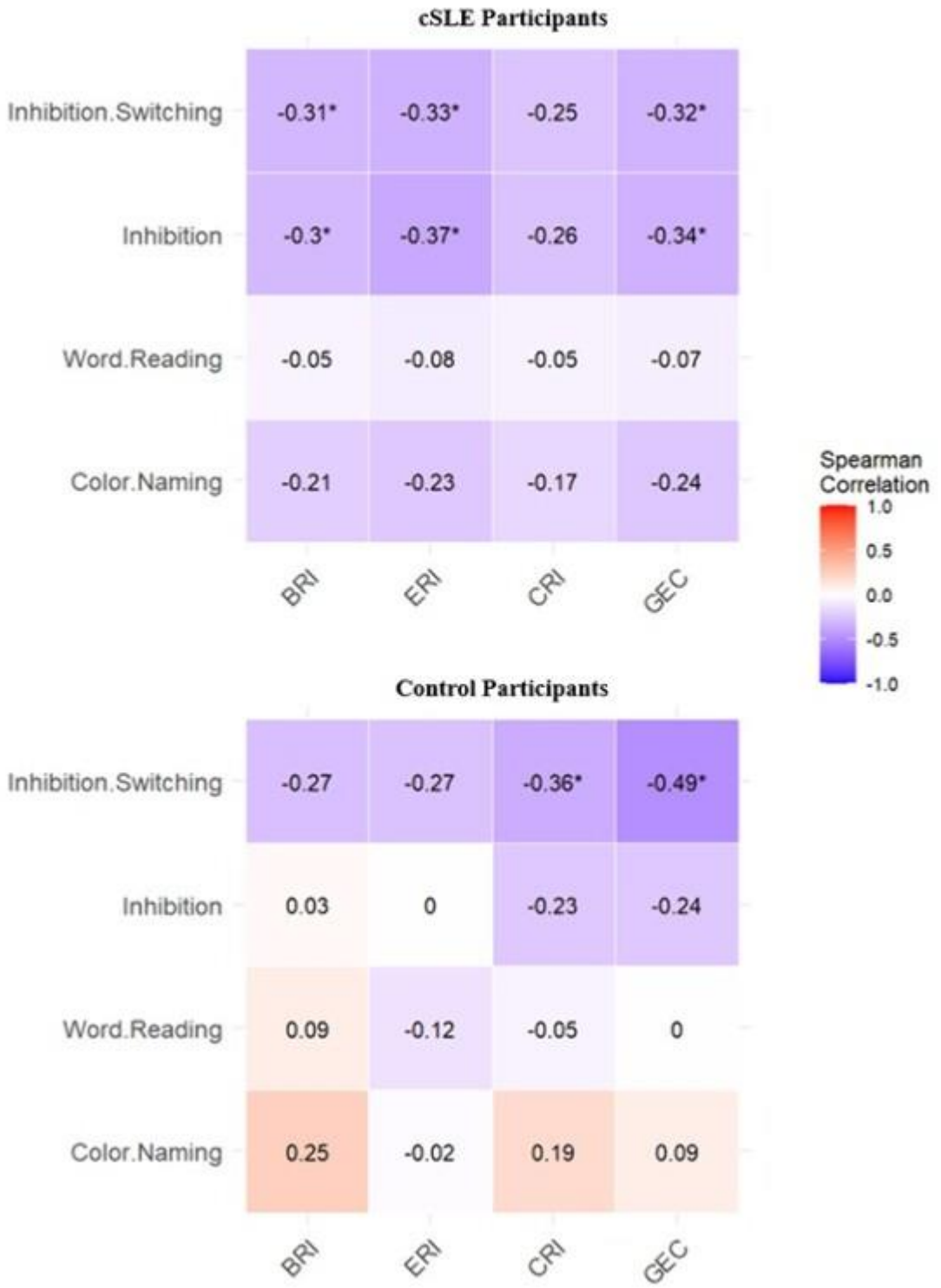

Figure 1: Spearman Rho correlation matrices depicting the associations between BRIEF-2-SR (higher scores indicating worse executive function) and D-KEFS (lower scores indicating worse executive function) measures for childhood-onset systemic lupus erythematosus (cSLE) participants and controls. * Denotes significance ($p < 0.05$)

Conclusions: Youth with cSLE in this cohort had worse performance-based EF measures compared to controls. Performance-based scores for cognitive inhibition and

flexibility correlated with self-rated daily EF scores in both groups, but more consistently across indices in the cSLE group. Further study is needed to determine the utility of questionnaires for self-rated daily EF as efficient screening tools to identify cSLE patients needing comprehensive neuropsychological assessment.

PV163 / #410

Poster Topic: *AS18 - Paediatric SLE*

PRESCRIBING OF MEDICATIONS WITH PHARMACOGENETIC GUIDANCE IN CHILDREN AND ADOLESCENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background/Purpose: Pharmacogenetics (PGx) focuses on the effect of genetic variations on metabolism and response to medications. At this moment, over 100 medications have clinical practice guidelines that provide recommendations on how genetic variations can be incorporated into clinical decision-making to improve efficacy and prevent adverse drug reactions. This study aims to determine how often medications with PGx guidelines are prescribed within a cohort of children and adolescents diagnosed and followed for systemic lupus erythematosus (SLE) at the Hospital for Sick Children Lupus Clinic.

Methods: We completed a retrospective cohort study of patients diagnosed and followed for SLE at SickKids between January 1997 and December 2017. All patients met ACR, SLICC, or EULAR/ACR SLE classification criteria and had clinical and medication data in the dedicated lupus database. We created a list of medications with clinical PGx guidelines (e.g., Clinical Pharmacogenetics Implementation Consortium [CPIC] and Dutch Pharmacogenetic Working Group [DPWG]) or clinical PGx recommendations in FDA-approved drug labels using the Pharmacogenomics Knowledgebase (www.pharmgkb.org). We used descriptive statistics to calculate the number of prescriptions of medications with PGx guidance, the proportion of the total prescriptions to PGx prescriptions, and the time to the first and second instance of PGx prescribing following SLE diagnosis using Kaplan-Meier analysis. Characteristics of the cohort such as age, sex, ethnicity, and SLE manifestations were also extracted and compared between people prescribed and not prescribed PGx medications ($P < 0.05$).

Results: Our cohort included 616 children and adolescents with SLE. The cohort was 80% female, with a median age at diagnosis of 14 years (IQR 11-15), with the largest

reported ethnic group being Europeans (38%). The most common SLE manifestations were malar rash (79%), lymphopenia (68%), and the presence of anti-dsDNA antibodies (66%). Patients prescribed a PGx medication within the first year after diagnosis showed a statistically increased prevalence of neuropsychiatric, renal, and musculoskeletal manifestations, and hypocomplementemia (Table 1). Patients were prescribed 219 distinct medications, including 43 with PGx guidance. The most commonly prescribed PGX medications were azathioprine (42%), omeprazole (33%), and lansoprazole (15%). Of the 616 patients, 413 (67%) were prescribed at least one PGx medication, with most individuals receiving prescriptions within the first year of SLE diagnosis (n=290, 47%).

Table 1: Cohort Demographic and Feature Characteristics

Features	Total Cohort N=616 (%)	Prescribed within the First Year N=290 (%)	P[a]
Female Sex (%)	495 (80)	241 (83)	0.36
Age at Diagnosis (years), Median [IQR]	14 [11, 15]	13 [12, 16]	1.00
Ancestry			0.17
European	235 (38)	108 (37)	
Asian	182 (30)	90 (31)	
African	66 (11)	30 (10)	
Other	24 (4)	10 (3)	
Undisclosed	79 (13)	37 (13)	
Clinical Features			
Neuropsychiatric	**141 (23)**	**106 (37)**	2.19 x 10-5*
Nephritis	**212 (34)**	**135 (47)**	5.70 x 10-4*
Class II	16 (3)	2 (1)	
Class III	71 (12)	50 (17)	
Class IV	93 (15)	65 (22)	
Class V	67 (11)	40 (14)	
Serositis	**90 (15)**	**53 (18)**	0.17
Pericarditis	51 (8)	31 (11)	
Pleuritis	73 (12)	40 (14)	
Mucocutaneous	**552 (90)**	**264 (91)**	0.55
Malar Rash	484 (79)	222 (77)	
Other Rash	233 (38)	108 (37)	
Alopecia	282 (46)	162 (56)	
Musculoskeletal	**423 (69)**	**221 (76)**	0.02*
Arthritis	419 (68)	221 (76)	
Myositis	32 (5)	16 (6)	
Laboratory Features			
Hematological	**490 (80)**	**245 (84)**	0.08
Thrombocytopenia	178 (29)	94 (32)	
Lymphopenia	420 (68)	214 (74)	
Leukopenia	316 (51)	166 (57)	
Neutropenia	52 (8)	25 (9)	
Hypocomplementemia	**370 (60)**	**203 (70)**	4.00 x 10-3*
Lupus Specific Antibodies	**479 (78)**	**241 (83)**	0.07
Cardiolipin	250 (41)	129 (44)	
Anti-DNA	408 (66)	207 (71)	
Lupus Anticoagulant	92 (15)	38 (13)	
Smith	209 (34)	114 (39)	

(a) Sex, SLE features, and ethnicity were analyzed with a Fisher's exact test, age was analyzed with Wilcoxon rank sum test. (*) Denotes statistical difference between the groups ($p < 0.05$)

Conclusions: In a large cohort study of children and adolescents with SLE, we observed that 68% of patients were prescribed a medication with PGx guidance during the course of their disease, with nearly half of these patients being prescribed within the

first year of SLE diagnosis. Future plans include expanding the cohort and follow-up by 5 years and completing analyses of genetic variants for the most commonly prescribed PGx medications using Stargazer, a star allele calling software. Our research aims to provide a rationale for the use of PGx in individualized care for children and adolescents with SLE.

PV164 / #580

Poster Topic: ***AS18 - Paediatric SLE***

COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN CHILDREN LIVING IN KHARKIV REGION (UKRAINE) DURING THE MILITARY TIME

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Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by the presence of autoantibodies to nuclear antigens, the deposition of immune complexes, and chronic inflammation in classic target organs. SLE is characterized by typical manifestations and the presence of key diagnostic features. Today, the main principle of monitoring patients with SLE is the treat-to-target (T2T) strategy, according to which systematic evaluation of clinical manifestations and autoantibody profiles should be carried out regularly at established intervals. Purpose: To study the course of SLE at the current stage in Ukraine, during wartime, in children living in the east of the country (Kharkiv region).

Methods: The medical histories of 8 patients who continued to live in the Kharkiv region (front-line territory of eastern Ukraine) were analyzed and compared with the clinical presentation of SLE until 2022. The groups of patients did not differ in terms of age, gender, and physical development. All children became ill before the war, the age of patients with SLE was 13.92 ± 0.39 years. The duration of the disease among the studied patients during the war was expectedly longer (4.49 versus 2.72 years, $p < 0.05$).

Results: During 2022-2024, 85.7% of patients experienced disease activation, the causes of which were staying in cold rooms directly in the cities of hostilities, changes in the treatment plan, lack of medication, and previous acute respiratory viral infections. Analysis of clinical manifestations of SLE in children during the examination showed that the course of SLE retained its clinical presentation. Despite the exacerbation of the process, fever, convulsive syndrome, manifestations of active carditis, arthritis were not noted. However, during the war, such severe manifestations of the disease as hemorrhagic syndrome in the form of subcutaneous hematomas, impaired consciousness (delirium), the development of pleurisy with the presence of pleural effusion in children were noted for the first time. Facial erythema of the “butterfly” type was presented somewhat more often (62.5% vs. 40.6%, $p < 0.05$). Despite the exacerbation of the pathological process, hematological indicators were

unchanged, anemia and thrombocytopenia did not occur, leukopenia remained at the previous frequency (6.25% and 25.0%, respectively). Among laboratory indicators, the level of C-reactive protein was significantly higher (3.47 mg among patients before 2022 and 15.03 mg - after 2022, $p < 0.05$). It was found that during wartime, children with SLE had lower values of C3-complement (0.99 versus 0.82 g/l; $p < 0.05$), higher levels of total antinuclear antibodies (1.48 versus 4.52 units, $p < 0.001$) and antibodies to native DNA (6.99 versus 22.61 units, $p < 0.001$). Rheumatoid factor (RF) positivity remained at the previous frequency (13.30% and 12.50%). The concentration of vitamin D (25-OH-vitamin D) was at the level of previous values, its moderate deficiency persisted both in the pre-war period ((23.96 ± 1.74) ng/l) and during the war ((21.22 ± 3.20) ng/l).

Conclusions: The study of the features of clinical manifestations of SLE in children during the war showed that during the war in Ukraine there was an exacerbation of the pathological process. The immune system indicators react most significantly. Changes in innate immunity were established - a decrease in C3 complement and an increase in autoimmune aggression with an increase in the production of antinuclear antibodies ($p < 0.001$) and antibodies to double-stranded DNA ($p < 0.001$).

PV165 / #571

Poster Topic: *AS18 - Paediatric SLE*

CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS – SINGLE CENTER'S 10-YEAR EXPERIENCE

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Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) is a rare, chronic auto-immune multisystem inflammatory disease that manifests before the age of 16 years. The course of the disease in children is more severe than in adults. The clinical presentation of cSLE is multifaceted, most commonly including constitutional, hematological, cutaneous, renal, and neuropsychiatric symptoms. The aim of the study was to characterize cSLE cohort in single center in Poland in years: 2014-2024.

Methods: A total of 35 Caucasian children (27 girls, 8 boys) diagnosed with cSLE according to SLICC 2012 criteria in Department of Pediatric Cardiology and Rheumatology Medical University of Lodz, Poland, were included in the retrospective analysis. Clinical features, laboratory and imaging test, as well as, kidney biopsy if necessary and treatment strategies were analyzed.

Results: The female-to-male ratio was 3.37:1. The median age at diagnosis was 14 years (7.5 to 18). The most common clinical symptoms were photosensitivity/malar rash/ (15/35 – 42.8%), oral ulcers (11/35 – 31.4%) and arthritis (9/35 – 25.7%). The severe course of cSLE was observed in 18/35 (51.4%) children. Central nervous system was affected in 14/35 (40%) children – 5 (14.3%) complained of headaches, 2 (5.7%) - depression, 2 (5.7%) – epilepsy. Proteinuria (>500mg/24h) associated with histopathological lupus nephritis (3- stage IV, 1- stage - II) was observed in 4/35 (11.4%) patients. In 9/35 (25.7%) children leukopenia was observed, 5 /35 (14.3%) children have anaemia and the same number thrombocytopenia. Antinuclear antibodies were positive (titer >1:80) in all children with cSLE, and above 1:320 in 27/35 (77.1%) patients. Fourteen (40%;) children had dsDNA antibodies; 2/35 (5.7%) patients with lupus nephritis were anti-dsDNA positive. Anti-phospholipid antibodies were detected in 8/35 (22.8%) children, including 3 patients with neuropsychiatric manifestations, and 1 child with neuropsychiatric symptoms had also anti-Sm antibodies. Low total activity of compliment (CH50) was found in 14/35 (40%) patients with cSLE. Six patients had Raynaud symptom and only 3/35 (8.6%) had microangiopathy confirmed by capillaroscopy.

Table 1. Clinical symptoms observed in study group of children with cSLE.

	Symptom	n
1.	photosensitivity/malar rash	14
2.	lupus discoid (DLE)	1
3.	oral ulcers	11
4.	alopecia	8
5.	arthritis	9
6.	serositis	1
7.	renal/proteinuria	4
8.	CNS/headaches	14/9
9.	anaemia	5
10.	leukopenia	9
11.	thrombocytopenia	5

Table 2. Immunological markers in study group of children with cSLE.

immunological marker positivity	**n**
1. ANA	35
2. anti-dsDNA	14
3. anti-Sm	3
4. antiphospholipid antibodies	
lupus anticoagulant	5
anticardiolipin antibodies	6
IgM	2
IgG	4
IgM and IgG	0
beta-2-glycoprotein	4

IgM	1
IgG	2
IgM and IgG	1
5. low complement	
C3	10
C4	4
CH50	14

All the patients with cSLE were treated with hydroxychloroquine and supplemented with vitamin D. Twenty three children (65.7%) required systemic corticosteroids, included 13/35 (37.1%) patients who received methylprednisolone intra venous pulses followed by oral prednisone. Seven children (20%) were treated with IVIG. Mycophenolane mophetyl was used in 8/35 (22.8%) cases, methotrexate - in 4/35 (11.4%). The observed complications were related to the prolonged use of glucocorticoids - cushingoid symptoms, such as obesity and fat tissue redistribution and stretch marks.

Conclusions: Our study confirms that the course of cSLE is severe. Neuropsychiatric symptoms are common in children population. Lupus nephritis requires the administration of steroids, which can be associated with adverse effects.

PV166 / #638

Poster Topic: ***AS18 - Paediatric SLE***

RESPONSE TO HYDROXYCHLOROQUINE IN IMMUNE THROMBOCYTOPENIA IN CHILDHOOD-ONSET SLE

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Background/Purpose: The management of immune thrombocytopenia in childhood-onset systemic lupus erythematosus (cSLE) is diverse and yet to be standardized. We aimed to analyze the efficacy and safety of hydroxychloroquine (HCQ) in the treatment of thrombocytopenia (platelet count <100× 10^9/L) associated with cSLE.

Methods: We retrospectively reviewed the medical records of patients who developed thrombocytopenia (platelet count <100 × 10^9/L) and were followed in the SLE clinic at The Hospital for Sick Children, between January 2015 and December 2022. Definite cSLE was defined by ANA titer ≥ 1:160 measured by immunofluorescence and ≥10 points according to the 2019 EULAR/ACR 2019 classification criteria, while patients with incipient cSLE were ANA positive, had clinical features of evolving SLE but achieved a score below 10. Complete response was defined as a platelet count >100 x 10^9/L with no bleeding. Partial response was defined as a platelet count >30 x 10^9/L with at least a two-fold increase of the baseline count and no bleeding. Qualitative data were analyzed using descriptive statistics.

Results: Of the 265 patient records reviewed (201 with definite cSLE and 64 with incipient cSLE), 55 (21%) patients had thrombocytopenia. Nine patients with thrombocytopenia secondary to other causes, such as medications related or infections, were excluded. Forty-six patients (70% female), with a median age of 12.9 years (IQR 10.6 - 14.9) and median platelet count of 16.5 × 10^9/L (IQR 6 - 61) at time of thrombocytopenia diagnosis were included. The median lowest platelet count was 6 × 10^9/L (IQR 2 - 31). Twenty-eight (61%) patients had definite cSLE, while 18 (39%) had incipient cSLE. Median SLEDAI score at cSLE diagnosis (for definite SLE) was 7 (IQR 5 - 12). Thirty-one (67%) patients were treated with corticosteroids and/or IVIG prior to commencing HCQ, and 10 of them (22%) also required one or more additional treatments for thrombocytopenia (i.e., azathioprine, mycophenolate mofetil, eltrombopag, romiplostim, rituximab, or cyclophosphamide). Thirteen (28%) patients achieved either a complete or partial response prior to initiating HCQ. Forty-one (89%) patients were treated with HCQ during their disease course. HCQ was initiated at a median of 6 months (IQR 2.7-12.2) after thrombocytopenia diagnosis at a median platelet count of 65 × 10^9/L (IQR 19-131). Twenty-six (63%) of the patients treated with

HCQ had a complete or partial response at 12 weeks after initiating HCQ. Fourteen (34%) patients required additional treatment for thrombocytopenia during this time. Forty-three (93%) patients had either complete (n=39) or partial response (n=4) after one year and/or at the end of follow-up, including 38 (93%) who received HCQ. The median follow-up time was 27 months (IQR 12.7-52). At the end of follow-up, only three patients required a second drug (either sirolimus, eltrombopag, mycophenolate mofetil, or azathioprine). Only one patient discontinued HCQ due to side effects (headache).

Table 1. Demographics of Patients Included in Analysis

	Incipient SLE		Definite SLE		Total	
	N	(%)	N	(%)	N	(%)
Total records reviewed	64	24%	201	76%	265	100%
Patients diagnosed with thrombocytopenia	19	7%	36	14%	55	21%
Patients with thrombocytopedia due to secondary causes	1	0%	8	3%	9	3%
Total patients included in analysis	18	7%	28	11%	46	17%
Female biological sex	10	56%	22	79%	32	70%
Duration of thrombocytopenia in months at time of SLE diagnosis (median, IQR)	2.8 (0.7-9.2)		1.9 (0.9-8.7)		2.2 (0.8-9.2)	
Antiphospholipid antibodies (one or more) present at SLE diagnosis	3	7%	7	15%	10	22%
Developed major organ involvement during their disease course	0	0%	9	20%	9	20%
Received HCQ	14	30%	27	59%	41	89%
Received steroids and/or IVIG therapy prior to starting HCQ	15	33%	16	35%	31	67%
Received other therapy* prior to starting HCQ	5	11%	5	11%	10	22%
Response** observed prior to starting HCQ	8	17%	5	11%	13	28%
Response** observed 3 months after starting HCQ	6	13%	20	43%	26	57%
Response** observed at patient's most recent clinical encounter	16	35%	27	59%	43	93%

HCQ=hydroxychloroquine, IQR=interquartile range, IVIG=intravenous immunoglobulin, SLE=systemic lupus erythematosus
* Treated with either one or a combination of azathioprine, mycophenolate mofetil, eltrombopag, romiplostim, rituximab, or cyclophosphamide
** Either complete or partial response

Conclusions: In a cohort of children with definite or incipient cSLE, we observed successful management of thrombocytopenia on HCQ monotherapy nearly two years after their onset, although two-thirds required immunosuppression at presentation. Further analysis will identify characteristics that predict response to HCQ monotherapy.

PV167 / #832

Poster Topic: *AS18 - Paediatric SLE*
Late-Breaking Abstract

PREVALENCE AND TIME TO CATARACT DEVELOPMENT IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Cataracts are significant ocular complications in childhood-onset systemic lupus erythematosus (cSLE). This study aims to evaluate the prevalence, time to cataract development, and describe demographic and clinical features in a cohort of cSLE patients.

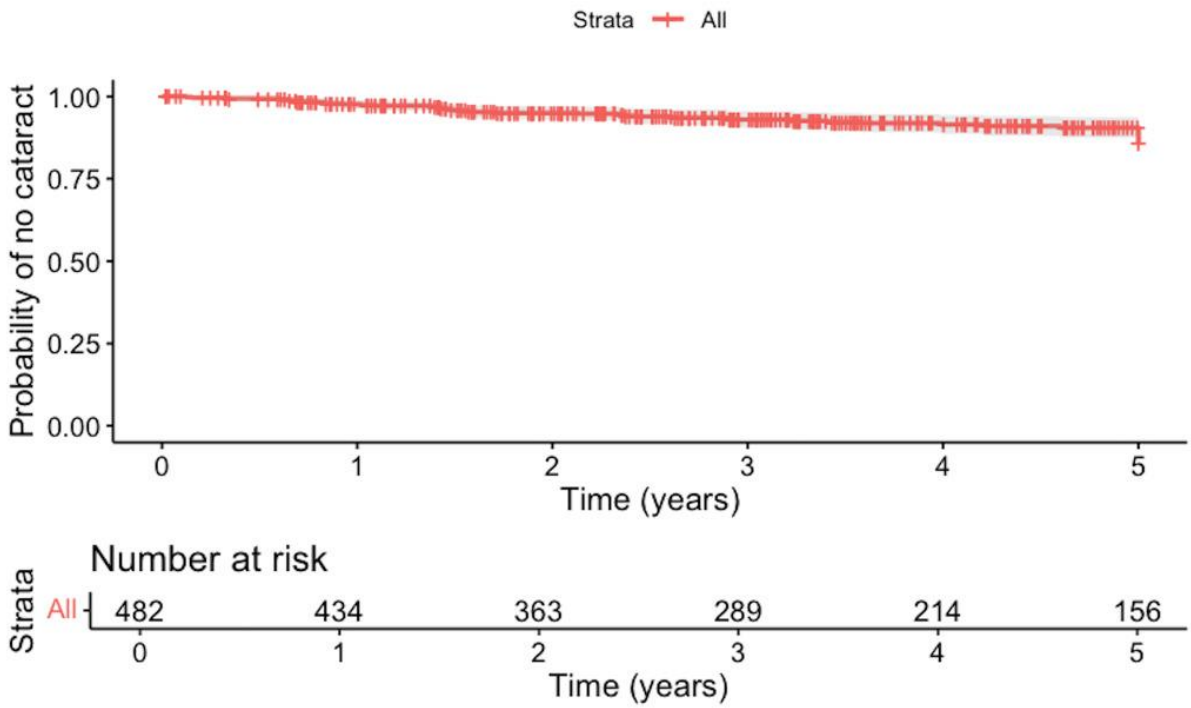
Methods: We conducted a retrospective analysis of patients who were followed for cSLE at a tertiary centre Lupus clinic from 1992 to 2023. All patients had prospectively collected data and follow-up until the age of 18 years. Demographic and clinical characteristics, including sex, self-reported ethnicity, age at SLE diagnosis, disease duration, and SLE-related manifestations, were compared between patients with and without cataracts. Cataracts were diagnosed by ophthalmologists or optometrists and documented in lupus clinical chart as part of the Systemic Lupus Erythematosus Collaborative Clinics Damage Index (SLICC-DI). We completed survival analysis of time from SLE diagnosis to first cataract and conducted t-tests to compare features of patients with and without cataracts ($P < 0.05$).

Results: Among the 482 cSLE patients included, 83% were female with a mean age at diagnosis of 13.1 ± 3.1 years and a mean follow-up time of 4.5 ± 3.0 years. The cohort was predominantly of European (28%) and East Asian (25%) ancestries, followed by South Asian (18%), American/Admixed (17%), and African (12%) ancestries (Table 1). The most common SLE-related manifestation was lupus nephritis, observed in 42% of patients, followed by arthritis (29%), serositis (16%), and neuropsychiatric systemic lupus erythematosus (NPSLE) (9%). A total of 43 (9%) patients developed cataracts. The majority of patients with cataracts were female (72%), with a longer mean disease duration (5.7 ± 2.8 years) compared to the non-cataract group (4.4 ± 3.0 years), and a younger mean age of SLE diagnosis (11.8 ± 2.9 years) than those without (13.3 ± 3.1 years). Patients with cataracts were more likely to have lupus nephritis (67% vs.

40%, *P* = 0.001). When we examined time from SLE diagnosis to first cataract, 35/43 (81%) developed cataracts within 5 years of SLE diagnosis (Figure 1).

Clinical and demographic cohort features (n = 482)

	Overall n = 482	**Catarct n = 43**	**Non-cataract n = 439**	***P***
Female, n (%)	398 (83)	31 (72)	367 (84)	0.091
Ethnicity, n (%) European East Asian South Asian American/Admixed African	136 (28) 121 (25) 85 (18) 83 (17) 57 (12)	7 (16) 13 (30) 10 (23) 11 (26) 2 (5)	129 (29) 108 (25) 75 (17) 72 (16) 55 (13)	0.103
Age of SLE diagnosis, mean ± SD, years	13.1 ± 3.1	11.8 ± 2.9	13.3 ± 3.1	0.005*
Disease duration, mean ± SD, years	4.5 ± 3.0	5.7 ± 2.8	4.4 ± 3.0	0.007*
Lupus nephritis, n (%)	204 (42)	29 (67)	175 (40)	0.001*
NPSLE, n (%)	43 (9)	4 (9)	39 (9)	1.000



Conclusions: In a multiethnic cohort of children and adolescents with cSLE, we observed that 9% developed cataracts within a mean of 4.2 years of follow-up. We also observed a higher prevalence of cataracts among those with younger age of SLE diagnosis, longer disease duration and lupus nephritis. Our next steps will include investigating the relative contributions of genetics and glucocorticosteroid exposure to cataract risk.

PV168 / #462

Poster Topic: ***AS18 - Paediatric SLE***

PREVALENCE OF CLINICAL AND SELF-REPORTED DIAGNOSES OF DEPRESSION AND ANXIETY IN PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Symptoms of depression and anxiety are common among patients with childhood-onset systemic lupus erythematosus (cSLE). In recent years, screening for depression and anxiety using validated self-report tools is increasingly part of routine clinical care. Comparing prevalence of mood disorders over time amid evolving perspectives on mental health requires retrospective chart review. However, identifying patients with depression and anxiety by retrospective chart review is challenging and requires consideration of both clinical documentation and patient-reported symptoms. This study aims to investigate the prevalence of clinical and self-reported diagnoses of depression and anxiety among children and adolescents diagnosed and followed for cSLE in the SickKids Lupus Clinic, using retrospective clinical chart review and self-report screening tools.

Methods: We completed a retrospective study of children and adolescents aged ≤ 18 years seen in a tertiary care Lupus Clinic between January 1, 2000, to December 31, 2023. All patients met ≥4 American College of Rheumatology (ACR) and/or Systemic Lupus International Collaborative Clinics (SLICC) criteria for SLE with data prospectively collected in a dedicated Lupus database. Additional information such as age of SLE diagnosis, sex, ancestry, and disease activity were extracted from the

database. Symptoms and diagnoses of depression and/or anxiety and use of psychotropic medication, before and after cSLE diagnosis, were extracted from clinical charts in ChartMaxx and EPIC. We identified patients with depression and/or anxiety as those with medical chart documentation of 1) a diagnosis and 2) persistent depression and/or anxiety symptoms over a course of at least two months. Self-reported depression and anxiety were identified by the Children's Depressive Inventory (CDI, CDI-2) and Multidimensional Anxiety Scale for Children (MASC, MASC-2), completed as clinical screening measures for patients seen by psychiatry. We classified individuals as positive for self-reported depression based on a total score >13 on the CDI and CDI-2, and for self-reported anxiety based on a total score >60 on the MASC and MASC-2, appropriate for referral to mental health services. We included patients who completed at least one self-report screen for depression or anxiety and retained the most severe score in analyses. Descriptive statistics were used for cohort demographics and cSLE features.

Results: We reviewed 491 patient clinical charts and identified 135 patients who completed at least one self-report questionnaire. The majority were females (86%) and the median age of cSLE diagnosis was 13 years (IQR 12-15). Most patients were of European (33%) and East Asian (24%) ancestry. The majority of patients completed the CDI (64%) and/or the MASC (25%), followed by MASC-2 (6%) and/or CDI-2 (5%). Of the 93 patients who completed a self-report screen for depression, 41 (44%) screened positive for depression; the majority who screened positive (68%) did not receive a diagnosis of depression. Of the 42 patients who completed a self-report screen for anxiety, 18 (43%) screened positive for anxiety; the majority who screened positive (55%) did not receive a diagnosis of anxiety. Psychotropic medication was initiated in 34% of patients after screening positive for depression and/or anxiety.

Conclusions: We found self-reported depression and anxiety to be prevalent among youth with cSLE. Future directions include examining scores for the Patient Health Questionnaire-4 (PHQ-4), Patient Health Questionnaire-9 (PHQ-9), and Generalized Anxiety Disorder 7-item scale (GAD-7). Concordance between clinical diagnosis and self-reported depression and anxiety will be assessed using chi-square statistics for categorical values and Wilcoxon rank-sum test for continuous variables.

Table 1. Demographic and clinical features of reviewed cSLE cohort (n = 135)

Variables	Total n = 135
Female sex (n (%))	116 (86)
Age at SLE diagnosis, years (median (IQR))	13 (12-15)
Genetically Inferred Ancestry (n (%))	
European	44 (33)
East Asian	33 (24)
African	14 (10)
South Asian	16 (12)
Admixed*	28 (21)
Clinical Features (n (%))	
Fever	44 (33)
Mucocutaneous	
Malar rash	98 (73)
Non-scarring alopecia	63 (47)
Oral nasal ulcers	44 (33)
Neuropsychiatric lupus (NPSLE)	55 (41)
Serosal	
Pericarditis	17 (13)
Pleuritis	13 (10)
Lupus nephritis	49 (36)
Arthritis	89 (66)
Myositis	7 (5)
Hematological	
Leukopenia	79 (59)
Coombs Positive Hemolytic Anemia	43 (32)
Thrombocytopenia	36 (27)
Laboratory Features (n (%))	
Antinuclear antibodies (ANA)	135 (100)
Antiphospholipid antibodies	
Anticardiolipin antibody	35 (26)
Lupus anticoagulant	19 (14)
SLE-specific antibodies	
Anti-dsDNA antibody	87 (64)
Anti-Smith antibody	50 (37)

* Admixed category represents patients who had <80% single ancestral proportion. Includes patients of Amerindian ancestry (n=6 (4)).

Table 2. Number of patients who completed the CDI, CDI-2, MASC, and/or MASC-2

Questionnaire	Patients, n (%) n = 135
CDI	86 (64)
CDI-2	7 (5)
MASC	34 (25)
MASC-2	8 (6)

Table 3. Number of patients who screened positive for depression on the CDI or CDI-2, and/or anxiety on the MASC or MASC-2

Questionnaire	Patients, n (%)
CDI or CDI-2 n = 93	41 (44)
MASC or MASC-2 n = 42	18 (43)

Note: Positive screen for depression on the CDI and CDI-2 indicated by a total raw score > 13; positive screen for anxiety on the MASC and MASC-2 indicated by a total raw score > 60.

PV169 / #263

Poster Topic: *AS19 - Patient-Reported Outcome Measures*

LIVING WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN 2024: LATIN AMERICAN EXPERIENCE BASED ON A PATIENT SURVEY

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Background/Purpose: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that significantly impacts patients' quality of life. In 2020, a survey was conducted by Lupus Europe to assess the burden of SLE among European patients(1). The reality of Latin America (LA) is highly diverse in terms of healthcare access and treatment availability, making it essential to describe these experiences from the patients' perspective.This study aimed to evaluate the burden of SLE from the perspective of LA patients in 2024.

Methods: In May 2024, as part of the international SLE awareness day, the Grupo Latinoamericano de Estudio del Lupus (GLADEL) disseminated an anonymous, bilingual online survey (in Spanish and Portuguese) to patients diagnosed with SLE through their physicians and various patient associations across LA countries.

Results: Data from 2,139 SLE respondents (95.9% female, median age: 38.0 years [IQR: 31.0–46.0], 25.5% Caucasian, 34.7% Mestizo, 20% Afrolatinoamerican, 10% indigenous and 6.8% other) from 15 LA countries were analyzed. The most commonly affected organs were the joints (68.1%), the skin (47.3%), and the kidney (35.6%). In 52.5% of the cases, a previous diagnosis other than SLE was reported. Regarding educational level, 40% had completed high school. At the time of the survey, 40% were employed, while 20% had stopped working due to lupus. Daily life activities were negatively impacted by lupus for 40% of respondents, with joint pain (17.5%) and fatigue (35%) being the most disruptive symptoms. Additionally, 35.6% of patients used antimalarials, 25% were on steroids (mean dose: 5 mg/day), 27.8% used immunosuppressants, and 5.4% were receiving biologic drugs. Notably, 35% of respondents agreed that they had access to specialized care and treatments appropriate for their condition.

Conclusions: CONCLUSIONS: Understanding patient perspectives is crucial for evaluating the impact of SLE and addressing challenges related to healthcare access and treatment. Incorporating patient feedback into regional healthcare policies should be prioritized. REFERENCE: 1-Cornet A, Andersen J, Myllys K, et al. Living with systemic lupus erythematosus in 2020: a European patient survey. Lupus Science & Medicine 2021;8:e000469. doi:10.1136/ lupus-2020-000469 Acknowledgements: LUPUS EUROPE for the support in adapting the survey to LA, to the GLADEL researchers and all patients who voluntarily participated in this survey and to the patient associations that made the survey available to patients.

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Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

EFFECT OF CENERIMOD ON QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: RESULTS FROM THE PHASE 2 CARE STUDY

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Background/Purpose: Cenerimod is an investigational highly selective $S1P_1$ receptor modulator with potential therapeutic benefits in autoimmune disease, including Systemic Lupus Erythematous (SLE). The Phase 2b CARE study was a double-blind, randomized, placebo-controlled trial evaluating the efficacy and safety of different doses of cenerimod (0·5 mg, 1 mg, 2 mg, or 4mg) in subjects with moderate-to-severe SLE, concurrently receiving stable background therapy. Cenerimod had a significant effect on the primary endpoint, the change in modified SLE disease activity index-2000 score (mSLEDAI 2K, which excludes leukopenia) from baseline to month 6. The largest difference vs placebo was obtained in the 4 mg arm and was nominally statistically significant (4 mg: -4.04 vs placebo: -2.85, P=0.029). Further, post-hoc subgroup analyses showed that 4 mg had a greater treatment effect size vs placebo (- 5·41 vs -2.62, P=0·0015) in patients with high IFN 1 gene expression at baseline. The CARE study also assessed health-related quality of life (QoL) as one of its endpoints, and the abstract presents the QoL results comparing cenerimod 4 mg to placebo.

Methods: The 36-Item Short Form Health Survey version 2 (SF-36v2) was one of the tools used to assess quality of life (QoL) in the CARE study. The data was collected using a paper clinical report form (CRF). Observed changes from baseline to month 6 were analyzed descriptively using the full analysis set. The SF-36v2 questionnaire covers 8 health domains and provides two component summaries, the physical and the mental components. A 2-point change in the physical component summary and a 3-point change in the mental component summary are considered as the minimal important differences (MIDs) indicating improvement in health status[1]. In this abstract, the results will focus on the two component summaries and on the mental health domain.

Results: Improvements were noted with cenerimod 4 mg vs placebo at month 6 across most of the SF-36v2 health domains. The mean [SD] change from baseline to month 6 with 4 mg was 4.72 [8.17] for the physical component summary (vs placebo, 2.60 [9.91]) (**Table 1**) and 2.73 [8.99] for the mental component summary (vs placebo, 2.51 [11.74]) (**Table 2**). In the subgroup of patients with high IFN-1 gene expression, the treatment effect was greater with a mean [SD] changes higher for 4 mg vs placebo in both physical (6.77 [7.80] vs 0.99 [9.81]) (**Table 1**) and mental components (3.14 [10.25] vs 0.75

[13.39]) (**Table 2**). For the SF-36 mental health domain at month 6, the mean [SD] difference was 3.02 with 4 mg vs 2.63 for placebo. In the high IFN-1 gene expression subgroup, the mean difference was 2.82 [9.76] for the 4 mg vs -0.07 [12.10] for the placebo.

Table 1: SF-36v2: observed value at baseline and change from baseline at Month 6: Physical Component

Time point statistic	Cenerimod 0.5 mg N=85	Cenerimod 1 mg N=85	Cenerimod 2 mg N=86	Cenerimod 4 mg N=85	Placebo N=86
Overall population					
Baseline					
N	85	82	84	83	84
Mean (SD)	35.97 (11.20)	36.09 (11.18)	35.62 (11.49)	33.52 (10.16)	35.17 (11.17)
Median (Q1, Q3)	35.70 (26.80, 43.40)	35.05 (27.20, 45.10)	34.60 (28.15, 43.50)	32.30 (27.10, 42.30)	34.80 (27.30, 43.65)
Change from baseline to month 6					
N	76	73	71	71	71
Mean (SD)	4.63 (9.80)	2.89 (8.51)	3.78 (7.70)	4.72 (8.17)	2.60 (9.91)
Median (Q1, Q3)	4.45 (-0.75, 10.65)	2.30 (-1.70, 7.30)	4.0 (-0.30, 9.20)	3.80 (-0.50, 9.90)	1.60 (-1.50, 6.40)
In high IFN 1 gene expression patients					
Time point statistic	**Cenerimod 0.5 mg N=42**	**Cenerimod 1 mg N=50**	**Cenerimod 2 mg N=39**	**Cenerimod 4 mg N=36**	**Placebo N=40**
Baseline					
N	42	50	39	36	38
Mean (SD)	35.58 (11.87)	36.99 (11.61)	36.45 (11.83)	33.34 (9.87)	37.35 (9.57)
Median (Q1, Q3)	35.6 (26.8, 43.4)	40.1 (27.9, 46.1)	33.8 (28.2, 48.1)	33.0 (26.2, 40.3)	37.8 (32.1, 44.1)
Change from baseline to month 6					
N	38	45	34	32	31
Mean (SD)	4.62 (10.27)	2.48 (8.41)	3.35 (8.60)	6.77 (7.80)	0.99 (9.81)
Median (Q1, Q3)	4.7 (-0.2, 10.1)	2.5 (-1.9, 7.7)	1.9 (-1.7, 9.4)	5.0 (1.3, 11.8)	0.6 (-3.0, 7.6)

SF-36v2,36-Item Short Form Health Survey version 2; IFN, Interferon

Table 2: SF-36v2: observed value at baseline and change from baseline at Month 6: Mental Component

Time point statistic	Cenerimod 0.5 mg N=85	Cenerimod 1 mg N=85	Cenerimod 2 mg N=86	Cenerimod 4 mg N=85	Placebo N=86
Overall population					
Baseline					
N	85	82	84	83	84
Mean (SD)	40.58 (11.75)	42.53 (10.41)	41.68 (11.76)	40.05 (11.50)	39.90 (12.78)
Median (Q1, Q3)	40.30 (31.10, 50.80)	41.80 (36.30, 50.70)	41.95 (34.50, 52.20)	39.50 (32.50, 49.20)	39.25 (31.10, 50.55)
Change from baseline to month 6					
N	76	73	71	71	71
Mean (SD)	2.80 (8.86)	0.39 (10.55)	1.84 (9.08)	2.73 (8.99)	2.51 (11.74)
Median (Q1, Q3)	2.50 (-1.90, 8.55)	1.20 (-5.40, 6.90)	1.30 (-4.90, 6.10)	1.90 (-2.10, 8.40)	2.20 (-5.0, 10.0)
In high IFN 1 gene expression patients					
Time point statistic	**Cenerimod 0.5 mg N=42**	**Cenerimod 1 mg N=50**	**Cenerimod 2 mg N=39**	**Cenerimod 4 mg N=36**	**Placebo N=40**
Baseline					
N	42	50	39	36	38
Mean (SD)	38.97 (12.32)	43.58 (9.81)	41.57 (10.44)	40.24(12.07)	40.38(13.06)
Median (Q1, Q3)	38.4 (30.1, 49.0)	43.1 (39.0, 50.6)	39.9 (34.8, 49.1)	39.6 (32.9, 51.5	42.4 (32.9, 50.7)
Change from baseline to month 6					
N	38	45	34	32	31
Mean (SD)	3.47 (9.29)	-1.55 (10.35)	1.39 (8.58)	3.14 (10.25)	0.75 (13.39)
Median (Q1, Q3)	2.5 (-1.7, 8.8)	-0.8 (-6.4, 6.4)	1.1 (-4.8, 5.4)	1.0 (-1.4, 9.1)	1.8 (-6.9, 9.9)

SF-36v2,36-Item Short Form Health Survey version 2; IFN, Interferon

Conclusions: Patients with cenerimod 4 mg groups showed meaning full improvements in the mental and physical components of the SF-36v2 scores compared to placebo at month 6. Further evaluation of the SF-36v2 scores will be performed in the phase III program. **Reference** User's manual for the SF-36v2 survey. 3rd ed. Lincoln (RD): Quality Metric Incorporated; 2011.

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Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

EFFECT OF CENERIMOD, AN S1P1 MODULATOR, ON FATIGUE IN SLE: RESULTS FROM THE PHASE 2 CARE STUDY

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Background/Purpose: Cenerimod is an investigational highly selective $S1P_1$ receptor modulator with potential therapeutic benefits in autoimmune disease. The Phase 2b CARE study (NCT03742037) evaluated the efficacy and safety of cenerimod at doses 0.5, 1, 2, and 4 mg in moderate to severe systemic lupus erythematosus (SLE) patients. Cenerimod had a significant effect on the primary endpoint, the change from baseline to month 6 in modified SLE disease activity index-2000 score (mSLEDAI 2K, which excludes leukopenia). The largest difference vs placebo was observed with 4 mg (- 4·04 vs - 2·85 from baseline) with a least square mean difference vs placebo of – 1·19 (P=0·029). In the subgroup of patients with high IFN-1 gene expression (approx. 50% of the population), 4 mg showed a greater treatment effect vs placebo (- 5·41 vs -2.62, P=0·0015). Based on these results, cenerimod 4 mg is selected for the ongoing phase 3 OPUS program (NCT05648500, NCT05672576). Fatigue, reported by 67% to 90% of SLE patients[1], is often the most bothersome symptom, impairing health-related quality of life. This outcome was measured in the CARE study, and the results of these analyses, focusing on patients treated with 4 mg (both the whole group and the IFN-1-high subgroup), are presented in this abstract.

Methods: Phase 2b CARE study was a multicenter, randomized, double-blind, placebo-controlled trial in which patients received once-daily oral cenerimod (one of four doses) or placebo, in addition to stable background SLE therapy, for 6 months. The fatigue scores were collected using the Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale score, and the fatigue component of the Lupus Quality of Life (QoL) questionnaire. Observed changes from baseline to month 6 were analyzed descriptively using the full analysis set.

Results: A total of 427 patients were randomized in the CARE study, with 85 patients each in the 0.5 mg,1 mg, and 4 mg arms and 86 patients in the 2 mg and placebo arms. The median age was 42 years (range 18–72); 406 (95%) patients were female, and 337 (79%) were White. In the overall study population, an increase in FACIT-Fatigue score, indicating improved fatigue, was observed in all treatment groups at month 6, with no dose-dependent trends. The median (IQR) change from baseline was 3 (0, 8) in the cenerimod 4 mg arm and 2 (-1.79, 9) in the placebo arm. In the subgroup analysis of patients with high IFN-1 gene expression, the median (IQR) change from baseline was

much better in the 4 mg arm, 5 (1, 9.5), than in the placebo arm, 1 (-5.33, 6) (**Table 1**). The results from the Lupus QoL fatigue scores (higher scores also indicate improved fatigue) showed similar trends. The median (IQR) change from baseline was 12.5 (0, 18.75) in the 4 mg arm and 3.125 (-6.25, 18.75) in the placebo arm in overall population. The 4 mg group exhibited a greater median (IQR) change of 15.63 (3.13, 25) compared to placebo 0 (-9.38, 12.5) in the high IFN-1 gene expression subgroup (**Table 2**).

Table 1: FACIT-Fatigue: observed value at baseline and change from baseline at Month 6

Time point statistic	Cenerimod 0.5 mg N=85	Cenerimod 1 mg N=85	Cenerimod 2 mg N=86	Cenerimod 4 mg N=85	Placebo N=86
Overall population					
Baseline					
N	85	84	85	82	84
Mean (SD)	31.07 (10.40)	31.78 (12.31)	29.17 (11.72)	28.52 (11.51)	28.21 (11.51)
Median (Q1, Q3)	29.25 (23.0, 38.0)	33.00 (23.42, 42.0)	29.00 (22.0, 37.0)	28.50 (20.0, 37.0)	26.50 (19.0, 36.0)
Change from baseline to month 6					
N	75	75	72	70	72
Mean (SD)	4.23 (9.08)	2.19 (9.65)	3.23 (9.48)	3.12 (7.81)	4.28 (9.85)
Median (Q1, Q3)	4.0 (-1.0, 11.0)	2.0 (-3.0, 7.0)	2.50 (-1.0, 8.21)	3.0 (0, 8.0)	2.0 (-1.79, 9.0)
In high IFN 1 gene expression patients					
Time point statistic	**Cenerimod 0.5 mg N=42**	**Cenerimod 1 mg N=50**	**Cenerimod 2 mg N=39**	**Cenerimod 4 mg N=36**	**Placebo N=40**
Baseline					
N	42	50	39	36	38
Mean (SD)	31.04 (10.90)	32.95 (12.28)	28.58 (11.61)	27.22 (10.64)	31.37 (11.22)
Median (Q1, Q3)	30.17 (23.0, 38.0)	33.50 (24.0, 43.0)	27.00 (23.0, 37.0)	26.00 (19.5, 34.5)	31.50 (25.0, 40.0)
Change from baseline to month 6					
N	38	44	33	32	31
Mean (SD)	3.47 (10.02)	1.75 (10.09)	2.63 (9.58)	5.37 (7.42)	2.26 (8.90)
Median (Q1, Q3)	2.50 (-1.0, 11.0)	1.54 (-3.0, 6.0)	2.00 (-1.0, 8.0)	5.00 (1.0, 9.50)	1.00 (-5.33, 6.00)

Table 2: Lupus QoL- Fatigue component: observed value at baseline and change from baseline at Month 6

Time point statistic	Cenerimod 0.5 mg N=85	Cenerimod 1 mg N=85	Cenerimod 2 mg N=86	Cenerimod 4 mg N=85	Placebo N=86
Overall population					
Baseline					
N	85	84	84	81	84
Mean (SD)	56.91 (24.83)	56.17 (25.04)	56.39 (26.72)	51.95 (25.69)	52.53 (28.70)
Median (Q1, Q3)	56.25 (43.75, 75)	59.37 (37.50, 75.0)	62.50 (37.50, 75.0)	56.25 (37.50, 68.75)	56.25 (25.0, 75.0)
Change from baseline to month 6					
N	76	76	72	71	72
Mean (SD)	8.47 (18.61)	6.33 (19.51)	8.56 (18.63)	8.86 (18.63)	5.46 (20.66)
Median (Q1, Q3)	6.25 (-6.25, 21.8)	3.12 (-6.25, 15.63)	6.25 (0, 18.75)	12.50 (0, 18.75)	3.125 (-6.25, 18.75)
In high IFN 1 gene expression patients					
Baseline					
N	42	50	38	36	39
Mean (SD)	55.06 (28.09)	58.25 (26.19)	57.40 (26.02)	49.47 (25.45)	57.21 (26.26)
Median (Q1, Q3)	56.25 (31.25, 81.25)	68.75 (37.50, 75.0)	62.50 (37.50, 75.0)	50.00 (34.38, 71.8)	62.50 (43.75, 75.0)
Change from baseline to month 6					
N	38	45	33	32	32
Mean (SD)	8.55 (20.46)	5.13 (19.04)	7.89 (17.28)	13.47 (19.89)	1.17 (18.61)
Median (Q1, Q3)	9.38 (-6.25, 18.75)	0.00 (-6.25, 12.50)	6.25 (0, 18.75)	15.63 (3.13, 25.0)	0.00 (-9.38, 12.50)

QoL, Quality of Life

Conclusions: Conclusion Improvements in mSLEDAI-2K scores in SLE patients treated with cenerimod 4 mg for 6 months were paralleled by relevant improvements in fatigue scores compared to placebo in the subgroup of patients with high IFN-1 gene expression. **Reference** Cornet A, et al. Lupus Sci Med. 2021 Apr;8(1):e000469

PV172 / #761

Poster Topic: *AS19 - Patient-Reported Outcome Measures*
Late-Breaking Abstract

ASSESSMENT OF FATIGUE IN A MONOCENTRIC ITALIAN COHORT OF PATIENTS AFFECTED BY SLE AND OTHER RHEUMATIC DISEASES (RDS) THROUGH VALIDATED QUESTIONNAIRES

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Background/Purpose: Fatigue is one of the most common and disabling symptoms which might impair quality of life (QoL) in patients affected by chronic diseases[1]. Previous data showed that 35-82% of patient with rheumatic diseases (RDs) reported fatigue[2]. Often, fatigue is associated with a perceived higher disease activity and it has been identified as one of the implicated factors in the failure to achieve the remission[3] We aimed to assess fatigue in our cohort of SLE and other RDs patients using validated questionnaires, to evaluate any differences in fatigue compared with healthy subjects and between various RDs subgroups. These represents the preliminary results of the IDEA-FAST project that aims to identify novel, objective and reliable digital endpoints of fatigue, by using mobile digital technologies in patients affected by neurodegenerative disorders and immune-mediated inflammatory diseases

Methods: We conducted a cross sectional observational monocentric study including patients with SLE, rheumatoid arthritis (RA), primary Sjögren syndrome (pSS) and healthy volunteers (HV) between August 2023 and July 2024. Patients with a primary diagnosis of major sleep disorder and fibromyalgia were excluded. Fatigue was rated on a visual analogue scale (fVAS:0-100 mm) and through FACIT-Fatigue and modified Mental Fatigue Scale (m-MFS). Additionally, all patients completed questionnaires investigating sleep quality (sqVAS and Medical Outcomes Study-Sleep Scale, MOS-SS), daily sleepiness (Epworth Sleepiness Scale, ESS), anxiety (Generalized Anxiety Disorder 2-item, GAD-2), depression (Patient Health Questionnaire-2, PHQ-2), QoL (EuroQoL 5 Dimensions 5 Levels, EQ-5D-5L) and social functioning (Social Functioning Questionnaires, SFQ)

Results: We enrolled 30 RA, 21 SLE, 14 pSS and 9 HV (**Table 1**). As expected SLE patients were younger and with a longer disease duration. A good construct validity was observed correlating fVAS scores with FACIT-Fatigue and m-MFS (rs:-0.81, $p<0.001$ and rs:0.42, p:0.002). Comparing the questionnaire scores RDs patients reported more fatigue, both physical and mental, and worst QoL and global health status (**Table 2**),

however no differences between the different RDs subgroups regarding the questionnaires scores were observed except for m-MFS, showing a higher mental fatigue in patients with SLE+pSS than RA patients. The female patients reported higher fVAS scores (meaning greater fatigue) as compared to males (39.0 [20.0-60.0] vs 14.0 [0.0-35.0], p:0.0125), while no significant correlations were found between fVAS scores and age, disease duration and Charlson Comorbidity Index. In SLE and pSS subgroups no correlations with disease activity were found. Finally, fVAS correlated positively with sqVAS (rs:0.36, p:0.004), ESS (rs:0,28, p:0.022), MOS-SS (rs:0.38, p:0.050), GAD-2 (rs:0.45, p<0.001), PHQ-2 (rs:0,31, p:0.028), SFQ (rs:0.41, p:0.003) and negatively with EQ-5D-5L index value (rs:-0.61, p:0.003). This implies that as fatigue worsens, sleep quality, anxiety and depressive symptoms, social functioning, quality of life and global health status worsen.

Table 2. Questionnaire scores.

	All patients n=65	Healthy volunteers n=9	p value	RA patients n=30	LES + pSS patients n=35	p value
FACIT-F (52-0)	42,0 [36,0-45,0]	48,0 [45,0-50,0]	0,004	42,5 [37,3-46,5]	40,5 [35,3-43,8]	0,144
fVAS (0-100)	35,0 [15,0-60,0]	3,0 [0,0-17,0]	0,006	31,5 [11,0-46,5]	38,0 [18,5-61,5]	0,125
m-MFS (0-42)	7,0 [3,9-13,9]	2,8 [0,9-4,3]	0,018	4,5 [3,0-8,5]	9,0 [6,0-15,5]	0,011
MOS-SS (0-100)	31,0 [18,1-43,6]	-	-	36,4 [28,2-46,0]	22,2 [15,6-34,2]	0,097
sqVAS (0-100)	47,5 [24,8-60,0]	36,0 [15,0-50,0]	0,294	46,0 [25,0-55,0]	50,0 [22,5-61,5]	0,871
ESS (0-24)	7,0 [5,0-11,0]	7,0 [3,0-12,0]	0,947	7,0 [3,0-10,0]	7,0 [6,0-11,0]	0,312
GAD-2 (0-6)	2,0 [0,0-3,0]	1,5 [1,0-2,8]	0,990	1,0 [0,0-2,0]	2,0 [1,0-3,0]	0,083
PHQ-2 (0-6)	1,0 [0,0-2,0]	0,5 [0,0-1,0]	0,143	1,0 [0,0-1,5]	2,0 [0,0-2,0]	0,306
EQ-5D-5L index value (1-0)	0,90 [0,81-0,95]	0,98 [0,95-1,0]	0,020	0,85 [0,76-0,95]	0,91 [0,84-0,96]	0,257
SFQ (0-24)	6,0 [3,8-7,3]	4,5 [3,3-5,0]	0,397	5,0 [2,0-6,5]	6,0 [4,0-8,0]	0,191

Continuous variables are expressed as median [1st-3rd quartile] and compared using Kruskal-Wallis test; categorical variables are expressed as n/number of available answers (%) and compared using ANOVA test.
Abbreviations: FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue; fVAS: fatigue Visual Analog Scale; m-MFS: modified-Mental Fatigue Scale; MOS-SS: Medical Outcomes Study Sleep Scale; sqVAS: sleep quality Visual Analogue Scale; ESS: Epworth Sleepiness Scale; GAD-2: Generalized Anxiety Disorder 2-item scale; PHQ-2: Patient Health Questionnaire-2; EQ-VAS: EuroQoL- Visual Analogue Scale; EQ-5D-5L: EuroQoL 5 Dimensions 5 Levels; SFQ: Social Functioning Questionnaire.

Table 1. Demographic and clinical characteristics.

	All patients n= 65	Healthy volunteers n= 9	p value	RA patients n=30	SLE patients n= 21	pSS patients n= 14	p value
Females	54/65 (83,1)	7/9 (77,8)	0,654	24/30 (80,0)	19/21 (90,5)	11/14 (78,6)	0,577
Age (years)	53,0 [46,0-59,0]	52,0 [29,0-60,0]	0,353	56,0 [50,3-63,0]	50,0 [42,0-55,0]	52,5 [46,8-57,3]	0,015
CCI	2,0 [1,0-3,0]	1,0 [0,0-2,0]	0,001	2,0 [2,0-3,0]	2,0 [1,0-2,0]	2,0 [1,0-3,0]	0,136
Age at disease onset (years)	37,0 [27,0-46,0]	-	-	44,5 [36,3-51,5]	24,0 [19,0-33,0]	40,0 [29,0-44,8]	<0,001
Disease duration (years)	13,0 [6,0-25,0]	-	-	11,0 [5,0-18,5]	21,0 [12,0-32,0]	12,5 [4,5-19,3]	0,017
Steroid use	22/65 (33,8)	-	-	10/30 (33,3)	9/21 (42,9)	3/14 (21,4)	0,410
PDN dose (mg/week)	20 [15,6-26,9]	-	-	20,0 [20,0-26,9]	20,0 [15,0-25,0]	20,0 [15,0-35,0]	0,807
HCQ use	30/65 (46,2)	-	-	6/30 (20,0)	17/21 (81,0)	7/14 (50,0)	<0,001
csDMARDs use	49/65 (75,4)	-	-	25/30 (83,3)	17/21 (81,0)	7/14 (50,0)	0,059
b/tsDMARDs use	16/65 (24,6)	-	-	14/30 (46,7)	2/21 (9,5)	0/14 (0,0)	0,004
DAS28	-	-	-	1,8 [1,5-2,2]	-	-	-
SLEDAI-2K	-	-	-	-	0,0 [0,0-2,0]	-	-
ESSDAI	-	-	-	-	-	1,0 [0,0-5,3]	-
Disease remission*	42/65 (64,6)	-	-	24/30 (80,0)	13/21 (61,9)	5/14 (35,7)	0,015

Continuous variables are expressed as median [1st-3rd quartile]; categorical variables are expressed as n/number of available data (%).
*Remission was defined according to DAS28 in RA patients (≤2,6); SLEDAI-2K in SLE patients (=0); ESSDAI in pSS patients (=0).
Abbreviations: CCI: Charlson Comorbidity Index; HCQ: Hydroxychloroquine; cs-DMARD: conventional synthetic-Disease Modifying Antirheumatic Drugs; b/ts DMARD: biologic/targeted synthetic-Disease Modifying Antirheumatic Drugs; DAS28: Disease Activity Score 28; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2000; ESSDAI: Eular Sjogren's Syndrome Disease Activity Index.

Conclusions: patients affected by SLE and other RMDs reported worse fatigue and quality of life than HV. A greater fatigue appears associated with female sex as well as with sleep disturbances, anxiety symptoms, depression, poorer social functioning and lower QoL, without differences according to the RD diagnosis nor disease activity indices. Future perspectives include the implementation of the results with the questionnaire scores obtained during subsequent follow-up visits and the data derived from the digital devices used in the field of IDEA-FAST study to evaluate the data

consistency REFERENCES. [1]L Chen et al. Annu Int Conf IEEE Eng Med Biol Soc. 2022; [2]Overman CL et al. Clin Rheumatol 2016; [3]Pollard LC et al. Rheumatology 2006.

PV173 / #295

Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

THE USE OF POLYSIMPTOMATIC DISTRESS SCALE IN A MULTICENTRIC COHORT OF SLE PATIENTS TO IDENTIFY PATIENTS WITH HIGH LEVELS TYPE 2 SYMPTOMS

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Background/Purpose: SLE is a chronic inflammatory systemic disease characterized by a complex clinical picture. It has been demonstrated that achieving remission or low disease activity is crucial to improve long term outcomes. However, in daily clinical practice, it is not rare to observe a relevant discordance between patient and physician global assessment, because of different illness perceptions. Recently, it has been proposed a different way to categorize SLE manifestations: classic inflammatory signs and symptoms has been labelled as type 1, whereas other frequent symptoms as fatigue, widespread pain, sleep disorder, brain fog with an unclear relationship to inflammation as type 2(1). The presence and severity of type 2 manifestations can be assessed with the use of Polysymptomatic distress (PSD) scale, derived from 2016 ACR Fibromyalgia Criteria (2). The aim of the present collaborative study was to assess the prevalence of type 2 in a multicenter cohort of SLE patients, to evaluate correlations with other PROs and to evaluate differences in clinical manifestations, disease activity, treatment and PROs performance in patients with or without high level type 2 SLE

Methods: Adult SLE patients consecutively followed in two Lupus Clinic from March to July 2024 were included.PSD score is obtained by summing the Widespread Pain Index and Symptom Severity Scale (range score 0-31), and high level type 2 is defined as ≥ 12 (2). Fatigue was assessed through FACIT-Fatigue, quality of life with EuroQoL 5 Dimensions 3 Levels (EQ-5D-3L) and Short Form-36 Health Survey (SF-36). Medical records including demographic data, clinical characteristics and outcomes measures were collected

Results: The study included 238 patients (92% women), Caucasian in 95%, with a median age of 47 years and a mean disease duration of 199 months. Concerning level of education 28.1% had a primary/middle school education, high school in 38.6% and 33.3% postsecondary education. The majority of patients were employed (68.7%),

followed by retired in 17.8%, unemployed 10% and 3.5% were students. 30 (12.7%) patients had a diagnosis of fibromyalgia. At the last evaluation mean SLEDAI was 1.48 (±1.77), mean SLE-DAS 1.34 (±1.94); 193 (81.4%) and 184 (80.3%) met the criteria for SLE-DAS or DORIS remission. We reported a mean PSD of 7.99 (±6.08) and, as shown in table 1, PSD score strongly correlated negatively with SF-36 domains, FACIT and EQ-5D-3L and patient global assessment, whereas it does not correlate with physician global assessment, disease activity or damage scores. Moreover, a significant positive correlation was found with BMI and disease duration. A high level type 2 (PSD≥12) was found in 58 patients (24.3%), and comparison between patients with and without high level type 2 is reported in table 2. No differences were found in cumulative clinical manifestations, disease activity or damage and ongoing SLE treatment, whereas patients with higher PSD were older, with a higher BMI and more frequently had a primary/secondary education. Moreover, they had a worse performance in all the PROs.

	r	P value
SF-36		
physical functioning	-0.61	<0.0001
role physical	-0.51	<0.0001
bodily pain	-0.71	<0.0001
general health	-0.47	<0.0001
vitality	-0.66	<0.0001
social functioning	-0.56	<0.0001
role emotional	-0.55	<0.0001
mental health	-0.61	<0.0001
FACIT-F	-0.75	<0.0001
EQ-5D-3L	-0.70	<0.0001
Patient global assessment	-0.47	<0.0001
Physician global assessment	-0.03	ns
SDI	0.03	ns
SLE-DAS	0.05	ns
BMI	0.27	<0.0001
Current age	0.21	0.0011
Duration of follow-up	0.18	0.0068

Table 1 Spearman correlations of PSD scores with PROs, demographic features and disease activity measures. Categorical variables were reported as proportion and/or percentage, continuous variables were expressed as mean (±standard deviation) values.

	PSD score ≤11 N = 180	PSD score ≥ 12 N = 58	P value
DEMOGRAPHIC FEATURES			
Females	162 (90)	57 (98.3)	0.05
Mean age	46 (±14)	51 (±13)	0.0297
Mean BMI	23.8 (±4.7)	26.5 (±6.7)	0.0056
Primary/middle school education	38 (21.7)	26 (49.1)	0.0000*
Retired	25 (14.2)	16 (29.6)	0.0170**
CUMULATIVE CLINICAL MANIFESTATIONS			
Cutaneous	96 (53.3)	31 (53.4)	ns
Ulcers	44 (24.4)	17 (29.3)	ns
Non scarring alopecia	44 (24.4)	12 (20.7)	ns
Sinovitis	99 (55.0)	28 (48.3)	ns
Serositis	34 (18.9)	14 (24.1)	ns
Renal	69 (38.3)	21 (36.2)	ns
Neurological	16 (8.9)	4 (6.9)	ns
Hematological	120 (66.7)	40 (69.0)	ns
PROS			
SF-36			
physical functioning	81.78 (±20.4)	49.91 (±26.8)	<0.0001
role physical	77.12 (±29.91)	46.12 (±31.6)	<0.0001
bodily pain	69.95 (±22.5)	36.08 (±18.7)	<0.0001
general health	48.16 (±18.2)	32.81 (±15.4)	<0.0001
vitality	56.53 (±19.6)	32.95 (±15.4)	<0.0001
social functioning	76.12 (±22.3)	51.94 (±26.26)	<0.0001
role emotional	80.79 (±26.3)	49.57 (±34.2)	<0.0001
mental health	69.94 (±18.6)	48.92 (±20.1)	<0.0001
FACIT-F	39.76 (±8.0)	24.25 (±9.7)	<0.0001
EQ-5D-3L media	0.76 (±0.2)	0.44 (±0.2)	<0.0001
ONGOING TREATMENTS			
GC	80 (44.4)	21 (36.2)	ns
HCQ	164 (91.1)	48 (82.8)	ns
cDMARDS	80 (44.4)	23 (39.7)	ns
Biological DMARDs	37 (20.6)	10 (17.2)	ns
Antidepressant/anti-anxiety	53 (29.4)	34 (58.6)	0.0001***
DISEASE ACTIVITY AND DAMAGE			
SLEDAI-2K	1.41 (±1.71)	1.69 (±1.94)	ns
SLE-DAS	1.25 (±1.88)	1.62 (±2.11)	ns
SLE-DAS remission	150 (83.8)	43 (74.1)	ns
SLE-DAS LDA	159 (88.8)	45 (77.6)	ns
DORIS remission	140 (80.9)	44 (78.6)	ns
SDI	0.76 (±1.34)	0.79 (±1.35)	ns

Categorical variables were reported as proportion and/or percentage, continuous variables were expressed as mean (±standard deviation) values. *OR3,47, 95% CI 1,82-6,63; **OR2,54, 95%CI 1,24-5,23, *** OR 3,40, 95%CI (1,84-6,27)

Conclusions: High level type 2 SLE symptoms occurred in nearly 25% and its occurrence was not related to classic disease manifestation or objective disease activity, but with other features as weight, age, concomitant depression/anxiety. Moreover, PSD performance strongly correlates with other PROs and has the advantage of being completed in a short time and therefore its use in daily practice could be more feasible. References (1)Pisetsky DS. Arthritis Care Res (Hoboken).2019Jun;71(6):735-741. (2) Wolfe F. Semin Arthritis Rheum 2016;46:319-329.

PV174 / #623

Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

WORK OUTCOMES AND PREDICTORS OF EARLY WORK CESSATION IN INDIVIDUALS LIVING WITH SYSTEMIC LUPUS ERYTHEMATOSUS: INSIGHTS FROM THE CANADIAN CANIOS COHORT

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Background/Purpose: Early work cessation is a significant contributor to the personal and societal costs associated with systemic lupus erythematosus (SLE). We sought to describe work status in people with diagnosed SLE and to identify factors associated with early work cessation.

Methods: We used data from the multicentre Canadian Network for Improved Outcomes in Systemic lupus erythematosus cohort (CaNIOS). Lupus symptoms were assessed using the self-reported SLE activity questionnaire (SLAQ). Health related quality of life which reflects health status was assessed using the Short-Form 36 physical and mental component scores (PCS and MCS respectively). Work status [working at least 10 hours per week, retired, full-time student, disabled, full-time homemaker] and hours worked/week (categorized as 1-15, 16-30, >30 hrs) were reported annually. We evaluated work status at baseline and during follow-up in participants of working age (defined as <66, the average retirement age in Canada). We defined incident SLE as having the baseline study visit within 12 months of diagnosis. Binary logistic regression analysis was used to identify variables associated with baseline work status. Models included gender, duration of lupus, achievement of high school education, SLAC, PCS and MCS.

Results: Work status was available for 2194 working age participants (90.6% women, mean age 43 (12.7) years, 1910/2170 (88%) completed high school, 693/1245(56%) had insurance for disability, 1040/1350 (77%) for prescription drugs, and 811/1267(64% for physiotherapy). At the baseline visit, for prevalent cases, 1158/(52.8%) were working, 214(9.8%) were retired, 225 (10.3%) were full-time homemakers, 145(6.6%) were full-time students and 363 (16.5%) were disabled. Of working age participants 269 had incident SLE. For the 269 incident SLE participants of working at the baseline visit 157 (58.4%) were working, 19 (7.1%) were retired, 27(10.1%) were full-time homemakers, 21 (7.8%) were full-time students and 33 (12.3%) were disabled. Work status was stable during follow-up as were overall hours worked (Figure). In the subset of participants with available data (N=407), high school completers (OR 3.0 (1.61,5.65), higher (better) PCS (1.07 (1.04, 1.09) and MCS (1.03 (1.01, 1.05), and higher SLAQ 1.045(1.01, 1.08) were associated with working at baseline; gender (OR 1.5(0.72,3.32) and disease duration OR 0.99(0.97, 1.01) were not.

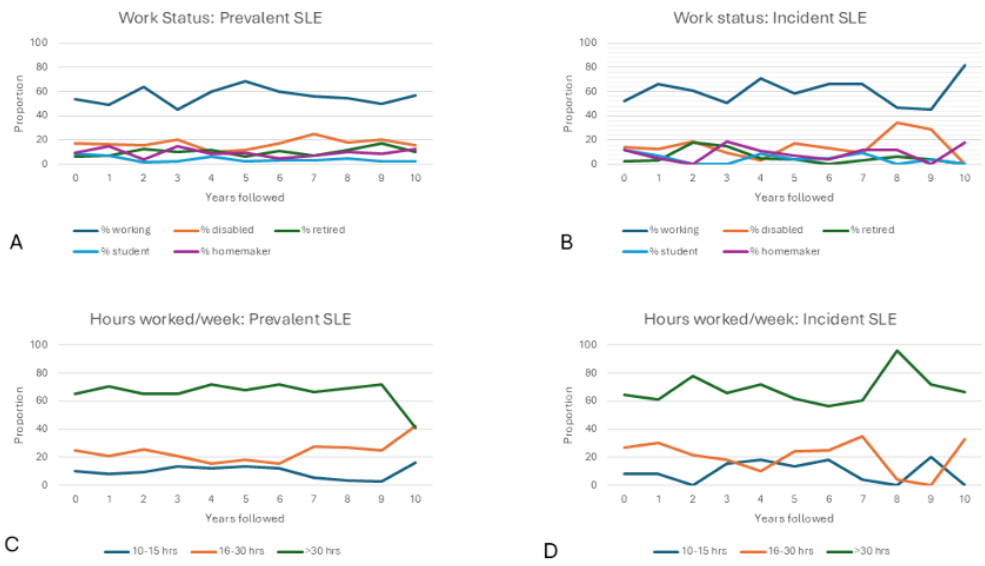

Figure: Employment status over time
A. Prevalent SLE, **B.** Incident SLE, **C.** Hours worked prevalent SLE, **D.** Hours worked incident SLE

Conclusions: Patients with SLE are employed at lower rates than the general Canadian population. Employment appears to be influenced by both demographic factors such as education and both physical and mental health status. Strategies to imporve employment rates for people with SLE are needed.

PV175 / #503

Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

TYPE 2 LUPUS IS THE MAJOR PREDICTOR OF FATIGUE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CROSS-SECTIONAL STUDY OF 200 PATIENTS

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Background/Purpose: * first and second authors listed share first authorship Fatigue is a major symptom in patients with systemic lupus erythematosus (SLE) significantly impacting health-related quality of life (HR-QoL). Causes of fatigue in SLE are multifactorial and not well understood. A novel framework categorizes SLE manifestations into type 1 and type 2. Type 1 manifestations can be ascribed to inflammation and captured in activity indexes, whereas type 2 symptoms (such as fatigue, pain, sleep, and mood disturbances) have no clear relation to disease activity. Type-2 SLE is defined using the polysymptomatic distress scale (PDSS). Objective: To identify predictors of fatigue in SLE patients.

Methods: Cross-sectional study of SLE patients fulfilling ACR/EULAR 2019 and/or SLICC 2012 classification criteria followed in a Rheumatology outpatient clinic. Inclusion was from December 2023 to May 2024.

Results: The study included 200 patients with SLE (female: 92.0%; mean age: 46.4±14.3 years; median age at diagnosis: 28.5 [16.0] years). Severe fatigue was present in 28.6%. In the study population, 87.5% fulfilled the LDA treatment target, 30.5% had type 2 SLE, 38.5% had organ damage, and 17.0% were diagnosed with fibromyalgia. Patients with severe fatigue had worse scores in both PDSS and aPDSS ($p<0.0001$). The aPDSS cut-off that better predicted SLE type 2 was ≥9.50 (sensitivity 96.9%, specificity 99.9%). Univariate analysis showed significant variables for severe fatigue: female sex ($p=0.04$), age ($p=0.02$), disease duration ($p=0.02$), SLE-DAS ($p=0.03$), type 2 SLE (PDSS and aPDSS definitions) ($p<0.001$), and fibromyalgia ($p<0.001$), while LDA was protective ($p<0.01$). SLEDAI and SDI were not significant. Multivariate analysis revealed type 2 SLE [OR 25.33; 95%CI(10.63-60.31); $p<0.001$) and diagnosis of fibromyalgia [OR 3.51; 95%CI(1.16-10.69); $p<0.05$] as independent predictors of severe fatigue. Similar findings were found when using aPDSS, [OR 16.16; 95%CI(7.22-36.13); $p<0.001$)] for type 2 SLE and [OR 4.44; 95%CI(1.51-12.26); $p<0.05$] for fibromyalgia.

Conclusions: In this cohort of SLE patients, type 2 lupus was the major predictor of severe fatigue. Physicians and patients should be careful not to attribute fatigue to inflammatory type 1 disease activity when the LDA treatment target is achieved. This should be taken into consideration for establishing the management strategy.

PV176 / #700

Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

LIVING WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN MAURITIUS: A NARRATIVE STUDY OF PATIENT EXPERIENCES

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Background/Purpose: Systemic Lupus Erythematosus (SLE), commonly known as Lupus, is a complex, chronic autoimmune disease characterized by the immune system attacking healthy tissue and organs. The condition presents a broad spectrum of physical, psychological, and social challenges, significantly affecting patients' quality of life. While advances in clinical research have improved diagnostic and therapeutic strategies, the personal and social dimensions of living with SLE remain underexplored, particularly in regions such as Mauritius where public awareness and systemic support may be limited. This study aimed to investigate the lived experiences of individuals diagnosed with SLE in Mauritius, focusing on their emotional, social, and practical challenges.

Methods: Employing a narrative methodology, data were collected through in-depth telephone interviews with 60 participants diagnosed with SLE. The interviews were designed to capture rich qualitative data on sociodemographic characteristics and personal reflections using open-ended questions. Participants represented diverse backgrounds, ensuring a comprehensive exploration of experiences. The analysis involved meticulous transcription, iterative reading, and thematic coding. The data were structured around three key domains informed by both existing literature and study findings: **Pre-Diagnosis**: Participants described the prolonged diagnostic journeys marked by misdiagnosis, lack of awareness, and frustration with the healthcare system. **Response to Diagnosis**: While receiving a diagnosis brought relief and validation of symptoms, it also elicited fear, denial, and anxiety about managing a lifelong condition. **Daily Challenges and Coping Mechanisms**: Six overarching themes emerged from these domains: **Pain and Fatigue**: The pervasive physical symptoms disrupted daily routines and social engagement. **Changes in Appearance**: Visible manifestations such as skin rashes and hair loss impacted participants' self-esteem and social confidence. **Impact on Relationships**: Strain on familial, social, and professional relationships was widely reported, with many citing stigma and lack of understanding from others. **Emotional Burden**: Participants experienced fear of disease progression, frustration with medical uncertainty, and struggles with mental health. **Economic Strain**: The financial burden of lifelong treatment, frequent medical visits, and reduced work capacity added significant stress. **Support Networks**: Many

participants emphasized the absence of sufficient emotional and practical support from family, employers, and even healthcare providers.

Results: The findings underscore the multifaceted impact of SLE on patients' lives, highlighting systemic gaps in awareness, early diagnosis, and support mechanisms. Participants called for enhanced public education about SLE, greater sensitivity from employers and medical professionals, and the establishment of community-based support groups.

Conclusions: This study contributes to the growing body of research on chronic illness in underrepresented populations, emphasizing the need for tailored interventions in Mauritius and across the African continent. Enhanced public health initiatives and patient-centered care models are crucial to addressing the unmet needs of individuals with SLE, fostering greater inclusion, and improving their quality of life.

PV177 / #114

Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

THE COVID-19 PANDEMIC REDUCED STRESS DIFFERENTLY IN PEOPLE WITH LUPUS BY POVERTY AND SOCIAL ISOLATION

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Background/Purpose: Background/Purpose Many people with systemic lupus erythematosus (SLE), particularly from communities of color in the U.S., suffer from substantial psychosocial and socioeconomic stressors. The COVID-19 pandemic had a significant impact on mental health. We evaluated the effect of the pandemic in PWL on stress by social isolation (SI) and poverty.

Methods: Methods Georgians Organized Against Lupus (GOAL) is a Centers for Disease Control and Prevention (CDC)-supported population-based cohort of validated SLE patients in Atlanta who completed annual surveys across multiple domains from surveys in 4 periods: pre-pandemic or baseline (8/20/2017-1/31/2020), early-pandemic (2/1/2020-9/18/2021), late-pandemic (9/19/2021-5/11/2023), and post-pandemic (5/12/2023-10/15/2024). The early and late pandemic periods coincide with the U.S. COVID-19 Public Health Emergency declaration divided in half. At baseline, we analyzed sociodemographics and validated measures of lupus characteristics and physical and psychological parameters, including poverty and PROMIS SI (see table). A mixed model for repeated measures was used to characterize time trends for the outcome (Perceived Stress Scale, PSS). The model was expanded through stratification to examine the possible effect modification of poverty and SI at baseline on longitudinal PSS trends across the periods (see figures).

Results: Results At baseline, out of 953 participants, most identified as female (94%) and Black (81.3%) and had a mean age of 47.5 years. Over 62% lived at or below 200% of the Federal Poverty Level (high poverty), and 29.5% (281 out of 953) had some SI (PROMIS score > 50). High-poverty individuals were mainly Black, younger, had no or government insurance (Medicare and/or Medicaid), and had higher disease activity and damage. Socially isolated individuals were mostly younger, poorer, and had higher disease activity and damage. Baseline stress was higher in those with SI and high poverty. From the pre- to early-pandemic period in the moderate-severe SI group, the mean PSS score declined by 2.67 (95% CI: 2.81-5.55) for those in the high poverty group compared to 2.17 (95% CI: 0.21-4.12) in the low poverty group. The PSS scores do not, over time, return to pre-pandemic levels. Those without SI had no significant changes in

stress over time. When stratified by poverty level, there is a suggestion of different stress trajectories by the degree of SI, though again, not reaching pre-pandemic levels.

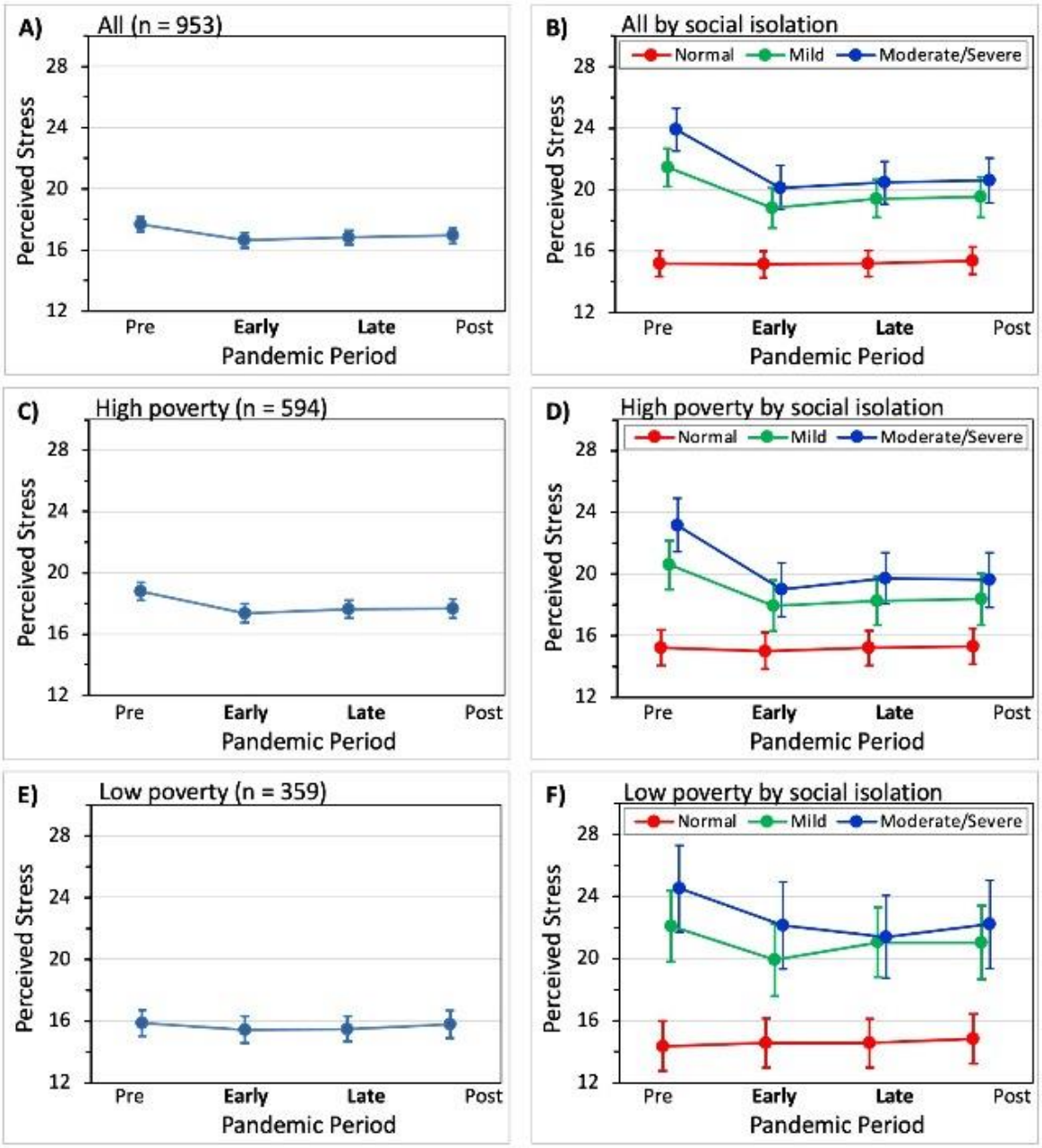
Conclusions: Conclusions Though this may be unexpected, improvement in stress with the pandemic in those with SLE may have indicated how severe stress had been for these individuals before the pandemic. The impact of SI on stress may be mediated through stigmatization and poor functional status. The pandemic may have reduced these factors by bringing people with SLE closer to the general population as the public isolated themselves, wore masks, and implemented occupational and other financial support measures. Improvement in stress was seen most in those with higher levels of SI and poverty, which may be subgroups to study further and target interventions. Additional research is needed into other related causal pathways, mitigating factors, biological mechanisms, and whether these improvements are durable. *Acknowledgements: This work was supported by the CDC grant U01DP006698.*

Table. Descriptive characteristics at baseline (before the pandemic)

Characteristic	Overall	Social Isolation				Poverty		
		Normal	Mild	Moderate-Severe	P-value	Low (≥ 200%)	High (< 200%)	P-value
	N = 953	n = 672	n = 154	n = 127		n = 359	n = 594	
Gender, n (%)					0.20			0.30
Male	57 (6.0)	38 (5.7)	14 (9.1)	5 (3.9)		18 (5.0)	39 (6.6)	
Female	896 (94.0)	634 (94.3)	140 (90.9)	122 (96.1)		341 (95.0)	555 (93.4)	
Race, n (%)					0.68¥			**< 0.001¥**
White	158 (16.6)	107 (15.9)	29 (18.8)	22 (17.3)		112 (31.2)	46 (7.7)	
Black	775 (81.3)	552 (82.1)	120 (77.9)	103 (81.1)		234 (65.2)	541 (91.1)	
Other	20 (2.1)	13 (1.9)	5 (3.2)	2 (1.6)		13 (3.6)	7 (1.2)	
Age, Mean ± SD	47.5 ± 13.9	48.6 ± 13.8	45.9 ± 14.6	43.9 ± 13.0	**< 0.001**	50.3 ± 13.3	45.8 ± 14.1	**< 0.001**
Age Quartile, n (%)					**0.008**			**< 0.001**
≤ 36.9	239 (25.1)	151 (22.5)	46 (29.9)	42 (33.1)		59 (16.4)	180 (30.3)	
36.9-47.5	238 (25.0)	161 (24.0)	42 (27.3)	35 (27.6)		97 (27.0)	141 (23.7)	
47.6-58.3	238 (25.0)	173 (25.7)	33 (21.4)	32 (25.2)		101 (28.1)	137 (23.1)	
> 58.3	238 (25.0)	187 (27.8)	33 (21.4)	18 (14.2)		102 (28.4)	136 (22.9)	
Poverty Level, n (%)					**< 0.001**			**< 0.001**
≤ 100% FPL	367 (38.5)	226 (33.6)	73 (47.4)	68 (53.5)		-	367 (61.8)	
101-200% FPL	227 (23.8)	170 (25.3)	32 (20.8)	25 (19.7)		-	227 (38.2)	
201-400% FPL	201 (21.1)	157 (23.4)	28 (18.2)	16 (12.6)		201 (56.0)	-	
> 400% FPL	158 (16.6)	119 (17.7)	21 (13.6)	18 (14.2)		158 (44.0)	-	
Insurance, n (%)					0.20			**< 0.001**
No Insurance	126 (13.2)	87 (12.9)	23 (14.9)	16 (12.6)		16 (4.5)	110 (18.5)	
Private	335 (35.2)	252 (37.5)	46 (29.9)	37 (29.1)		232 (64.6)	103 (17.3)	
Medicare and/or Medicaid	492 (51.6)	333 (49.6)	85 (55.2)	74 (58.3)		111 (30.9)	381 (64.1)	
Lupus Activity (SLAQ), Mean ± SD	15.0 ± 8.7	13.3 ± 8.0	17.0 ± 8.1	22.0 (9.1)	**< 0.001**	12.8 ± 7.9	16.4 ± 9.0	**< 0.001**
Lupus Activity (SLAQ Score Groups), n (%)					**< 0.001**			**< 0.001**
Mild: 0-10	323 (33.9)	276 (41.1)	34 (22.1)	13 (10.2)		154 (42.9)	169 (28.5)	
Moderate: 11-16	255 (26.8)	186 (27.7)	44 (28.6)	25 (19.7)		108 (30.1)	147 (24.7)	
Severe: ≥ 17	375 (39.3)	210 (31.3)	76 (49.4)	89 (70.1)		97 (27.0)	278 (46.8)	
Lupus Damage (BILD), Mean ± SD	4.1 ± 3.7	3.8 ± 3.6	4.4 ± 3.9	4.9 ± 3.7	**0.004**	3.5 ± 3.6	4.4 ± 3.7	**< 0.001**
Lupus Damage (BILD Score Groups), n (%)					**0.029**			**0.007**
None (0)	128 (13.4)	100 (14.9)	19 (12.3)	9 (7.1)		58 (16.2)	70 (11.8)	
Mild (1-2)	252 (26.4)	182 (27.1)	44 (28.6)	26 (20.5)		108 (30.1)	144 (24.2)	
Severe (≥ 3)	573 (60.1)	390 (58.0)	91 (59.1)	92 (72.4)		193 (53.8)	380 (64.0)	
Perceived Stress, n (%)					**< 0.001**			**< 0.001**
Low: 0-13	295 (31.0)	277 (41.2)	11 (7.1)	7 (5.5)		152 (42.3)	143 (24.1)	
Moderate: 14-26	543 (57.0)	371 (55.2)	114 (74.0)	58 (45.7)		174 (48.5)	369 (62.1)	
High: 27-40	115 (12.1)	24 (3.6)	29 (18.8)	62 (48.8)		33 (9.2)	82 (13.8)	

SLAQ, Systemic Lupus Activity Questionnaire; BILD, Brief Index of Lupus Damage; FPL, U.S. Federal Poverty Level; Pearson's Chi-squared test for categorical variables; One-way ANOVA or 2-sample t test for continuous variables; ¥ Based on Fisher's exact test; Social Isolation based on PROMIS scoring: Normal (< 55), Mild (55-60), and Moderate-Severe (≥ 60)

Figures. Perceived stress across pandemic periods by baseline social isolation and poverty



Models in figures B, D, and F were adjusted for gender, race, age, poverty, insurance, Systemic Lupus Activity Questionnaire (SLAQ), Brief Index of Lupus Damage (BILD)

PV178 / #702

Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

ASSOCIATION BETWEEN IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE OUTCOMES AND DISEASE ACTIVITY IN SLE: A REAL-WORLD COHORT STUDY

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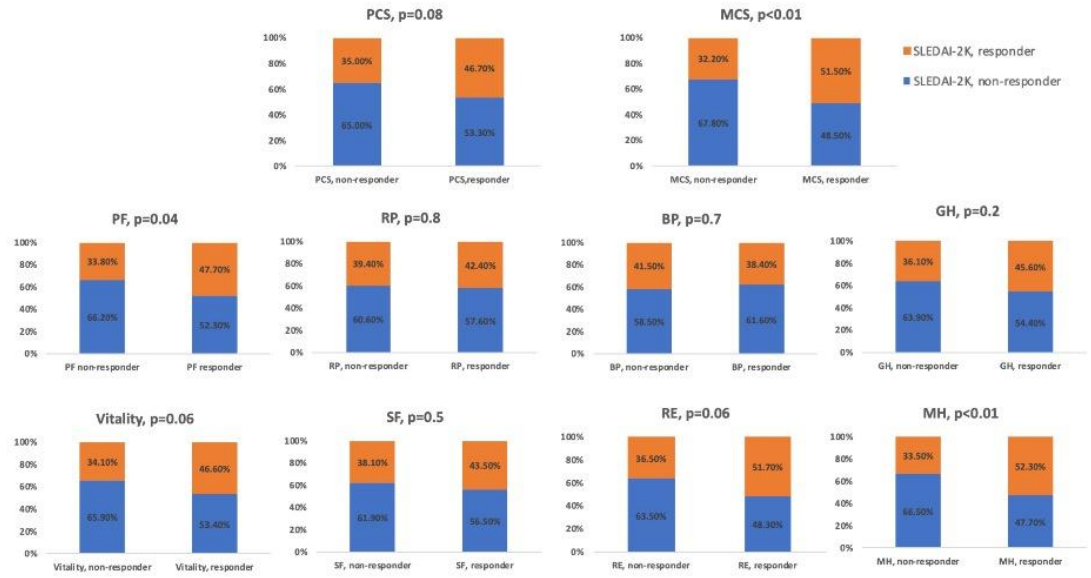
Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder associated with significant morbidity and mortality. The use of patient-reported outcome (PRO) measures in SLE to assess health-related quality of life (HRQoL) is particularly relevant for capturing aspects of the disease that are not fully reflected by traditional disease activity measures, such as Type 2 SLE features. This study aimed to evaluate the association between clinically important improvements in HRQoL scores, assessed by the Short Form 36 (SF-36), and disease activity, assessed by SLEDAI-2K, in patients with SLE in a real-world clinical setting.

Methods: This was a retrospective analysis of prospectively collected data in SLE patients followed at a single center in Toronto. Clinical and laboratory data were collected every 3-6 months, with SF-36 annually. We included patients with active disease (defined as SLEDAI-2K ≥ 6) from 2005- 2024 (marking the advent of mycophenolate mofetil use), with the availability of baseline and one-year follow-up data for SF-36. Minimum clinically important differences (MCID) in SF-36 scores were defined as increases in SF-36 Physical (PCS) and Mental Component Summary (MCS) scores by ≥2.5, individual domain scores by ≥5, and minimum important difference (MID) for SLEDAI-2K as a decrease by ≥4. Associations between improvements in SF-36 (2 summary, 8 domain) scores and SLEDAI-2K responses at one year were analyzed using chi-square tests. Two separate regression models were used to study the least squares mean differences in SLEDAI-2K scores for PCS and MCS score responders versus non-responders at one year.

Results: Among 247 patients included, median age was 37.1 years (IQR 28.5–46.5) at the study visit, female-to-male ratio of 8.8:1, and median SLE duration from diagnosis of 9.25 years (IQR 4.39–16.07). The median SLEDAI-2K score was 8 (IQR 6–12), with common organ involvements being mucocutaneous (46.6%), renal (44.9%), and

musculoskeletal (23.5%). Most patients had active serology (79.4%) and a median SDI of 1 (IQR 0–2) at the study visit. The majority received hydroxychloroquine (83%), with mycophenolate mofetil (49.4%) being the most commonly prescribed immunosuppressant, followed by azathioprine (44.9%). Among MCS score responders, a significantly greater proportion achieved SLEDAI-2K responses compared to MCS non-responders (52 of 101, 51.5 % vs 47 of 146, 32.2%, p<0.01). This association was not observed between PCS score responders and non-responders. For individual SF-36 domains, significantly more patients who reported clinically meaningful improvements in physical function (53 of 111, 47.7 vs. 46 of 136, 33.8%, p=0.04) and mental health (45 of 86, 52.3% vs. 69 of 189, 33.5%, p<0.01) domains also achieved SLEDAI-2K responses. No significant differences were reported for other domains, although there was a trend in vitality and role emotional responders to achieve SLEDAI-2K responses (**Figure 1**). In the two regression models, a significant difference in SLEDAI-2K scores from baseline to one year was observed between PCS responders vs. non-responders (-5.13 and -3.09, p<0.01) and MCS responders vs. non-responders (-5.19 and -3.14, p<0.01).

Figure 1: Proportion of SLEDAI-2K responders and non-responders in patients reporting improvements ≥ MCID versus non-responders in SF-36 summary and domain scores



Conclusions: In patients with active SLE, clinically important improvements in disease activity were notable among those who reported clinically meaningful improvements in MCS scores, physical function, and mental health domains of the SF-36 at one year. Those who demonstrated clinically meaningful improvements in both, SF-36 MCS and PCS scores had greater reductions in SLEDAI-2K scores at one year. These findings indicate that improvements in some aspects of HRQoL are associated with significant reductions in disease activity in SLE patients.

PV178a / #270

Poster Topic: ***AS19 - Patient-Reported Outcome Measures***

A VISUAL JOURNEY THROUGH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disese that can manifest in a varaitey of ways, This study aims to explore the personal journey of living with Systemic Lupus Eryhematosus (SLE) from the perspective of an individual patient. By sharing personal experiences,the study seeks to increase awareness of the disease highlight the challenges faced by patients, and emphasize the importance of self -documentation in managing SLE. the project aims to bridge this gap by utilizing a unique approach : a visual diary.Over the past four years , the reasercher ,the journalist and film maker living with SLE,has meticulously documented their daily healthy journey through photographs nd videos. The visual records capture the evolution of various SLE manifestations, incluing skin lesions,hair loss and other systemic symptoms. **Significance:** By sharing this visual narrative, the project seeks to: Increase public awareness of SLE: Visual story telling can effectively convey the complexities of the disease to broader audience, challanging misconceptions and fostering empathy. **Enhance patient -Physician Communications:** Visual documentation can aid in diagnosis, treatment planning, and disease monitoring.and to emphasize the importance of patient perspectives in driving reaserch and treatment development , particularly in relation to quality of life and patient reported outcomes. **Advance medical research** :The dataset of visual records may contribute to a deeper understanding of disease progression and treatment respnse. **Empower Patients**: Sharing personal experiences can provide support and inspiration to others living with chronic illnesses.Ethical considerations:The project adheres to ethical guidlinesfor reaserch involving human subjects.

Methods: The project involves a qualitative, autoethnographic approach.The researcher's daily visual records serve as primery data sources. These visual data will be analized using thematic analysis to identify patterns and themes related to the disease's impact on the individual's physical and emotional well-being.

Results: The patients initial symptoms included localized itching and marking on the right leg and arm, which rapidly progressed to more severe manifestations.As the condition worsened, the patient experienced significient pysical and emotional challenges, such as scalpsores,facial skin peeling, pain, fatigue, and mood disturbances. These symptoms significantly impacted the patient's quality of life and ability to peform daily activities.

Conclusions: This multimedia project chronicles a four -year journey with Systemic Lupus Erythematosus (SLE). By visual documenting the disease's progression, from initial skin manifestations to systemic impacts , this work aims to raise awareness and understanding of SLE. The project underscores the importance of early diagnosis, timely intervention, and patient advocacy. Through a combinantion of photography and videography, it offers a unique perspective on the lived experience of SLE, challenging societal perceptions and inspiring hope for individuals facing similar challenges.

PV179 / #524

Poster Topic: ***AS20 - Precision Medicine***

CLINICAL MANIFESTATIONS AT DIFFERENT FOLLOW-UP TIME POINTS IN AUTOANTIBODY-DEFINED SLE SUBGROUPS.

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Background/Purpose: The heterogeneity of SLE has impaired the advancement in diagnostic strategies, tailored treatments, and prognostic tools for this disease. Defining SLE subgroups based on autoantibody profiles can reduce such heterogeneity and reveal important differences [1]. Here, we studied a Norwegian inception cohort, with longitudinal follow-up at two years and 11 years (in median IQR[7-13]) after diagnosis.

Methods: We clustered 102 SLE patients, as previously,[1] based on 10 autoantibodies at diagnosis (Table1, Fig1A). The autoantibodies were measured using ELISA or immunoprecipitation, we assumed positivity if one of them was positive. Using logistic or linear regression, we tested associations between clusters and 13 clinical manifestations at diagnosis, two-year, and last-visit. We tested associations between the clusters and SLEDAI and some of its components: acute cutaneous lupus, cardiovascular disease, lung, or muscle-skeletal involvement for the last follow-up. Analyses were done in R v4.3.3.

Results: Four clusters explained most variability based on the Silhouette index (**Fig1**). The patients in subgroup 2 have a higher risk of photosensitivity at diagnosis (OR:12.5 95%CI:2.1-252.8) and two years after (OR:8.1 95%CI:1.7-76.8). In comparison, photosensitivity was less common in subgroup 3 compared to the rest of patients at two years (OR:0.3 95%CI:0.09-0.7)(**Fig2B**). Acute cutaneous lupus was more frequent in subgroup 2 at the last visit (OR:3.7 95%CI:1.2-14.1), lung involvement was more frequent in subgroup 1 (OR:14.5 95%CI:11.4-543.2), although it did not reach significance (p-value=0.053). SLEDAI significantly differed among the subgroups at diagnosis being higher for subgroups 4 and 3 (respectively: OR:1.5 95%CI:1.3-1.8; OR:1.3 95%CI:1.1-1.5), conversely lower for subgroups 2 and 1 (respectively: OR:0.7 95%CI:0.6-0.9; OR:0.7 95%CI:0.6-0.8). At the last visit, SLEDAI was significantly lower for subgroup 3 (OR:0.7 95%CI:0.5-0.9).

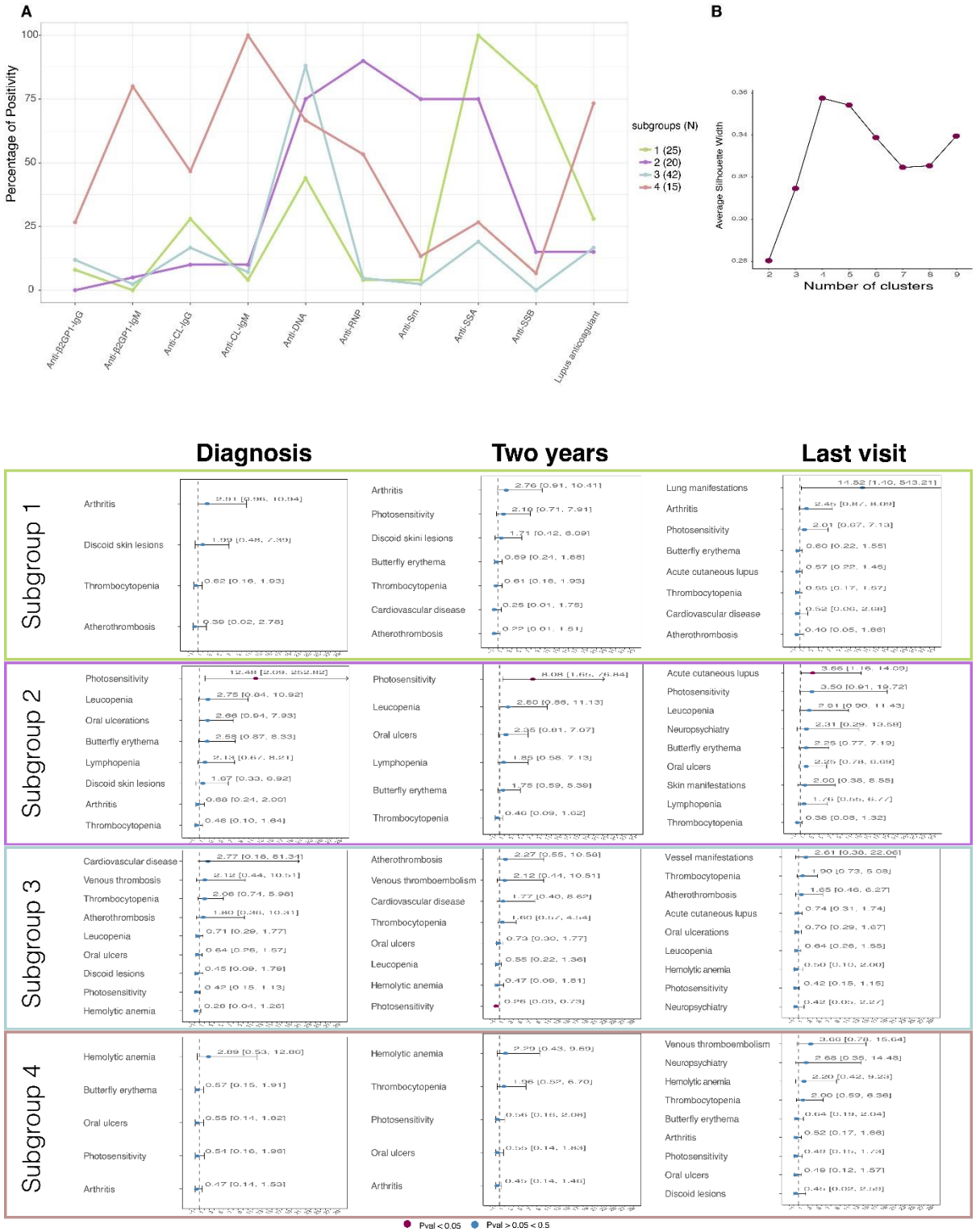
A
Percentage of Positivity
100
75
50
25
0
Anti-B2GP1-IgG
Anti-B2GP1-IgM
Anti-CL-IgG
Anti-CL-IgM
Anti-DNA
Anti-RNP
Anti-Sm
Anti-SSA
Anti-SSB
Lupus anticoagulant
subgroups (N)
1 (25)
2 (20)
3 (42)
4 (15)
B
Average Silhouette Width
Number of clusters
Diagnosis
Two years
Last visit
Subgroup 1
Arthritis
Discoid skin lesions
Thrombocytopenia
Atherothrombosis
Photosensitivity
Leucopenia
Oral ulcerations
Butterfly erythema
Lymphopenia
Discoid skini lesions
Cardiovascular disease
Lung manifestations
Acute cutaneous lupus
Subgroup 2
Oral ulcers
Skin manifestations
Subgroup 3
Cardiovascular disease
Venous thrombosis
Venous thromboembolism
Vessel manifestations
Subgroup 4
Hemolytic anemia
Neuropsychiatry
Pval < 0.05
Pval > 0.05 < 0.5

Table1. Characteristics of the SLE cohort from Norway.

	All	Subgroups			
		1	2	3	4
		anti-SSA/SB	anti-DNA, -RNP, -Sm, -SSA	anti-DNA	anti-B2GP1 IgM, -CL IgM, Lupus anticoagulant
n (%)	102 (100)	25 (24.5)	20 (19.6)	42 (41.2)	15 (14.7)
Female, n(%)	94 (92.2)	23 (92)	18 (90)	39 (92.9)	14 (93.3)
Age at diagnosis, median [IQR]	32 [24-44]	30 [25-41]	26.5 [20.8-37.3]	40 [26.5-46.5]	27 [23.5-34.5]
SLEDAI at diagnosis, median [IQR]	8 [4-14]	5 [4-11.5]	8 [4.3-10]	10 [4-16]	12 [5.5-17-5]
SLEDAI two years follow-up, median [IQR]	2 [0-4]	2 [0-5.5]	2 [0-5]	2 [0-4]	4 [2-4.8]
SLEDAI last visit follow-up, median [IQR]	2 [0-4]	2 [0-4]	2 [0-4.5]	1.5 [0-2.8]	2 [0-3.5]
Anti-DNA	73 (71.6)	11 (44)	15 (75)	37 (88.1)	10 (66.7)
Anti-RNP	29 (28.4)	1 (4)	18 (90)	2 (4.8)	8 (53.3)
Anti-Sm	19 (18.6)	1 (4)	15 (75)	1 (2.4)	2 (13.3)
Anti-SSB	24 (23.5)	25 (100)	15 (75)	8 (19.0)	4 (26.7)
Anti-SSA	52 (51)	20 (80)	3 (15)	0	1 (6.7)
Anti-CL IgG	23 (22.5)	7 (28)	2 (10)	7 (16.7)	7 (46.7)
Anti-CL IgM	21 (20.6)	1 (4)	2 (10)	3 (7.1)	15 (100)
Anti-B2GP1 IgG	11 (10.8)	2 (8)	0	5 (11.9)	4 (26.7)
Anti-B2GP1 IgM	14 (13.7)	0	1 (5)	1 (2.4)	12 (80)
Lupus anticoagulant	28 (27.5)	7 (28)	3 (15)	7 (16.7)	11 (73.3)

Conclusions: Patients with SLE from Norway can be grouped into four based on their antibody profile at the time of the diagnosis. Regardless of the limited sample size, the observations indicate that antibody-defined subgroups are a tool to reduce SLE-heterogeneity and improve perspective to study this disease. **Reference:** Diaz-Gallo LM, et al. ACR Open Rheumatol. 2022;4(1):27-39.

PV180 / #508

Poster Topic: ***AS20 - Precision Medicine***

CONFIRMATION OF EIGHT ENDOTYPES OF LUPUS BASED ON WHOLE BLOOD RNA PROFILES

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Background/Purpose: We previously described a classification system of persons with SLE based on whole blood (WB) mRNA profiles and a random forest (RF) algorithm to predict individual patient endotypes.[1.] Here, we apply this algorithm prospectively in an independent set of patients to validate its use as a staging biomarker.

Methods: WB from 101 patients participating in three clinical trials meeting ACR or SLICC criteria for SLE classification was obtained at baseline, and RNA isolated and sequenced. Gene expression values were used as input to Gene Set Variation Analysis (GSVA) and the RF algorithm was applied using GSVA enrichment scores of 32 informative gene sets as input. Composite scores summarizing gene expression perturbations were assigned to each patient using a ridge logistic regression algorithm. Binary classifiers characterizing patients in the prospective cohort into each endotype were additionally constructed and Shapley Additive Explanations (SHAP) analysis was employed to explain the contribution of molecular features to the RF algorithmic decision.

Results: Eight SLE endotypes were identified by the algorithm.[

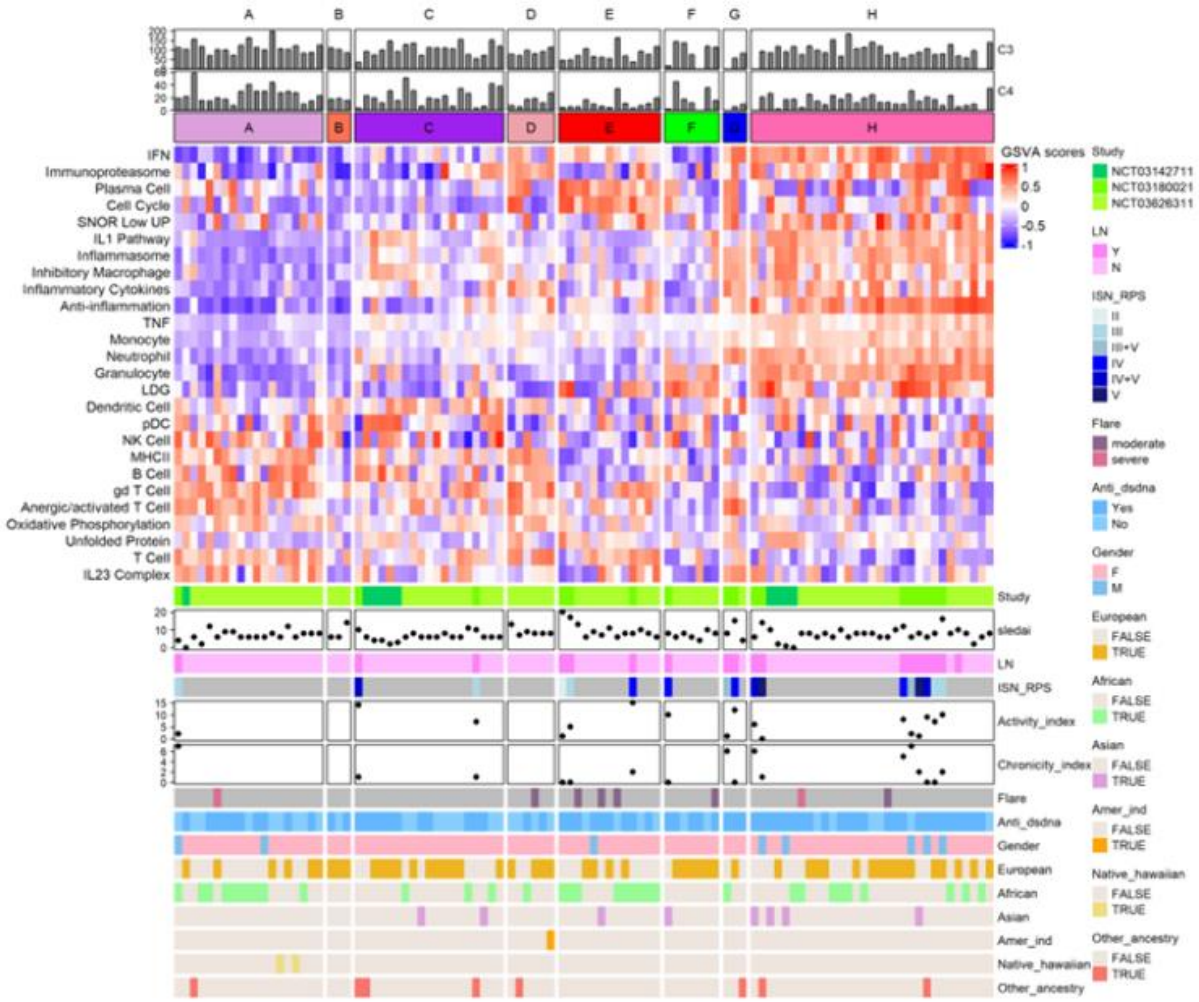

Figure 1. Identification of Eight Endotypes Among 101 SLE Patients
GSVA enrichment scores of 26 immune/inflammatory modules show the molecular profiles for each of the 101 SLE patients according to endotype membership, which was identified by a random forest algorithm using the enrichment scores. Clinical metadata for each patient (x-axis) was annotated as shown. Heatmap constructed in R v 4.3.3 using the ComplexHeatmap package v. 2.18.0. LN=lupus nephritis; ISN_RPS=International Society of Nephrology/Renal Pathology Society.

] Patterns of gene enrichment in the identified endotypes mirrored those found in the previously reported endotypes.[1.] Differences in clinical characteristics, including serum complement levels, autoantibody positivity, and the presence of nephritis, were observed between patients in various endotypes. Patients with active, contemporaneous nephritis were disproportionately assigned to the more molecularly perturbed endotypes. Composite scores were significantly, but modestly, inversely correlated with complement but not SLEDAI or anti-dsDNA titer. SHAP analysis revealed specific important features and patterns of features per endotype and per patient contributing to the RF models' classification decision.

Conclusions: The identification of eight molecular endotypes of lupus based on WB gene expression was validated in an independent dataset of diverse patients. Endotyping SLE patients based on transcriptional profiles can provide important status

(presence of nephritis) information and provide novel molecular insights in support of personalized management.

PV181 / #691

Poster Topic: ***AS20 - Precision Medicine***

LOW-DOSE INTERLEUKIN-2 THERAPY IN ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (LUPIL-2): A MULTI-CENTER, DOUBLE-BLIND, RANDOMIZED AND PLACEBO-CONTROLLED PHASE 2 TRIAL

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Background/Purpose: A regulatory T cell (Treg) insufficiency due to shortage of interleukin-2 (IL-2) is central to the pathophysiology of systemic lupus erythematosus (SLE). We performed an international, multi-center, double-blind, randomized, placebo-controlled phase 2 proof-of-concept trial to evaluate the safety and efficacy of low-dose IL-2 therapy in patients with SLE having moderate-to-severe disease activity while receiving standard-of-care treatment.

Methods: We randomly assigned 100 patients in a 1:1 ratio to receive either 1.5 million IU/day of subcutaneous IL-2 (ILT-101) or placebo for 5 days followed by weekly injections for 12 weeks. Clinical efficacy was assessed at week-12 in a predefined hierarchical analysis of (1) the SLE responder index-4 (SRI-4) response as a primary endpoint, and (2) of relative and (3) of absolute changes in the SELENA-SLEDAI scores as key secondary endpoints. Multi-color flow cytometry was applied at defined time points to assess changes in Treg and other immune cells.

Results: Although the primary endpoint was not met in the intention-to-treat population (ILT-101: 68%, placebo: 58%; p=0.3439), which was due to a 100% SRI-4 response rate in placebo-treated patients at two study sites from the same country (n=14 in total), a post-hoc analysis on a prespecified per-protocol population that also excluded patients from these two sites (n=53) revealed a statistically significant difference at week-12 in favour of ILT-101 for the SRI-4 response rate (ILT-101: 83.3%; placebo: 51.7%; p=0.0168) and for the two key secondary endpoints ($p<0.05$). This was accompanied by significant differences ($p<0.05$) in several secondary and exploratory endpoints, such as proportions of SRI-6 and SRI-8 responders, patients in remission and changes in glucocorticoids. Notably, a significant and robust difference in the SRI-4 response rate was already evident at week-8 (ILT-101: 79.2%; placebo: 41.4%; p=0.0051). ILT-101 was

safe and well-tolerated and no generation of anti-drug antibodies was observed. Treatment with ILT-101, but not with placebo, led to a selective and sustained expansion of the CD25hi Treg population and clinical benefit was associated with the magnitude of the Treg response.

Conclusions: The post-hoc hierarchical analysis of the primary and key secondary endpoints in a per-protocol population, complemented by the exploratory analyses of multiple other secondary endpoints, consistently support that low-dose IL-2 therapy is beneficial in active SLE. Our data also imply that clinical efficacy of low-dose IL-2 therapy is driven by the activation and expansion of the Treg population, which adds confidence in the pathophysiological concept of an impairment of the Treg-IL-2 axis in SLE. The results of this trial (1) in conjunction with encouraging data from several other studies (2) warrant the further development of low-dose IL-2 therapy as precision medicine for SLE and other autoimmune diseases, and provide a valuable scientific basis for the design of confirmatory phase 3 clinical trials in SLE. **References:** 1) Humrich JY et al. Ann Rheum Dis. 2022; 81(12):1685-1694. doi: 10.1136/ard-2022-222501. 2) Akbarzadeh R, Riemekasten G, Humrich JY. Curr Opin Rheumatol. 2023;35(2):98-106. doi: 10.1097/BOR.0000000000000924. **Trial registration number:** NCT02955615 **Funding:** Funding was provided by ILTOO Pharma (trial sponsor) and the French National Research Agency (ANR-16- RHUS- 0001, RHU IMAP).

PV182 / #43

Poster Topic: ***AS20 - Precision Medicine***

MODULAR GENE EXPRESSION CHANGES IN THE SLEEK PHASE 2 STUDY OF UPADACITINIB AND ABBV-599 IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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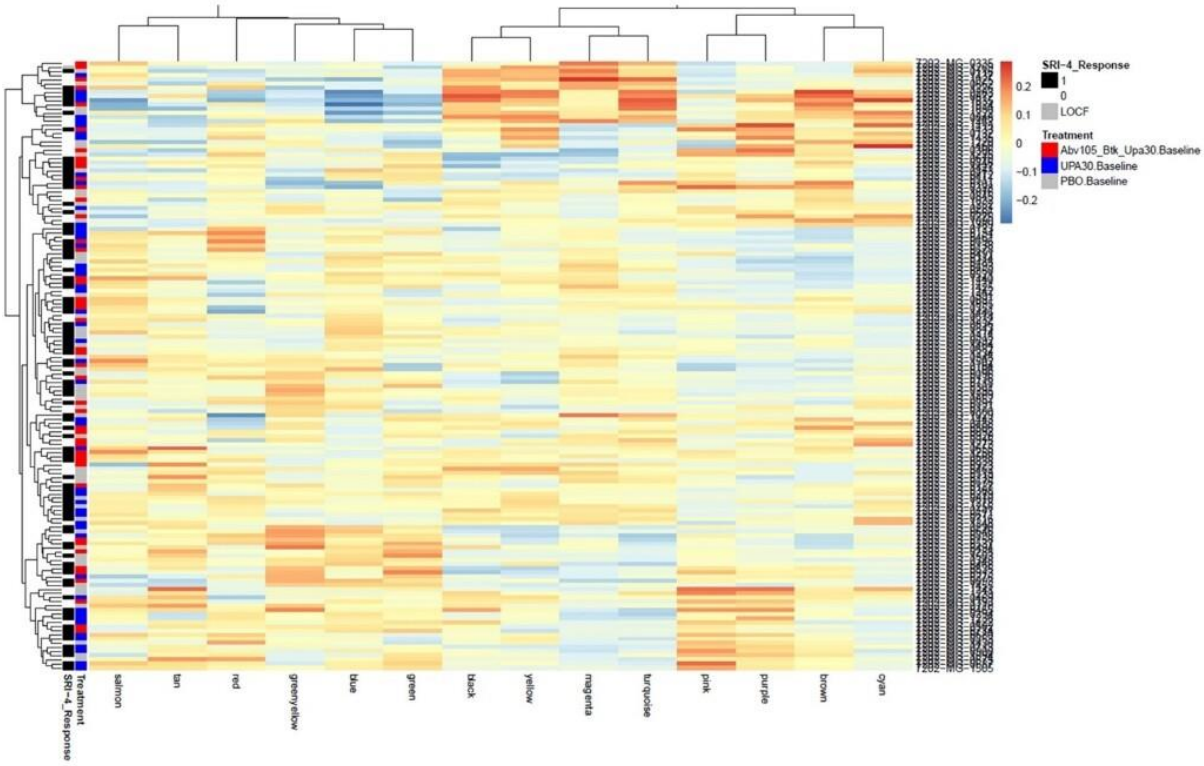
Background/Purpose: In systemic lupus erythematosus (SLE), targeting both type I interferon (IFN) and B-cell pathways should be a promising therapeutic approach since each provides independent and additive contributions to pathology. Upadacitinib (UPA) is a Janus kinase (JAK) inhibitor acting at several receptors both directly and indirectly transmitting IFN signals. Elsubrutinib inhibits Bruton's tyrosine kinase (BTK) associated with B-cell signaling. A phase 2 SLE trial (NCT03978520) of UPA, elsubrutinib, or combination (ABBV-599) found that both UPA and ABBV-599 met the 24-week endpoint of SLE Responder Index 4 (SRI-4). However, in the overall population, efficacy of UPA alone was comparable to ABBV-599. To characterize the mechanism of action of UPA and ABBV-599 in patients with SLE.

Methods: This randomized, double-blind, phase 2 trial collected blood at baseline, and weeks 2, 12, 24, and 48. RNAseq analysis was compared from 147 patients who received placebo, UPA (30mg once daily (QD)), or ABBV-599 (elsubrutinib 60mg + UPA 30mg QD). Limma mixed-model analyses were used to determine differentially expressed genes between timepoints and to predict responders/non-responders totherapy. Weighted gene co-expression network analysis (WGCNA) was used to construct gene networks and to determine changes of these networks (significance by paired Wilcoxon test). Total immunoglobulin G (IgG), immunoglobulin M (IgM), and anti-double-stranded DNA (anti-dsDNA) IgG concentrations were measured from serum using an immunoturbidimetric assay and enzyme linked immunosorbent assay. Immune cell subsets and counts were identified using flow cytometry.

Results: Differentially expressed genes (FDR <.05) for all timepoints compared with baseline were detected for both UPA and ABBV-599 , but not placebo. Distinct differences between UPA and ABBV-599 in the number of differentially expressed genes at all timepoints suggested unique mechanisms for the drugs. WGCNA of the 147 baseline samples formed 14 modules of highly correlated genes and 12 of these modules overlapped previously identified WGCNA-derived SLE gene modules. Module trait correlation demonstrated significant relationships between module scores and clinical traits (P<.01; R >.3), but not with response to treatment, in agreement with

baseline heterogeneity of gene module expression for responders demonstrated by hierarchical clustering (**Figure 1**). The change in module eigengene values demonstrated that the BTK inhibitor led to a significant increase in neutrophil module scores, and flow cytometry demonstrated a significant increase in the percentage of neutrophils in ABBV-599, but not UPA–treated patients. However, ABBV-599 did not demonstrate a unique effect on B-cell modules, with comparable significant impacts of both UPA and ABBV-599 on post-baseline decrease in total IgG, anti-dsDNA antibodies and increase in B cells by flow cytometry. As expected, UPA significantly changed gene module values for type I IFN compared with placebo and also decreased the expression of basophil, cell cycle, and cytotoxic T-cell gene modules.

Figure 1. Baseline heterogeneity in SLE gene module expression



SLE, systemic lupus erythematosus; LOCF, last observation carried forward; PBO, placebo; SRI-4, SLE Responder Index 4; UPA, upadacitinib

Conclusions: ABBV-599 increased neutrophil and other myeloid cell gene module scores compared to UPA, but this effect could have neutral impact related to its role in neutrophil extravasation. The BTK inhibitor in combination with UPA had little additional effect on B cells compared to UPA alone. In addition to the expected decreased expression of type I IFN gene modules, UPA treatment was associated with decreased basophil, cytotoxic T-cell, and cell cycle gene modules accounting for its efficacy in SLE patients with different baseline gene expression patterns.

PV183 / #357

Poster Topic: ***AS20 - Precision Medicine***

BELIMUMAB REDUCES THE RISK OF FLARES ASSOCIATED WITH THE BAFF OVEREXPRESSING TNFSF13B GENE VARIANT: A HINT FOR PERSONALIZED TREATMENT IN SLE.

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Background/Purpose: The TNFSF13B gene functional variant (BAFFvar) is an insertion-deletion (GCTGT→A) introducing an alternative polyadenylation motif generating a truncated/shorter gene transcript that escapes miRNA inhibition, yielding increased production of soluble BAFF (Steri M., et al. NEJM 2017). The consequent overexpression of BAFF, in turn, up-regulates humoral immunity, increases the production of autoantibodies, and increases the risk of developing SLE. The present study investigates if BAFF-var status influences the risk of overall and renal SLE flares and whether patients stratified according to BAFF-var status might show a differential benefit from anti-BAFF treatment.

Methods: This study used data from patients included in a monocentric SLE inception cohort between 1 January 2006 and 31 December 2022. Inclusion criteria were: (a) SLE classified according to the ACR/EULAR 2019 and/or SLICC 2012 and/or ACR 1997 criteria; (b) evaluation in at least three consecutive visits (not less than two visits every 12 months); (c) genotyping for BAFFvar. Demographic, clinical, serologic, and treatment variables were recorded. Flare was defined as the onset of a new SLE manifestation or worsening of a preexisting clinical manifestation resulting in a therapy change. Renal flares were nephritic (≥10 RBCs/hpf with or without a decrease in eGFR by ≥10%, irrespective of changes in proteinuria) or nephrotic (doubling of proteinuria to >1g/24h or to >2g/24h depending on the previous complete or partial response). Kaplan-Meier curves were used to analyze the association between BAFFvar and overall or renal SLE flares. Multivariate Cox-regression models were built, including demographic, clinical, and serologic data and past or ongoing treatment as covariates.

Results: 194 (89.2% female) out of 256 screened patients were analyzed (Table 1). The mean age was 41.1 (± 14.8) years, the mean number of follow-up visits was 17 (± 8) and 119 (61.3%) were BAFFvar
carriers.

TABLE 1. Baseline characteristics of the lupus cohort at entry into the study.

FEATURES	VALUE
Age in years, mean (± SD)	41.1 (± 14.8)
Sex, female/male (%)	177/17 (90/10)
Disease duration in years, median IQR	8.96 (0 – 9.0)
Follow-up in years, mean (± SD)	8.8 (± 4.6)
Number of visits, mean (SD)	16.9 (± 8.1)
Cumulative manifestations *	
Constitutional	136 (70%)
Mucocutaneous	147 (75.8%)
Neuropsychiatric	23 (11.9%)
Musculoskeletal	182 (93.8%)
Cardiorespiratory	68 (35.0%)
Gastrointestinal	4 (2.1%)
Ophthalmic	5 (2.6%)
Hematologic	86 (44.3%)
Renal	53 (27.3%)
SLEDAI, median (range)	2 (0 – 6)
SDI, median (range)	0 (0 – 5)
Medications**	
Prednisone	188 (96.9%)
Hydroxychloroquine	165 (85.0%)
Immunosuppressants	128 (66%)
Biologics	3 (1.5%)

* According to BILAG domains ** Previous or ongoing at baseline. LA: Lupus anticoagulant. ACl: Anticardiolipin antibodies IgM/IgG. aB2GPI: anti-B2-glycoprotein I IgM/IgG.

During follow-up, 119 patients (56.2%) experienced at least one flare, with 60 patients (30.9%) having more than one flare. The median number of flares was higher (p=0.038) in BAFF-var carriers (1; IQR 0-2) than in BAFF-wt carriers (0; IQR 0-1). Cox regression model showed BAFFvar (HR 1.5 per copy variant; 95%CI 1.2 - 2.0; p = 0.002), disease duration <1 year (HR 0.46; 95%CI 0.30 – 0.71; p<0.001), DORIS remission (HR 0.41; 95%CI 0.24 – 0.71; p = 0.001), renal (HR 1.7; 95%CI 1.1 – 2.6; p = 0.017), and musculoskeletal (HR 5.3; 95%CI 1.3 – 21.5; 0.019) involvement as baseline factors independently associated with the risk of flare development. Out of 38 patients with biopsy-confirmed LN, 33 (86.8%) were female, 21 (55.3%) were BAFFvar carriers, and 24 (63.2%) were diagnosed with proliferative lupus nephritis class III or IV. Flares occurred in 12 (33.3%) patients, with 22 flares (5 nephritic and 17 nephrotic). The BAFFvar was independently associated with the risk of renal flare (HR 9.3; 95%CI 1.8 to 49.5; p=0.008). Out of 35 patients treated with belimumab after a flare, 9 had at least one flare during a median 48-month follow-up (total of 11 flares). Patients with BAFFvar had a flare rate of 13.6% (3/22), while BAFFwt carriers had a flare rate of 46.1% (6/13) (HR 0.22; 95%CI 0.05-0.90; p=0.035).

Conclusions: Belimumab reduces the risk of overall and renal SLE flares conferred by the BAFFvar. BAFFvar identifies patients at higher risk for flare and those best

responders to belimumab and may represent a potential predicting and prognostic biomarker for personalized treatment in SLE patients.

PV184 / #644

Poster Topic: ***AS21 - Pregnancy and Reproductive Health***

PREVENTION OF RECURRENT IDIOPATHIC HYDROPS FETALIS; IS IT RELATED TO THROMBOSIS AND INFLAMMATION?

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Background/Purpose: Hydrops Fetalis (HF) involves abnormal fetal fluid accumulation with placental thickening, often due to non-immune causes (85%), with approximately 70% of them are result of cardiovascular, chromosomal, or infectious factors. The remainder are of unknown causes, defined as idiopathic non-immune (i-NIHF). Pathogenesis of HF includes tissue hypoxia, immunological and complement pathways activation, which are usually accompanied by local inflammation. Recurrence of HF suggests that it might be of a heritable origin. Despite advanced in-utero therapy, mortality as high as 50-95% for most non-immune HF cases, especially those with idiopathic type having the worst prognosis. Therefore, prevention is the utmost important approach to preserve fetal vitality and improve pregnancy outcomes.

Methods: Presenting a case-series of women with recurrent miscarriages attributed to i-NIHF that were treated with standard anti-phospholipid syndrome (APS) prophylaxis protocol, which is used for prevention of fetal loss. The therapeutic regimen includes low-dose aspirin (LDA) 100mg daily, or daily subcutaneous injections of low molecular weight heparin (LMWH), dose of 40-60 mg Enoxaprin (Clexan), or a combination of both. Due to severe history of recurrent fetal loss, and their failure of repeated trials for productive pregnancy and advancing age with time, an addition of corticosteroids (CS) was recommended for all women (prednisone 30 mg daily for 1st to 20 mg for 2nd and 10 mg with tapering close to delivery).

Results: Table1 summarizes a case-series of 5 young females (age; 29-38 years old) with normal thrombophilia tests and no definitive APS diagnosis who had recurrent miscarriages, who were referred to the rheumatology clinic for suspected autoimmunity or APS. They had a total of 23 pregnancies that resulted in only one successful birth of a healthy but premature baby. All women had various obstetrical events including recurrent early spontaneous abortions (during the first 10 weeks), intra-uterine fetal death (IUFD) (during 2nd-3rd trimester of pregnancy), and a total of eight episodes of i-NIHF that were identified (ranges between 22-30 weeks). One woman had three episodes of i-NIHF, another had two, and the rest had one each. During follow-up, two of those cases had some autoimmune features such as arthralgia, mild rash, Raynaud's phenomenon, and occasional low titers of anti-nuclear antibodies (ANA), so were treated with Hydroxy-chloroquine (400 mg/day) and a low dose of prednisone (5

mg/day). All five cases received the treatment protocol (LDA, LMWH,CS) given immediately after conception. Following this protocol, a total of 12 pregnancies were uneventful and resulted in the delivery of eleven healthy babies and one with mild HF who survived with no further complications. Interestingly, the occurence of i-NIHF was almost entirely prevented by the treatment protocol.

	Normal live-birth *n*	Preterm *n, (w)*	Spontaneous abortions (<10 w) *n*	IUFD *n, (w)*	i-NIHF *n, (w)*
Pregnancies before APS prophylaxis (n = 23)	1	1, (30)	11	2, (22,30)	8, (22-30)
Pregnancies on APS prophylaxis (n = 12)	11	0	0	0	1*, (30)

Table 1. Outcome of case-series of i-NIHF before and after treatment with APS prophylaxis protocol. **mild HF, born, healthy male*. w = gestational age in weeks.

Conclusions: Idiopathic non-immune hydrops fetalis is a serious condition with high mortality rate and limited effective therapy. Therefore, prevention is of crucial importance. It may recur repeatedly and even occur in addition to other pregnancy morbidities. The true mechanism of pathogenesis for this serious condition is still unclear, this study presents a series of cases which may suggest a possible explanation; a combination of intra-uterine inflammtory and micro-thrombotic processes at the level of placenta. In summary, a prophylactic regimen for APS, involving anti-platelets, anti-coagulant and anti-inflammatory therapy during pregnancy, shows promising effects, and promotes the need for further investigation.

PV185 / #628

Poster Topic: ***AS21 - Pregnancy and Reproductive Health***

FIRST CASES IN THE LUPUS PREGNANCY CLINIC OF A TERTIARY UNIVERSITY HOSPITAL IN 2024

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Background/Purpose: Pregnancy in systemic lupus erythematosus (SLE) requires specialized management to minimize maternal and fetal complications. In 2024, we established a dedicated lupus pregnancy clinic within our rheumatology department at a tertiary university hospital. This study reports the first six pregnancies managed in this clinic.

Methods: Six pregnant patients with SLE were followed during their gestations. Three were anti-Ro/SSA positive, two were positive for antiphospholipid antibodies (aPL), and one was negative for both anti-Ro/SSA and aPL. All patients were in remission or had low disease activity at conception.
• Anti-Ro/SSA positive patients received hydroxychloroquine (HCQ) and low-dose prednisone (5–10 mg/day) during the first trimester. Routine obstetric care included fetal heart rate monitoring at 16, 20, and 24 weeks, along with uterine artery Doppler assessments.
• aPL-positive patients: One with prior thrombosis received HCQ and therapeutic heparin. The other received prophylactic heparin and aspirin.
• The anti-Ro/SSA and aPL-negative patient was treated solely with HCQ. No patient received teratogenic medications or biologic therapies during pregnancy.

Results: All six pregnancies resulted in successful outcomes, with no maternal or fetal complications. There were no cases of fetal congenital abnormalities, intrauterine growth restriction, or neonatal issues. Routine monitoring and close collaboration with obstetrics ensured optimal outcomes.

Conclusions: Close interdisciplinary management of pregnancies in SLE patients, with disease control and tailored treatments, maximizes the likelihood of successful outcomes and minimizes complications. Our experience underscores the importance of dedicated lupus pregnancy clinics in achieving these goals.

PV186 / #574

Poster Topic: ***AS21 - Pregnancy and Reproductive Health***

SYSTEMIC LUPUS ERYTHEMATOSUS PREGNANCIES: TRENDS IN DISEASE MANAGEMENT AND MATERNAL – FETAL OUTCOMES COMPARING TWO TIME PERIODS (1988-2012 VS 2013-2022)

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Background/Purpose: In the last decades, Systemic Lupus Erythematosus (SLE) pregnancies outcome has greatly improved thanks to pregnancy planning, preconception counselling, multidisciplinary follow-up and availability of compatible drugs. However, patients are burdened by an increased risk of disease flares and adverse maternal-fetal outcomes. The aim of this study was to assess how SLE pregnancies management has changed over time and how this has affected the maternal-fetal outcome.

Methods: Retrospective data of SLE pregnancies prospectively followed in a pregnancy clinic were collected from preconception counselling throughout the three trimesters. Twin pregnancies were excluded. Pregnancies from two different time intervals were compared: Group 1 (1988 – 2012) and Group 2 (2013-2022). Statistical analysis was performed using Mann-Whitney, Fisher or chi-square test when appropriate. $p<0.05$ was considered significant.

Results: 204 pregnancies in 141 SLE patients were included. Compared to Group 1 (n=103), Group 2 (n=101) showed higher age at conception (30 *vs* 33 years; $p = 0.013$), lower frequency of Caucasian patients and lower rate of performed preconception counselling (90% *vs* 63%, $p < 0.0001$) (Table 1). Moreover, pregnancies in Group 2 showed: lower median disease activity (SLEPDAI) and higher median C4 levels in each trimester (Table 1); higher rate of hydroxychloroquine usage (66% *vs* 92%; $p < 0.0001$); lower rate of glucocorticoids usage (84% *vs* 67%; $p = 0.011$) with lower median weekly dose (50mg *vs* 25mg; $p<0.00001$). No statistically significant differences were observed in disease history, pattern of organ involvement, immunosuppressive treatment and maternal - fetal outcome between the two groups (Table 1).

Table 1

	Group 1 Pregnancies 1988-2012 (n = 103)	Group 2 Pregnancies 2013-2022 (n = 101)	p-value
DEMOGRAPHIC FEATURES			
Age at SLE diagnosis, years (median; IQR)	24 (20-28)	22 (20-27)	0.110
Age at conception, years (median; IQR)	30 (28-35)	33 (28-36)	0.013
Disease duration at time of conception, years (median; IQR)	5 (3-9)	8 (3-13)	0.005
ART, n (%)	4 (4%)	8 (8%)	0.250
Ethnicity, n (%)			
Caucasian	89 (86%)	76 (75%)	0.040
Performed pre-conception counselling, n (%)	93 (90%)	64 (63%)	< 0.0001
DISEASE ACTIVITY			
Pre-conception data (median; IQR)			
Disease activity (SELENA-SLEDAI)	2.6 (0-4) n=85	1.5 (0-2) n=74	0.003
C3 values	91 (78-106) n=88	87 (78-104) n=78	0.600
C4 values	14 (10-18) n=88	16 (12-20) n=78	0.009
First trimester (median; IQR)			
Disease activity (SLEPDAI)	2.3 (2-4) n=92	1.5 (0-2) n=74	0.003
C3 values	91 (78-106) n=88	87 (78-104) n=78	0.600
C4 values	14 (10-18) n=88	16 (12-20) n=78	0.009
Second trimester (median; IQR)			
Disease activity (SLEPDAI)	2.3 (0-4) n=91	1.5 (0-2) n=85	0.030
C3 values	105 (83-117) n=90	111 (94-123) n=84	0.009
C4 values	14 (11-20) n=90	18 (14-23) n=84	0.003
Third trimester (median; IQR)			
Disease activity (SLEPDAI)	1.9 (0-4) n=86	1.3 (0-2) n=76	0.090
C3 values	109 (97-129) n=84	113 (101-128) n=79	0.300
C4 values	16 (11-20) n=84	18 (14-22) n=79	0.003
MATERNAL-FETAL OUTCOME			
Live births, n (%)	91 (88%)	90 (90%)	0.860
Fetal losses, n (%)			
Early miscarriage (< 10th gestational week)	8 (8%)	9 (10%)	0.800
Late miscarriage (> 10th gestational week)	4 (4%)	1 (1%)	0.180
Perinatal deaths, n (%)	0 (0%)	1 (1%)	0.500
Preterm deliveries, n (%)			
Early preterm deliveries (≤ 34th GW)	1 (1%)	3 (4%)	0.370
Late preterm deliveries (> 34th GW)	11 (12%)	19 (20%)	0.120
SGA (< 5th percentile), n (%)	6 (7%)	12 (13%)	0.130
Hypertensive disorders of pregnancy, n (%)			
Pre-eclampsia	5 (5%)	4 (4%)	1.000
Eclampsia	2 (2%)	0 (0%)	0.500
HELLP syndrome	0 (0%)	0 (0%)	1.000

Legend: IQR: Interquartile range; ART: Assisted Reproductive Techniques; SLEPDAI: SLE Pregnancy Disease Activity Index; SGA: Small for Gestational Age; GW: Gestational Week; HELLP: Hemolysis, Elevated Liver enzymes, Low Platelets

Conclusions: Our data show how the approach to SLE pregnancies management has changed over time thanks to increasing knowledge and awareness in this field, as highlighted by recent recommendations. Despite the decreased use of corticosteroids, the increased use of hydroxychloroquine, and the lower disease activity observed in more recent pregnancies, pregnancy outcome was not improved. This can be related to a lower rate of preconception counselling (probably due to the increasing number of

patients referred to our pregnancy clinic when already pregnant) in this group but also to the higher age at conception, the higher disease duration, and the high number of non-caucasian patients, that are known to have a more difficult-to-treat disease because of their ethnicity and social status.

PV187 / #637

Poster Topic: ***AS21 - Pregnancy and Reproductive Health***

STUDY DESIGN AND RECRUITMENT INTO THE BELIMUMAB MOTHERTOBABY PREGNANCY EXPOSURE STUDY: AN OTIS AUTOIMMUNE DISEASES IN PREGNANCY PROJECT

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Background/Purpose: Belimumab is a human monoclonal antibody that inhibits B lymphocyte stimulator protein (BLyS). Among other countries, belimumab is approved in the United States (US) and Canada for systemic lupus erythematosus (SLE) and lupus nephritis in people 5 years of age and older. Data on belimumab exposure during pregnancy is limited. The OTIS Pregnancy Exposure Registry is a US based study designed to monitor pregnancy and infant outcomes among people in the US and Canada. Pregnancy registries are an important component of post-marketing surveillance to assess the safety of new medications. Presented is an overview of the study design and recruitment into this pregnancy study. The study will monitor pregnancies for the occurrence of major structural birth defects, spontaneous abortion, elective termination, stillbirth, preterm delivery, pattern of 3 or more minor structural defects, small for gestational age, postnatal growth and developmental performance at approximately 1 year of age, and serious infections in the first year of life in pregnancies exposed to belimumab, relative toa disease comparison (DC) group of pregnant participants with SLE.

Methods: This research study is a North American, prospective cohort study comparing pregnancy outcomes in participants exposed to belimumab to a DC group without belimumab exposure. Women with SLE who have been exposed to belimumab during pregnancy, or within three months of the last menstrual period, and who have not had any abnormal prenatal screening or diagnostic test indicating a major structural defect as eligible for enrollment. Those who do not meet the eligibility criteria are eligible for a “case series” cohort. These data may be used to illuminate any findings in the cohort study. Recruitment began in November 2022 and will continue through 2027, with a goal of 200 participants in each cohort. The study captures data on exposures, outcomes and covariates through maternal interviews and maternal and pediatric medical records, a dysmorphology exam, and developmental screening of the child using the

Ages and Stages online questionnaire. Disease severity is captured with information from medical records.

Results: Between November 10, 2022 and November 1, 2024, 30 participants were enrolled (17 belimumab-exposed, 9 DC, and 3 in the belimumab-exposed case series).

Conclusions: With the help of rheumatologists and other providers specializing in the care of patients with SLE, this study will collect information that will help healthcare professionals and their patients make informed treatment decisions during pregnancy.

PV188 / #82

Poster Topic: ***AS21 - Pregnancy and Reproductive Health***

SEXUAL HEALTH CHALLENGES IN PRIMARY ANTIPHOSPHOLIPID SYNDROME: EXPLORING PREVALENCE AND CLINICAL CORRELATES

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Background/Purpose: Antiphospholipid syndrome (APS) is a systemic thromboinflammatory disease with various forms of presentation. There is limited information on sexual function in patients with APS, and it is unclear whether it may be associated with chronic disease damage or if other clinical parameters can predict issues in this area of sexual health.

Methods: We conducted a cross-sectional study at two tertiary referral centers in Mexico City and Monterrey from January to May 2024. The study included patients aged ≥ 16 years who met the revised Sapporo criteria for APS and had been sexually active within the past six months. Patients with other autoimmune diseases, prothrombotic disorders, or chronic viral infections were excluded. All participants completed the Changes in Sexual Functioning Questionnaire-14 (CSFQ-14), which assesses various domains of sexuality, and had their ankle-brachial index (ABI) measured. Additionally, we asked three questions: 1) Do you think you have sexual dysfunction? 2) Would you be interested in being referred to a specialist if you have any alteration in your sexual function? and 3) Do you consider that your illness influences your sexual function? The damage index for patients with thrombotic antiphospholipid syndrome (DIAPS) was calculated, and additional demographic, clinical, and serological variables were recorded.

Results: We included 47 APS patients in the study. The mean age was 40.9 ± 10.9 years, with 87.5% being women, and the median disease duration was 7.0 years (IQR 7-14). Thrombotic APS was present in 68% of the patients. Most patients (70%) were taking vitamin K antagonists, and 30% were taking hydroxychloroquine. The two main comorbidities were obesity (25.5%) and dyslipidemia (23%). The average cumulative damage measured by DIAPS was 2, and the mean ABI was 0.97 ± 0.16. Sexual dysfunction was identified in 34% of patients based on their CSFQ-14 total score, with pleasure being the most affected domain (94%). Patients with sexual dysfunction had lower educational levels (12.8 vs. 15.8 years, p = 0.01), a higher history of immunosuppressant use (p = 0.03), greater history of thrombocytopenia (p = 0.04), and

were more likely to believe they had sexual dysfunction (p = 0.01). However, they were less inclined to seek help from a sexual function specialist if needed (p = 0.003). When stratifying patients by gender, we found that more women experienced sexual dysfunction in the desire/frequency domain compared to men (70% vs. 30%, p = 0.05). Notably, a correlation was observed between total ABI and both the frequency domain (r = 0.31, p = 0.03) and the arousal/erection domain (r = 0.29, p = 0.04). Complementary variables are shown in Table 1 and Figure

Characteristics	Total n = 47	Sexual dysfunction n = 16 (34%)*	No sexual dysfunction n = 31 (66%)	p
Women, n (%)	38 (81)	14 (87.5)	24 (77)	0.40
Age, years, mean ± SD	40.9 ± 10.9	44.3 ± 13.6	39.2 ± 9.0	0.13
Scholarship, years, mean ± SD	14.8 ± 3.9	12.8 ± 2.4	15.8 ± 4.2	**0.01**
Time since APS diagnosis, years, median (IQR)	7 (4-14)	7 (5.5-14.5)	10 (3-14)	0.98
Obstetric APS, n (%)	12/38 (31)	3/14 (21)	9/24 (37.5)	0.40
Thrombotic APS, n (%)	32 (68)	9 (56)	23 (74)	0.20
History of thrombocytopenia, n (%)	17 (36)	9 (56)	8 (26)	**0.04**
Current use of vitamin k antagonist, n (%)	33 (70)	8 (50)	25 (81)	**0.02**
Current use of antimalarial, n (%)	14 (30)	2 (12.5)	12 (39)	0.09
Current use of prednisone, n (%)	8 (17)	2 (12.5)	6 (19)	0.70
Current use of immunosuppressive therapy, n (%)	16 (34)	7 (44)	9 (29)	0.31
Previous use of immunosuppressive therapy, n (%)	14 (30)	8 (50)	6 (19)	**0.03**
Current prednisone dose, mg/day, mean ± SD	2.4 (9.2)	0.5 (1.35)	3.5 (11.2)	0.30
Cumulative dose of prednisone in the last year, mg, mean ± SD	0.53 (1.5)	0.12 (0.45)	0.74 (1.8)	0.18
Menopause, n (%)	4/38 (10)	1/14 (7)	3/24 (12.5)	1.0
Overweight, n (%)	38 (81)	14 (87.5)	24 (77)	0.40
Obesity, n (%)	12 (25.5)	2 (12.5)	10 (32)	0.17
Type 2 diabetes, n (%)	4 (8.5)	1 (6)	3 (10)	0.10
Hypertension, n (%)	4 (8.5)	2 (12.5)	2 (6.5)	0.60
Dyslipidemia, n (%)	11 (23)	3 (19)	8 (26)	0.72
Other comorbidities, n (%)	13 (28)	6 (37.5)	7 (23)	0.30
Belief of having sexual dysfunction, n (%)	8 (17)	6 (37.5)	2 (6.5)	**0.01**
Desire to see a specialist, n (%)	42 (89)	11 (69)	31 (100)	**0.003**
Believes that APS influences sexual function, n (%)	21 (45)	7 (44)	14 (45)	0.092
Current smoking, n (%)	8 (17)	3 (19)	5 (16)	1.00
Previous smoking, n (%)	21 (45)	8 (50)	13 (42)	0.60
Normal ABI, n (%)	11 (35.5)	6 (27)	5 (56)	0.21
Total ABI, points, mean ± SD	0.97 (0.16)	0.94 (0.2)	0.99 (0.14)	0.31
Creatinine, mg/dl, median (IQR)	0.71 (0.65-0.85)	0.73 (0.66-0.89)	0.71 (0.65-0.83)	0.79
Cholesterol, mg/dl, median (IQR)	158.5 (134-189)	156 (122-182)	171 (143.5-205.5)	0.10
Hemoglobin, g/dl, median (IQR)	14 (12.8-15)	14.2 (13.2-14.8)	13.9 (12.3-15)	0.72
Lymphocyte, cell/mm^3 x10^3, median (IQR)	1680 (1340-2240)	1605 (1290-2140)	1765 (1410-2440)	0.43
Antiphospholipid triple positive, n (%)	22 (47)	6 (37.5)	16 (52)	0.36
aGAPSS score, points, median (IQR)	9 (5-13)	9 (4-12.5)	9 (7-13)	0.2
Total DIAPS score, points, median (IQR)	2 (0-4)	2 (0-4)	2 (0-4)	0.9

Table 1. Baseline demographic, clinical and laboratory characteristics of patients with APS

***Based on CSFQ-14 total score**

1.

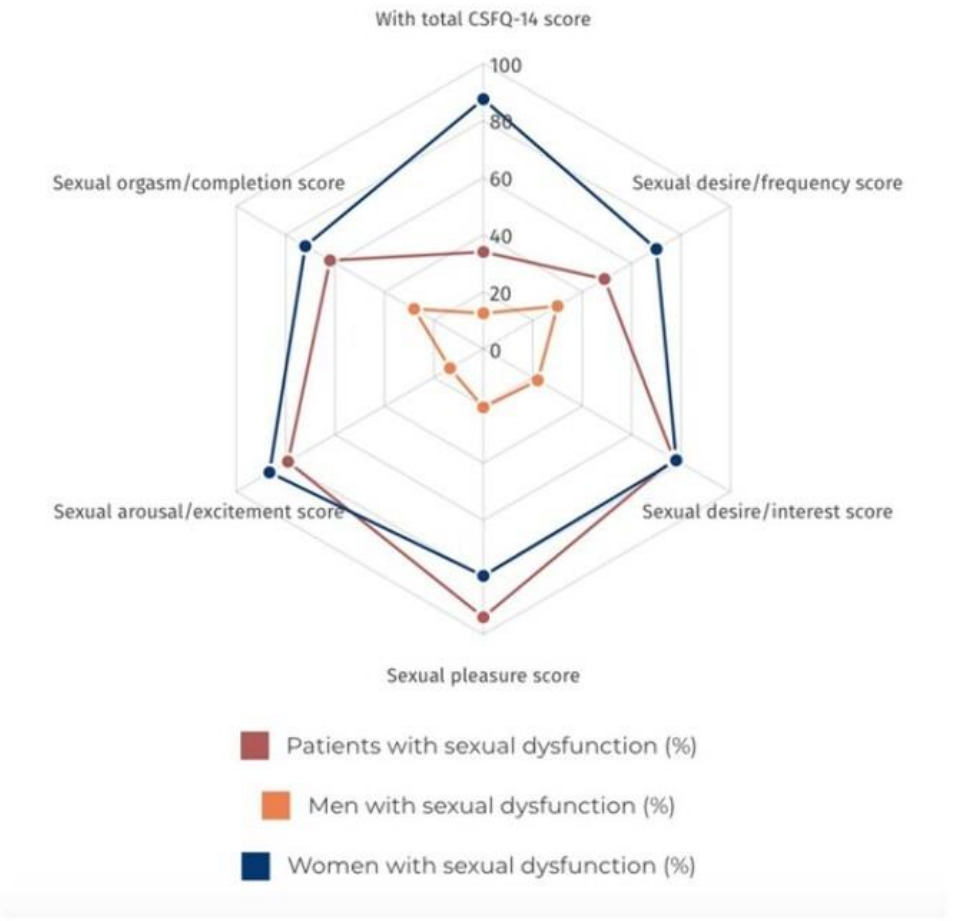

Figure 1. Patients with sexual dysfunction categorized by gender. Sexual dysfunction was assessed using the CSFQ-14 cut-off points for both the total score and the different domains.

Conclusions: This study is the first to outline the prevalence and clinical manifestations of sexual dysfunction in individuals with APS. Sexual function is impaired in these generally young patients who have few comorbidities and low chronic organ damage. Rheumatologists should consider this issue during regular visits and inquire about their patients' sexual health. Further research is needed to determine the underlying pathophysiological mechanisms of this condition, but endothelial damage and thrombotic alterations may play a role. We are grateful to all the patients who kindly participated.

PV189 / #70

Poster Topic: ***AS21 - Pregnancy and Reproductive Health***

ENHANCING INTERDISCIPLINARY COLLABORATION IN THE MANAGEMENT OF PREGNANCY IN PATIENTS WITH SYSTEMIC AUTOIMMUNE/AUTOINFLAMMATORY RHEUMATIC DISEASES: THE IMPACT OF JOINT RHEUMATOLOGY AND OBSTETRICS MEETINGS

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Background/Purpose: Background Management of pregnancy in patients with systemic autoimmune/autoinflammatory rheumatic disease (SARD) requires close collaboration between rheumatologists and obstetricians. However, regular face-to face meeting is not held even academic institutions due to difficulties in scheduling and lack of sufficient participants from obstetric department due to less interests. Objectives Recognizing the need for increased collaboration, monthly interdepartmental meetings were initiated to share information and improve patient outcome. education for young clinicians. The primary goal was to make as needed communication easier and strengthen meticulous collaboration between the rheumatology and obstetrics departments to improve the management of pregnant patients with SARDs.

Methods: Joint meetings between the two departments were held at a tertiary medical facility. To continue the meeting with sufficient participants, 5 principles were established as follows; 1. Starting at 16:30 sharp on Wednesday and finish by 16:55. 2. Members of rheumatology department comes to Obstetric staff area in time. 3. All cases of infertility treatment, pregnancy, and delivery are discussed and to facilitate the discussion, a designated rheumatology fellow prepares 1 slide for each patient and present all cases. 4. Encouragement to participate on site but option of remote attendance via Microsoft teams is available. 5. Mini-lectures and confirmation of consensus in care are done at the end as far as time allows. At the end of FY2022, a survey of staff in both departments was conducted regarding these meetings. Based on the feedback from the survey, bi-directional mini-lectures on pregnancies complicated by RMDs were initiated starting in FY2023.

Results: In FY2022-2023, there were discussions on a total of 197 pregnancy cases, and 10 infertility treatment cases. Details of the cases delivered in our hospital in FY 2022-2023 are shown in Table 1. SLE was the most common background disease among pregnant women, followed by rheumatoid arthritis and antiphospholipid antibody syndrome. There were no serious adverse pregnancy outcomes (APOs) for the mothers, and the three cases of premature birth had uneventful postnatal courses leading to discharge. Improvements in interdepartmental collaboration included 1)

standardized protocols for corticosteroid coverage and 2) coordinated aspirin prescribing. According to the staff survey, 68.4% felt that their understanding of pregnancy management had deepened and 94.7% felt that interdepartmental collaboration had improved. Based on the results of the questionnaire, mini-lectures for mutual understanding were initiated; a total of eight lectures were held in FY2023 on the most requested topics.

Conclusions: Conclusion The implementation of joint meetings between rheumatology and obstetrics has greatly enhanced communication and is a critical step in patient care. In the context of progressive work style reforms, the sustained practice of these concise and effective meetings promises not only to deepen mutual understanding among professionals, but also to significantly improve the standard of care for our patients. Looking ahead, this collaborative model sets a promising precedent for interdisciplinary teamwork in health care.

PV189a / #296

Poster Topic: ***AS22 - SLE Heterogeneity***

AUTOANTIBODIES IN A MULTI-INSTITUTIONAL INDIAN INCEPTION COHORT (INSPIRE): PREVALENCE, CLUSTER ANALYSIS AND PHENOTYPE ASSOCIATION

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Background/Purpose: In SLE the prevalence of autoantibodies is variable across different ethnic group and data on Indian population is limited. Thus, we assessed the prevalence and association of different autoantibody clusters with clinical features in an Indian SLE inception cohort for research.

Methods: INSPIRE cohort is a cohort with 2503 patients accrued till October 2022 and currently 6 monthly follow up is ongoing. At inclusion antibodies were assayed using Immunoline (Euroimmune, Germany) or ELISA. To determine autoantibody clusters, an unsupervised random forest algorithm was built with 10000 trees and the resulting proximity matrix was used to generate a distance matrix between individual autoantibodies. Odds ratios were used to identify associations between autoantibody/autoantibody clusters and clinical manifestations.

Results: A total of 2503 patients (mean age 27.69±10.19 years, 2292 [91.57%] females) were enrolled in the cohort. At the baseline, organ involvement (%) was as follows: constitutional features (68.23), alopecia (77.82), oral ulcers (49.74), acute cutaneous lupus (59.41), subacute/discoid lupus (12.4), arthritis (68.27), pleural effusion (20.94), pericarditis (12.39), nephritis as per active sediments and/or proteinuria (41.23),

delirium (1.31), psychosis (2.27), seizures (7.39), autoimmune haemolysis (14.54), leukopenia (31.2), thrombocytopenia (24.85). Proliferative nephritis (class III, IV or combination of III/IV and V) was seen in 396, and non-proliferative lupus nephritis in 235. The median SLEDAI at baseline was 12 (IQR 6-18).

Antibodies to the DNA nucleosome complex were the most common with anti-dsDNA in 70.19%, anti-nucleosome in 42.02% and anti-histone in 35.6%. This was followed by antibodies to the ribonuclear complex with anti-Sm (32.16%), anti-RNP (52.01%), anti-Ro52 (37.95%), anti-Ro60 (42.14%) and anti-La (12.26%). Other positive antibodies included anti-Ribosomal P (32.16%), anti-AMA-M2 (8.35%), anti-Scl70 (2.83%) anti-PCNA (4.55%), anti-PM/Scl (2.16%), anti-CENP-B (1.48%) and anti Jo-1 (0.99%). IgG autoantibodies (>40 GPL) to anticardiolipin and β2 glycoprotein1 were present in (10.06%) and (8.4%) patients respectively and 8.86% had lupus anticoagulant.

Antibodies to dsDNA, histones and nucleosomes showed association with proliferative nephritis, oral ulcers and arthritis, anti-Ro antibodies had association with alopecia and serositis, antibodies to Sm, RNP and Ribosomal P showed association with mucocutaneous disease. Antibodies to Sm, nRNP, Ro and La were protective for proliferative nephritis.

Four clusters of autoantibodies were identified. Cluster 1 had antibodies to dsDNA, histone and nucleosome and accounted for 932 (45.84%) patients. Cluster 2 had antibodies to Sm, nRNP, Ro52, Ro60 and Ribosomal P and accounted for 989 (48.65%) patients. Cluster 3 had autoantibodies to cardiolipin, β2GP1, lupus anticoagulant, La as well as AMA-M2 and accounted for 98 (4.62%) patients. Cluster 4 was a predominantly negative cluster which included antibodies to Scl-70, Jo-1, PCNA, PM-SCL and CENP-B and accounted for 18 (0.89 %) patients.

Cluster 1 was associated (odds ratio) with clinically significant proteinuria (1.54) and proliferative lupus nephritis (2.06), pleural effusion (1.29), leukopenia (1.37) and with reduced risk of pericarditis (0.72). Cluster 2 was associated with increased seizures (1.36) and pericarditis (1.52) as well as lower risk of proteinuria (0.74), proliferative nephritis (0.56), leukopenia (0.82) and thrombocytopenia (0.78). Cluster 3 was associated with lower risk of proteinuria (0.57), proliferative nephritis (0.36), pleural effusion (0.41) and leukopenia (0.52).

Conclusions: The prevalence of anti-Sm and Ribosomal P antibodies is higher in Indian population, and they show association with mucocutaneous disease. While antibodies and Cluster 1 associated with DNA had an association with nephritis.

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PV190 / #379

Poster Topic: ***AS22 - SLE Heterogeneity***

SEX DIFFERENCES IN SYSTEMIC LUPUS ERYTHEMATOSUS: A COMPREHENSIVE ANALYSIS OF CLINICAL AND TREATMENT DISPARATIES IN A MULTICENTER LONGITUDINAL COHORT

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with female predominance. Due to its lower prevalence in men, SLE is less well understood in male patients. This study aimed to examine disparities in clinical manifestations, treatment, and outcomes between female and male patients with SLE using data from a multicenter longitudinal cohort.

Methods: Prospectively collected data from a 13-country cohort were analyzed. Demographics, fulfilment of 1997 American College of Rheumatology (ACR) classification criteria, disease activity (SLEDAI-2K, flare), medications, lupus low disease activity state (LLDAS) and DORIS remission attainment, and SLICC/ ACR damage index (SDI) were compared between female and male patients using Chi-squared tests (categorical variables) and Kruskal-Wallis (continuous variables) tests.

Results: A total of 4,106 SLE patients were studied. 328 (8.0%) were male, who were more likely to be non-Asian (14.5% vs 10.8%, p=0.04), active smoker (22.3% vs 3.9%, p<0.01), have shorter disease duration (7.0 years vs 8.0 years, p=0.01), and live in countries with a high gross domestic product (GDP ≥ $50,000 per capita) (58.5% vs 48.2%, p<0.01) (**Table 1**). At study enrolment, disease activity (SLEDAI-2K 4.0 vs 4.0, p=0.86) was similar between male and female patients., while female patients had more frequent use of anti-malarials (78.7% vs 72.0%, p=0.01), mycophenolate mofetil (32.0% vs 22.6%, p<0.01), and cyclophosphamide (6.7% vs 4.1%, p=0.03) Organ damage (defined as SDI>0) was present in 43% of males and 37% of females (p=0.07) at study enrolment with more frequent damage in peripheral vascular domain observed in male patients (6.0% vs 2.7%, p<0.01). Over a follow-up duration of 2.5 (IQR 1.0-5.1) years, male patients were more likely to receive anti-malarial (86.3% vs 78.2%, p<0.01) and mycophenolate mofetil (43.0% vs 36.7%, p=0.03), but less likely to experience flares (46.6% vs 53.7%, p=0.02). The frequency of organ damage accrual (defined as increase in SDI≥1) and treat-to-target state attainment was similar between male and female patients **(Table 1)**. Over 42,347 clinical visits, clinical disease activity (defined as clinical SLEDAI-2K>0) was observed in 16,804 (39.7%) visits (**Figure 1**). Male patients had more visits with active disease in renal domain (29.2% vs 22.3%, p<0.01), including patients without renal involvement at baseline (17.4% vs 10.1%, p<0.01). Visits with active disease in mucocutaneous domain (12.5% vs 11.3%, p=0.03) and vasculitis (0.9% vs 0.6%, p=0.04) were also more frequent among male patients. In contrast, female patients had more visits with activity in musculoskeletal (3.1% vs 4.5%, p<0.01) and hematological domain s(5.2% vs 6.3%, p=0.02). LLDAS was attained in 19441 (45.9%) visits overall. In clinical visits not in LLDAS, Pred >7.5mg/D (51.7% vs 48.0%, p<0.01) and SLEDAI>4 (53.0% vs 49.4%, p<0.01) occurred more frequently among male patients. Renal activity was observed in over half (52.6% vs 44.2%, p<0.01) of non-LLDAS visits in male patients.

Table 1: Clinical characteristics of the study cohort

	Females n=3,778	Males n=328	
	n (%) or median [IQR]		*p-value*
Age at SLE diagnosis (years)	29 [21, 38]	30 [20, 46]	0.07
Disease duration (years)	8.0 [3.0, 15.0]	7.0[2.0, 12.0]	0.01*
Study observation period (years)	2.5 (1.0, 5.1)	1.8 (0.9, 4.7)	0.02*
Asian ethnicity	3355 (89.2%)	277 (85.5%)	0.04*
Current smoker at enrolment	145 (3.9%)	71 (22.3%)	<0.01*
GDP (PPP) per capita ≥$50,000	1822 (48.2%)	192 (58.5%)	<0.01*
ACR classification criteria fulfilled	3500 (92.6%)	291 (88.7%)	0.01*
Medications use at study enrolment			
Glucocorticoids	2996 (79.3%)	253 (77.1%)	0.40
Anti - malarial	2722 (72.0%)	258 (78.7%)	0.01*
Immunosuppressants	2171 (57.5%)	204 (62.2%)	0.09
Azathioprine	862 (22.8%)	58 (17.7%)	0.03*
Methotrexate	172 (4.5%)	11 (3.4%)	0.31
Leflunomide	47 (1.2%)	6 (1.8%)	0.37
Mycophenolate mofetil	855 (22.6%)	105 (32.0%)	<0.01*
Calcineurin inhibitor	266 (7.0%)	31 (9.5%)	0.11
Cyclophosphamide	156 (4.1%)	22 (6.7%)	0.03*
Medication exposure during study period			
Glucocorticoids (ever)	3207 (84.9%)	278 (84.8%)	0.95
Anti - malarial (ever)	2955 (78.2%)	283 (86.3%)	<0.01*
Immunosuppressants (ever)	2648 (70.1%)	240 (73.2%)	0.24
Azathioprine (ever)	1190 (31.5%)	87 (26.5%)	0.06
Methotrexate (ever)	295 (7.8%)	20 (6.1%)	0.26
Leflunomide (ever)	88 (2.3%)	11 (3.4%)	0.25
Mycophenolate mofetil (ever)	1388 (36.7%)	141 (43%)	0.03*
Calcineurin inhibitor (ever)	472 (12.5%)	44 (13.4%)	0.63
Cyclophosphamide (ever)	293 (7.8%)	35 (10.7%)	0.06
Disease activity indicator and treatment target attainment			
SLEDAI-2K at enrolment	4.0 [2.0, 6.0]	4.0 [0.0, 6.0]	0.86
Time adjusted mean – SLEDAI-2K	2.9 [1.3, 4.7]	2.8 [1.1, 4.8]	0.36
Any flare (mild/ moderate or severe) at enrolment	469 (12.4%)	38 (11.6%)	0.66
Any flare (mild/ moderate or severe) at least once during study period	2027 (53.7%)	153 (46.6%)	0.02*
LLDAS at enrolment	1834 (48.9%)	148 (45.7%)	0.26
LLDAS (ever)	2968 (78.8%)	252 (77.1%)	0.47
DORIS remission at enrolment	1037 (27.7%)	78 (24.1%)	0.16
DORIS remission (ever)	2339 (62.1%)	191 (58.4%)	0.19
Organ damage at study enrolment[#]	1281 (37.8%)	123 (43.3%)	0.07
Ocular domain	312 (9.2%)	23 (8.1%)	0.53
Neuropsychiatric domain	26 (7.9%)	29 (10.2%)	0.18
Renal domain	261(7.7%)	30 (10.6%)	0.09
Pulmonary domain	114 (3.4%)	6 (2.1%)	0.26
Cardiovascular domain	124 (3.7%)	16 (5.6%)	0.10
Peripheral vascular domain	91 (2.7%)	17 (6.0%)	<0.01*
Gastrointestinal domain	14 (0.4%)	2 (0.7%)	0.47
Musculoskeletal domain	425 (12.5%)	33 (11.6%)	0.65
Skin domain	102 (3.0%)	10 (3.5%)	0.63
Other	200 (5.9%)	17 (6.0%)	0.10

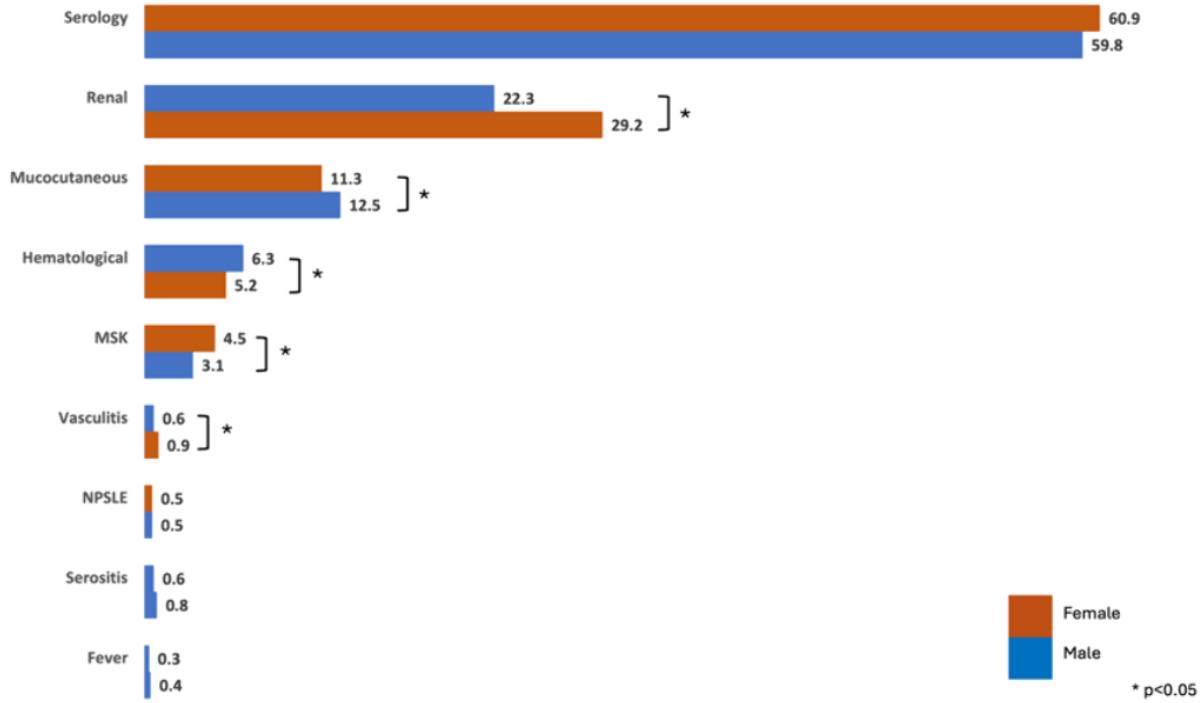
GDP (PPP) = gross domestic product purchasing power parity per capita; SDI= SLICC/ACR damage index; SLEDAI-2K = SLE disease activity index – 2K

[#]Organ damage assessed in 3674 patients.

[##]Damage accrual assessed in 2970 patients.

P-values were estimated using Chi-squared tests for categorical variables and Kruskal-Wallis tests for continuous variables.

Figure 1: Disease activity by SLEDAI organ domains in 42,347 visits



MSK = musculoskeletal; NPSLE = neuropsychiatric SLE.

Conclusions: Renal activity is more frequent in male patients with SLE, with males having more frequent clinical visits for active renal disease compared to females. Further studies are required to understand the mechanisms behind the differences between male and female SLE patients.

PV191 / #129

Poster Topic: ***AS22 - SLE Heterogeneity***

RELATIONSHIP BETWEEN AUTOANTIBODY-DEFINED SYSTEMIC LUPUS ERYTHEMATOSUS SUBGROUPS AND CLINICAL MANIFESTATIONS: PRELIMINARY FINDINGS FROM ILUPUS STUDY

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Background/Purpose: Characterization of systemic lupus erythematosus (SLE) patients using autoantibody profiles has successfully identified less heterogeneous subgroups of patients with multifaceted clinical manifestations. These subgroups are associated with distinct clinical manifestations, immunological markers, and genetic factors, leading to the identification of more homogeneous, clinically actionable SLE subgroups. However, these findings have been predominantly derived from individuals of White European descent, underscoring the necessity to replicate these studies in populations with diverse ancestral backgrounds. Hence, we aimed to subgroup Malay SLE patients based on their autoantibody profiles.

Methods: This is cross-sectional study comprising a total of 191 Malay SLE patients meeting the 2019 EULAR/ACR Classification Criteria. The sera samples of the participants were subjected for autoantibody profiling based on the 15 SLE-associated autoantibodies (i.e. anti-Rib.P_protein IgG /anti-histones IgG /anti-nucleosome IgG /anti-SSB IgG /anti-Ro52 IgG /anti-SSA IgG /anti-Sm IgG /anti-nRNP_Sm IgG /anti-cardiolipin IgG /anti-cardiolipin IgM /anti-β2glycoprotein IgG /anti-β2glycoprotein IgM /anti-phosphatidylserine IgG /anti-phosphatidylserine IgM) using immunoblot and ELISA methods. Unsupervised cluster analysis and logistic regression were used to define autoantibody-based SLE subgroups and explore their clinical associations.

Results: Our data showed 93% of the 191 SLE patients were female, with a mean age of 41.14 (±12.11) years. Four distinct clusters were identified: Cluster 1 (26.18%) was characterized by anti-Ro52 IgG (78%) and anti-SSA IgG (88%) autoantibodies; Cluster 2 (35.08%) by anti-nRNP_Sm IgG (68.1%); Cluster 3 (12.04%) by anti-histone IgG, anti-nucleosome IgG, and anti-nRNP_Sm IgG (91.3%); and Cluster 4 (26.70%) was autoantibody-negative. Cluster 2 was associated with organ damage (OR 3.00, 95% CI 1.11-8.92), and Cluster 3 with active disease (SLEDAI-2K≥6) (OR 5.65, 95% CI 1.30-29.99), mucocutaneous manifestations (OR 9.94, 95% CI 2.29-55.12), and renal involvement (OR 6.67, 95% CI 1.14-54.87).

Conclusions: Our findings in Malay SLE patients reinforce the concept of subgrouping clinically heterogeneous SLE patients according to their autoantibody profiles is a promising strategy for precision medicine. Our results support subgrouping by autoantibody profiles and highlight the need for further research in diverse populations to validate these subgroups across ethnicities.

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Poster Topic: ***AS22 - SLE Heterogeneity***

EVALUATING FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS: INSIGHTS FROM THE ISLA COHORT USING THE FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY-FATIGUE SCALE

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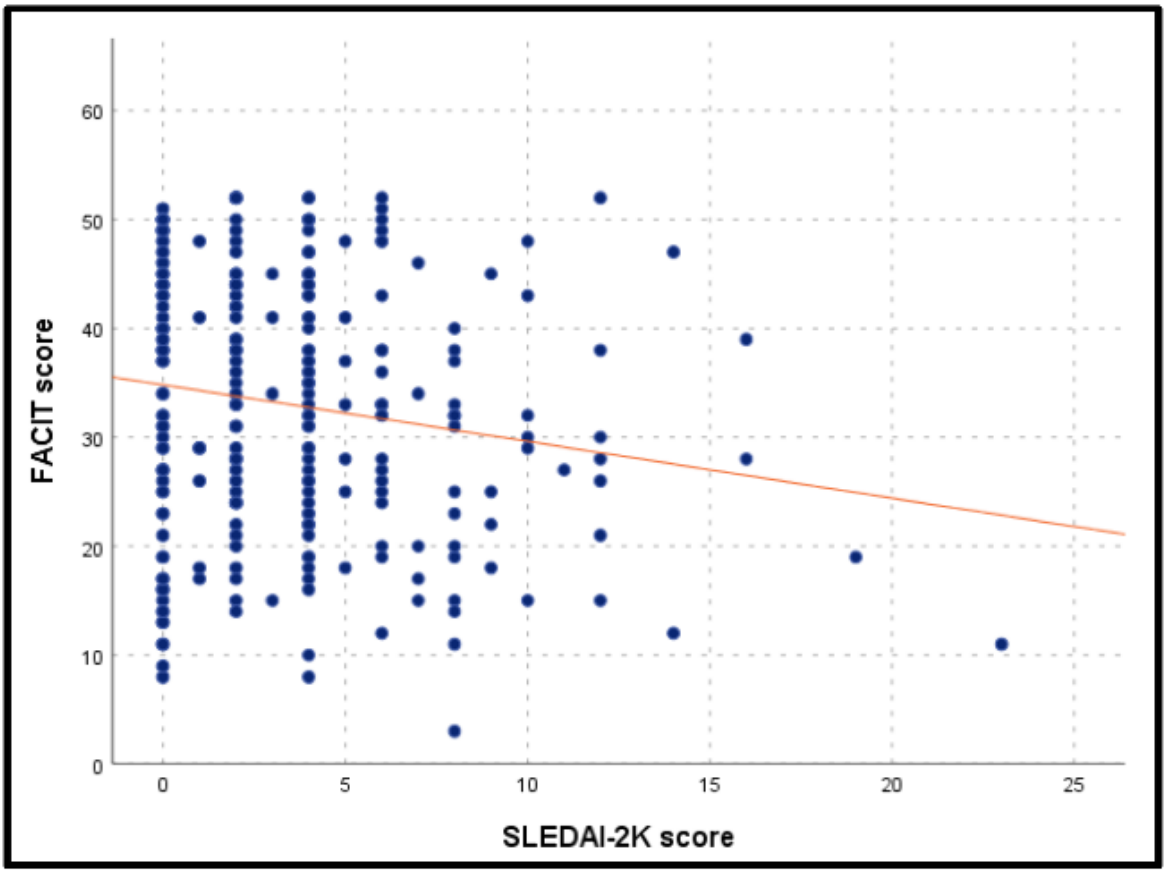
Background/Purpose: The prevalence of fatigue among patients with systemic lupus erythematosus (SLE) varies between 67% and 90%, representing a multifaceted phenomenon that significantly impacts overall functionality. Despite its prevalence, fatigue is often an overlooked characteristic in clinical assessments. This condition is inherently complex, and numerous measurement tools exist. Notably, the Functional Assessment of Chronic Disease Therapy (FACIT) Fatigue Scale, a crucial tool in this study, has been validated for use in this patient population. Consequently, the objective of this study is to evaluate fatigue within a cohort of Guatemalan lupus patients utilizing the FACIT scale.

Methods: A cross-sectional study was conducted on 268 patients diagnosed with SLE at a single rheumatology center in Guatemala, specifically within the Lupus cohort of the Guatemalan Social Security Institute in the Autonomous Unit (ISLA). Participants completed the FACIT fatigue questionnaire during the last follow-up evaluation in 2024, with prior authorization for using the scale by FACIT.org. Fatigue was defined as a score of less than 30 points. The study characterized participants based on the presence or absence of fatigue. Subsequently, we examined the correlation between disease activity by the SLEDAI-2K and the scores obtained from the FACIT fatigue scale. Additionally, the frequency of responses to the statements within the FACIT scale was described according to its measurement scale.

Results: The study revealed that 40.67% of the patients experienced moderate to severe fatigue, with 93.6% being women. In patients with fatigue, the mean FACIT score was recorded at 20.72, while 52.3% presented active disease, indicated by a mean SLEDAI-2K value of 4.17. The Pearson correlation analysis between disease activity, measured by the SLEDAI-2K, and fatigue, as assessed by the FACIT, revealed a coefficient of -0.16, suggesting a low negative correlation, as illustrated in **Graphic 1**. Furthermore, an examination of the statements included in the FACIT scale indicated that the statements with the worst ratings were "I feel tired, weak, listless ('washed out'), I am tired," and "I can do my usual activities" **Table 1**.

	No fatigue N: 159	Fatigue N: 109	P valor
Mean Age (+/- SD) *	40.43 (10.69)	42.4 (12.49)	0.029
Mean SLE disease duration (+/- SD) *	10.74 (8.37)	11.49 (7.29)	0.21
Female n (%)	143 (89.9)	102 (93.6)	0.29
Mean FACIT score (+/- SD)	41.31 (6.57)	20.72 (5.99)	0.12
Active disease n (%)	74 (46.5)	57 (52.3)	0.35
Mean Sledai-2K score (+/- SD)	3.23 (3.24)	4.17 (4.34)	0.025
Corticosteroid	127 (79.9)	90 (82.6)	0.58
Corticosteroid means doses (+/- SD) **	7.15 (8.10)	8.61 (10.62)	0.040

*** Time in Years, ** mg**



***Pearson correlation coefficient -0.16.**

N: 268	I feel fatigued	I feel weak all over	I feel listless ("washed out")	I feel tired	I have trouble starting things because I am tired	I have trouble finishing things because I am tired	I have energy	I am able to do my usual activities	I need to sleep during the day	I am too tired to eat	I need help doing my usual activities	I am frustrated by being too tired to do the things I want to do	I have to limit my social activity because I am tired
Score n (%)													
Not at all	38 (14.2)	65 (24.3)	58 (21.6)	38 (14.2)	72 (26.9)	77 (28.7)	38 (14.2)	72 (26.9)	70 (26.1)	163 (60.8)	140 (52.2)	112 (41.8)	104 (38.8)
A little bit	62 (23.1)	62 (23.1)	67 (25)	64 (23.9)	61 (22.8)	62 (23.1)	86 (32.1)	97 (36.2)	72 (26.9)	49 (18.3)	60 (22.4)	58 (21.6)	65 (24.3)
Somewhat	65 (24.3)	62 (23.1)	67 (25)	56 (20.9)	56 (20.9)	64 (23.9)	92 (34.3)	57 (21.3)	59 (22)	32 (11.9)	33 (12.3)	30 (11.2)	40 (14.9)
Quite a bit	77 (28.7)	62 (23.1)	57 (21.3)	79 (29.5)	57 (21.3)	47 (17.5)	47 (17.5)	29 (10.8)	45 (16.8)	21 (7.8)	23 (8.6)	40 (14.9)	34 (12.7)
Very much	26 (9.7)	17 (6.3)	19 (7.1)	31 (11.6)	22 (8.2)	18 (6.7)	5 (1.9)	13 (4.9)	22 (8.2)	3 (1.1)	12 (4.5)	28 (10.4)	25 (9.3)

Conclusions: Fatigue is a prevalent symptom among individuals with lupus within our population and exhibits a low negative correlation with disease activity. This relationship indicates that the FACIT score decreases as the disease activity score

increases, demonstrating greater fatigue levels in patients experiencing high disease activity. A critical implication of this fatigue is the difficulty in performing daily activities. Given these findings, it is imperative to recognize that fatigue should not be underestimated as a clinical symptom, and the ongoing monitoring of patients is essential to address this issue effectively.

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Poster Topic: *AS22 - SLE Heterogeneity*

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH SLE ACROSS 5 REGISTRIES – THE LUPUSNET FEDERATED DATA NETWORK

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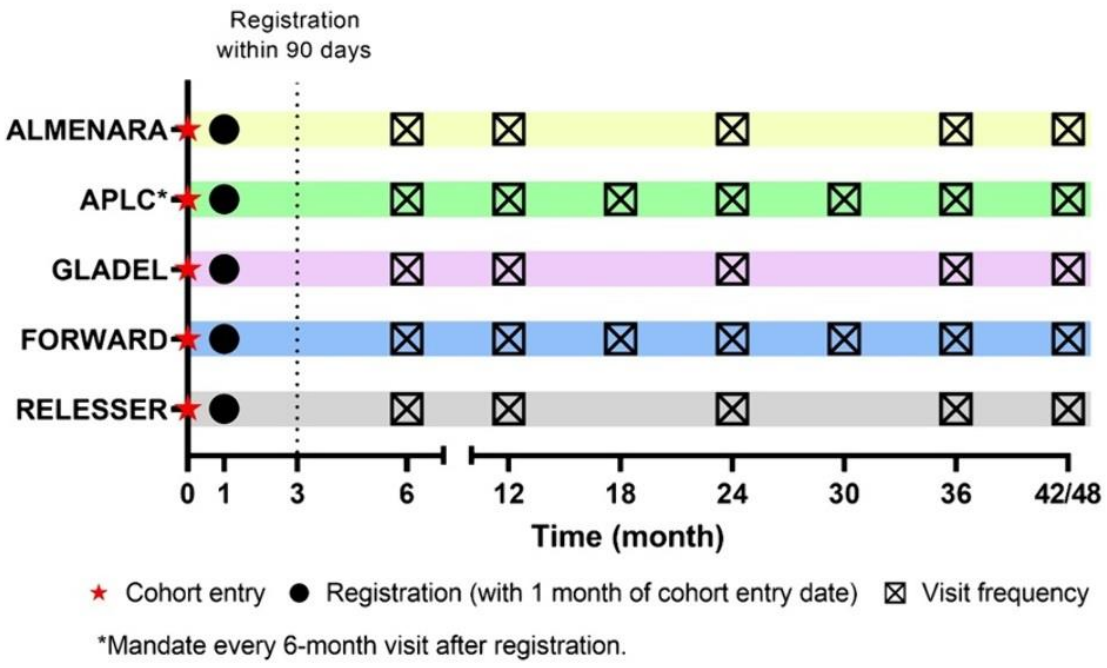
Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with a broad range of clinical manifestations and a high unmet need across patient populations. Real-world data on SLE are scattered across many registries worldwide, with heterogeneous data collection. The Lupus Federated Data Network (LupusNet) is an interdisciplinary international initiative that aims to combine and harmonize data from existing SLE registries to create a global, federated network of SLE databases with

a larger number of patients, greater data consistency, and the potential to address gaps in the understanding of SLE.

Methods: Data from 5 registries representing > 10,000 patients with SLE from 4 regions contributed to LupusNet: APLC (Asia Pacific), RELESSER (Europe), FORWARD (North America), and Almenara and GLADEL (Central and South America). LupusNet uses a federated data network approach and a privacy-by-design method, where the data remains with the respective registries and the analysis occurs at the local center; only aggregated results are shared. **Figure 1** illustrates the schedule of patient visits for clinical assessments (including the Systemic Lupus Erythematosus Disease Activity Index [SLEDAI]) in each registry. Demographic and clinical variables (e.g., disease activity/severity, clinical events, biopsies/histology, biomarkers, treatment history, comorbidities, medications, and patient-reported outcomes) were mapped and harmonized to the Observational Medical Outcomes Partnership Common Data Model v5.4. This study describes the baseline demographics, patient characteristics, and disease activity based on the SLEDAI in LupusNet during ± 90 days of registration.

Figure 1. Frequency of Patient Visits by Registry



Results: A total of 10,267 patients were included and mapped in LupusNet. Of those, 3,908 patients were in Asia Pacific, 1,806 in Europe, 3,066 in North America, and 1,487 in Central and South America. Select baseline demographics and characteristics of patients with SLE are presented in **Table 1**. Disease activity based on the SLEDAI questionnaire was assessed at registration from 4 registries that collected these data. Across registries, the majority of the patients were females; the duration from SLE diagnosis to the registry entry ranged from 5 to 10 years. Heterogeneity and variability in

disease manifestations determined from SLEDAI responses were observed across registries, particularly in relation to arthritis, nephritis (i.e., proteinuria, pyuria, hematuria, and urinary casts), increased anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibody, and leukopenia.

Table 1. Baseline Demographics and Patient Characteristics in LupusNet

Characteristic	ALMENARA (N = 507)	APLC (N = 3908)	FORWARD (N = 3066)	GLADEL (N = 980)	RELESSER (N = 1806)
Follow-up duration, mean (SD), years	5.7 (4.2)	3.0 (2.5)	4.4 (5.4)	1.0 (0.7)	4.0 (2.6)
Sex, female, n (%)	468 (92)	3597 (92)	2799 (91)	876 (89)	1625 (90)
Age at enrollment, mean (SD), years	41.6 (13.1)	40.6 (13.5)	47.4 (14.1)	36.8 (12.3)	48.4 (13.7)
Age at diagnosis, mean (SD), years	34.9 (13.6)	31.1 (12.8)	36.5 (14.3)	29.2 (11.6)	35.2 (13.8)
Disease duration, mean (SD), years	11.7 (7.5)	13.1 (8.9)	15.2 (10.8)	8.7 (7.8)	17.3 (9.6)
Duration from SLE diagnosis to registry entry, mean (SD), years	6.8 (6.4)	10.1 (8.4)	11.4 (9.5)	7.7 (7.7)	13.3 (8.9)
Race, n (%)					
Asian	< 10 (< 0.2)	3442 (88)	45 (2)	0	0
Black	< 10 (< 0.2)	0	345 (11)	78	0
Other	496 (98)	142 (4)	1162 (38)	654 (67)	1806 (100)
White	< 10 (< 0.2)	305 (8)	1527 (50)	241 (25)	0
Ethnicity, n (%)					
Hispanic or Latino	0	< 10 (< 1)	144 (5)	0	0
Mixed ancestry	496 (98)	< 10 (< 1)	0	649 (66)	0
Missing	11 (2)	3898 (100)	1051 (34)	331 (34)	1806 (100)
Not Hispanic or Latino	0	0	1871 (61)	0	0

If < 10 patients, actual number masked.

Conclusions: Mapping patient characteristics from LupusNet allows researchers to analyze a larger population of patients with SLE across different geographical regions. These findings demonstrate a high degree of variability in disease activity measured by SLEDAI across registries, likely due to differences in recruitment strategy, treatment strategy/access, healthcare system, and race/ethnicity. Compared to individual registries, this network of collective SLE databases allows further study to better understand disease heterogeneity, patient populations, and treatment patterns with the goal of improving outcomes for patients with SLE across the globe.

PV194 / #729

Poster Topic: *AS22 - SLE Heterogeneity*
Late-Breaking Abstract

MINORITIES ARE UNDER-REPRESENTED IN SLE CLINICAL TRIALS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background/Purpose: With numerous emerging treatments for systemic lupus erythematosus (SLE), it is crucial that populations in trials reflect the diversity of those affected by SLE. Data from North American and European cohorts show that the of SLE in prevalence of Black populations can be higher than White populations in some locations relative to background population ethnicities. The objectives of this study were to examine the racial composition of clinical trials in SLE from 2014 to 2024, assessing whether these trials accurately represent the diversity of SLE populations.

Methods: A systematic review of the literature was conducted using EMBASE, PUBMED, Web of Science, and Cochrane CENTRAL from Jan 1, 2014 – May 14, 2024. Randomized trials of pharmaceutical interventions in SLE patients were included. Studies were excluded if they had less than 50 participants, were not in English, did not report on race/ethnicity. Revman 5.4 and SPSS were used for statistical analysis.

Results: 2505 studies were identified, 63 were included. The pooled proportion of women was 91%. Caucasians represented 61% of those included in trials compared to only 14% of Blacks, 37% of Hispanics and Asians only 14%. Indigenous patients represented 8% whereas none were Pacific Islanders. There was a paucity of information on educational status, income, employment, urban/rural address, or marital status.

Conclusions: Standardized reporting of SES surrogates should occur (i.e. education, household income). Minorities seem under-represented in RCTs. Greater effort is needed to ensure that SLE research trials are generalizable to patients and equitable with respect to patient diversity.

PV195 / #239

Poster Topic: *AS22 - SLE Heterogeneity*

CLUSTER ANALYSIS OF AUTOANTIBODIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with diversity of autoantibodies and clinical manifestation. The identification of patient clusters by autoantibody profile can predict prognosis and mortality. The aim of this study is to define and describe serological clusters and their clinical and epidemiological characteristics, as well as their association with comorbidities, disease activity, severity and damage.

Methods: Descriptive, observational and multicenter study that includes patients with SLE from the Spanish national registry RELESSER. 1740 patients were included in the cross-sectional study and 718 in the prospective study (with annual follow-up during 5 years). The autoantibodies selected for cluster analysis were anti-DNA, anti-Sm, anti-RNP, anti-Ro, anti-La and antiphospholipid antibodies. Cluster analysis was carried out using Gower distance. To compare the distributions of categorical variables, Chi-square tests were used or Fisher's exact test in cases of low expected frequencies. For continuous variables, non-parametric tests such as Kruskal-Wallis or ANOVA were applied, depending on the data distribution and homogeneity of variances.

Results: Four serological clusters were defined. Cluster 1 (absence of anti-extractable nuclear antigen antibodies; 44.54% of the patients) was characterized by lower frequency of vasculitis (6.6%), leukopenia (49.1%) and lymphopenia (48.0%). Cluster 2 (antiphospholipid antibodies; 12.24%) was represented by higher frequency of high blood pressure (35.5%), hemolytic anemia (13.5%), thrombocytopenia (39.9%), vasculitis (12.5%), visual disturbances (9.1%) and higher use of immunoglobulins (10.3%) and oral anticoagulants (39.0%). Cluster 3 (anti-Ro and anti-La; 26.67%) had the lowest frequency of lupus nephritis (24.9%). Patients from cluster 4 (anti-Smith and anti-ribonuclear proteins; 16.55%) were younger at disease onset (median age of 29.2 years) and had the highest frequency of lupus nephritis (38.5%), leukopenia (66.0%), lymphopenia (62.2%), hypocomplementemia (89.5%), myositis (5.6%) and cutaneous manifestations. Besides, they had a higher frequency of osteoporosis (11.0%) and severe infections (26.4%) and a higher use of glucocorticoids (93.5%), azathioprine (42.0%), cyclophosphamide (25.5%) and mycophenolate mofetil (24.0%). Regarding disease activity assesed by SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), at visit 1 of the longitudinal study, patients in cluster 4 had the highest scores: 2.5 ± 3.37 (1.70 ± 3.09 in cluster 1 ($p=0.18$), 2.18 ± 4.26 in cluster 2 ($p=0.4$), 1.86 ± 2.50 in cluster 3 ($p=0.011$). After 5 years of follow-up, no differences were observed between clusters. Concerning damage assessed by SLICC/ACR DI, patients in cluster 2 exhibited the highest scores at visit 1: 1.93 ± 2.30 (1.42 ± 1.81 in cluster 1 ($p=0.018$), 1.13 ± 1.72 in cluster 3 ($p<0.001$), 1.67 ± 1.92 in cluster 4 ($p=0.4$)). After 5 years of follow-up, a

significant increase was observed across all clusters (p<0.001), with differences persisting at the end of follow-up (p=0.049). Regarding severity measured by Katz, patients in cluster 4 had the highest scores at visit 1: 5.24 ± 2.09 (4.45 ± 2.13 in cluster 1 (p<0.001), 4.57 ± 2.20 in cluster 2 (p=0.019), 4.35 ± 1.69 cluster 3 (p<0.001)). The differences persist between clusters after follow-up (p=0.005). As for mortality, 21 deaths were recorded: 5 in cluster 1 (1.74%), 6 in cluster 2 (5.50%), 6 in cluster 3 (2.97%) and 4 in cluster 4 (3.36%), with no significant differences between clusters (p=0.427).

Table 1. Epidemiological characteristics and comorbidities

	Cluster 1 (n=775)	Cluster 2 (n=213)	Cluster 3 (n=464)	Cluster 4 (n=288)	TOTAL (n=1740)	*p*
Age at diagnosis (median [Q1, Q3])	32.6 [24.2, 43.6]	32.8 [23.2, 41.3]	33.2 [25.3, 43.0]	29.2 [23.3, 38.0]	32.1 [24.1, 42.3]	0.001
Sex, n (%)						
Female	675 (87.3%)	185 (86.9%)	440 (94.8%)	263 (91.3%)	1563 (89.9%)	<0.001
Male	98 (12.7%)	28 (13.1%)	24 (5.2%)	25 (8.7%)	175 (10.1%)	
Ethinicity, n (%)						
African American	1 (0.1%)	0 (0%)	1 (0.2%)	1 (0.4%)	3 (0.2%)	
Asian	3 (0.4%)	0 (0%)	2 (0.4%)	2 (0.7%)	7 (0.4%)	
Caucasian	703 (93.4%)	195 (94.2%)	430 (94.7%)	249 (88.3%)	1577 (93.0%)	0.227
Latin american	41 (5.4%)	11 (5.3%)	18 (4.0%)	26 (9.2%)	96 (5.7%)	
Others	5 (0.7%)	1 (0.5%)	3 (0.7%)	4 (1.4%)	13 (0.8%)	
Tobacco, n (%)						
Previously	167 (23.5%)	48 (24.1%)	92 (21.5%)	52 (19.3%)	359 (22.3%)	0.358
Smoker	141 (19.9%)	37 (18.6%)	69 (16.1%)	47 (17.4%)	294 (18.3%)	
Never	402 (56.6%)	114 (57.3%)	267 (62.4%)	171 (63.3%)	954 (59.4%)	
Alcohol, n (%)						
Nowadays	6 (0.8%)	0 (0%)	3 (0.7%)	2 (0.7%)	11 (0.7%)	0.693
Previously	23 (3.2%)	8 (3.9%)	9 (2.0%)	6 (2.2%)	46 (2.8%)	
Never	700 (96.0%)	195 (96.1%)	428 (97.3%)	262 (97.0%)	1585 (96.5%)	
Diabetes Mellitus, n (%)	35 (4.6%)	13 (6.3%)	11 (2.4%)	12 (4.2%)	71 (4.2%)	0.103
High blood pressure, n (%)	230 (29.7%)	75 (35.5%)	102 (22.2%)	81 (28.4%)	488 (28.2%)	0.002
Dyslipidemia, n (%)	245 (32.7%)	75 (36.6%)	127 (28.3%)	82 (29.5%)	529 (31.5%)	0.138
Congestive heart failure, n (%)	27 (3.5%)	7 (3.3%)	9 (2.0%)	8 (2.8%)	51 (3.0%)	0.471
Tumor and lymphoma, n (%)	47 (6.1%)	13 (6.2%)	21 (4.5%)	16 (5.6%)	97 (5.6%)	0.675
Osteoporosis, n (%)	44 (5.8%)	16 (7.5%)	28 (6.1%)	31 (11.0%)	119 (7.0%)	0.025
Infections, n (%)	143 (19.6%)	49 (23.8%)	80 (18.1%)	72 (2.4%)	344 (20.8%)	0.032

Table 2. Clinical characteristics

	Cluster 1 (n=775)	Cluster 2 (n=213)	Cluster 3 (n=464)	Cluster 4 (n=288)	TOTAL (n=1740)	p
Fever, n (%)	18 (2.3%)	8 (3.8%)	14 (3.0%)	13 (4.5%)	53 (3.1%)	0.285
Weight loss, n (%)	65 (8.5%)	22 (10.4%)	27 (5.9%)	33 (11.5%)	147 (8.5%)	0.040
Lymphadenopathy, n (%)	63 (8.2%)	21 (9.9%)	40 (8.7%)	47 (16.4%)	171 (9.9%)	<0.001
Splenomegaly, n (%)	29 (3.8%)	14 (6.7%)	11 (2.4%)	13 (4.5%)	67 (3.9%)	0.063
Inflammatory rash, n (%)	447 (58.1%)	119 (56.7%)	306 (66.5%)	205 (71.2%)	1077 (62.4%)	<0.001
Oral ulcers, n (%)	291 (38.6%)	77 (36.5%)	199 (44.0%)	127 (45.2%)	694 (40.9%)	0.064
Alopecia, n (%)	245 (31.9%)	75 (35.4%)	167 (36.2%)	129 (45.6%)	616 (35.8%)	<0.001
Arthritis, n (%)	78 (10.2%)	24 (11.3%)	46 (10.0%)	39 (13.8%)	187 (10.9%)	0.4
Myositis, n (%)	22 (2.9%)	9 (4.3%)	8 (1.7%)	16 (5.6%)	55 (3.2%)	0.025
Alveolar hemorrhage/ Pulmonary vasculitis, n (%)	5 (0.7%)	2 (1.0%)	0 (0%)	2 (0.7%)	9 (0.5%)	0.164
Pneumonitis, n (%)	26 (3.4%)	5 (2.4%)	15 (3.3%)	11 (3.8%)	57 (3.3%)	0.836
Myocarditis, n (%)	3 (0.4%)	2 (1.0%)	2 (0.4%)	2 (0.7%)	9 (0.5%)	0.599
Pericarditis, n (%)	12 (1.6%)	4 (1.9%)	7 (1.5%)	5 (1.7%)	28 (1.6%)	0.96
Vasculitis, n (%)	50 (6.6%)	26 (12.5%)	46 (10.1%)	33 (11.6%)	155 (9.1%)	0.009
Lupus nephritis, n (%)	228 (29.9%)	58 (27.4%)	113 (24.9%)	110 (38.5%)	509 (29.7%)	0.001
Seizures, n (%)	35 (4.6%)	17 (8.1%)	17 (3.7%)	15 (5.3%)	84 (4.9%)	0.096
Organic brain syndrome, n (%)	16 (2.1%)	5 (2.4%)	6 (1.3%)	10 (3.5%)	37 (2.1%)	0.248
Lupus headache, n (%)	41 (5.4%)	15 (7.1%)	20 (4.3%)	22 (7.7%)	98 (5.7%)	0.184
Transverse myelitis, n (%)	7 (0.9%)	3 (1.4%)	3 (0.7%)	2 (0.7%)	15 (0.9%)	0.767
Cranial or peripheral neuropathy, n (%)	22 (2.9%)	6 (2.9%)	16 (3.5%)	9 (3.2%)	53 (3.1%)	0.947
Visual disturbances, n (%)	35 (4.6%)	19 (9.1%)	9 (1.9%)	11 (3.9%)	74 (4.3%)	<0.001
Hemolytic anemia, n (%)	60 (7.9%)	28 (13.5%)	23 (5.1%)	28 (9.9%)	139 (8.1%)	0.002
Leukopenia, n (%)	375 (49.1%)	112 (53.3%)	278 (61.5%)	188 (66.0%)	953 (55.7%)	<0.001
Lymphopenia, n (%)	365 (48.0%)	106 (51.2%)	250 (54.7%)	176 (62.2%)	897 (52.5%)	<0.001
Thrombocytopenia, n (%)	155 (20.7%)	81 (39.9%)	86 (19.3%)	65 (23.8%)	387 (23.2%)	<0.001
Hypocomplementemia, n (%)	555 (72.4%)	174 (82.1%)	348 (75.7%)	257 (89.5%)	1334 (77.3%)	<0.001

Table 3. Treatments

	Cluster 1 (n=775)	Cluster 2 (n=213)	Cluster 3 (n=464)	Cluster 4 (n=288)	TOTAL (n=1740)	*p*
Glucocorticoids, n (%)	641 (86.4%)	176 (88.0%)	365 (84.7%)	259 (93.5%)	1441 (87.3%)	0.005
Methotrexate, n (%)	137 (18.6%)	37 (18.6%)	95 (22.1%)	56 (20.1%)	325 (19.8%)	0.516
Leflunomide, n (%)	31 (4.2%)	11 (5.5%)	20 (4.7%)	8 (2.9%)	70 (4.3%)	0.529
Anti-TNF, n (%)	12 (1.6%)	4 (2.0%)	9 (2.1%)	3 (1.1%)	28 (1.7%)	0.743
Abatacept, n (%)	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)	1
Azathioprine, n (%)	218 (29.5%)	68 (34.5%)	127 (29.7%)	116 (42.0%)	529 (32.3%)	<0.001
Cyclophosphamide, n (%)	159 (21.6%)	45 (22.6%)	73 (17.0%)	71 (25.5%)	348 (21.2%)	0.047
Mycophenolate Mofetil, n (%)	112 (15.3%)	31 (15.5%)	73 (17.1%)	66 (24.0%)	282 (17.2%)	0.011
Mycophenolic acid, n (%)	18 (2.5%)	3 (1.6%)	14 (3.3%)	10 (3.7%)	45 (2.8%)	0.463
Antimalarials, n (%)	612 (82.6%)	155 (77.1%)	379 (88.6%)	252 (90.3%)	1398 (84.8%)	<0.001
Immunoglobulins, n (%)	22 (3.0%)	20 (10.3%)	19 (4.5%)	12 (4.4%)	73 (4.5%)	<0.001
Rituximab, n (%)	54 (7.3%)	19 (9.5%)	41 (9.6%)	22 (8.0%)	136 (8.3%)	0.496
Acetylsalicylic acid, n (%)	217 (34.7%)	127 (69.8%)	133 (34.7%)	79 (32.4%)	556 (38.7%)	<0.001
Oral anticoagulants, n (%)	88 (12.0%)	78 (39.0%)	57 (13.4%)	40 (14.5%)	263 (16.1%)	<0.001

Conclusions: In our cohort, the serological profile constitutes a crucial factor for the clinical stratification of patients and predicting their prognosis. Nevertheless, further studies are required to facilitate a more precise identification and comprehensive understanding of these patients.

PV196 / #120

Poster Topic: ***AS22 - SLE Heterogeneity***

CLINICAL SIGNIFICANCE OF INTERFERON STATUS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: PRELIMINARY DATA

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Background/Purpose: Studies of systemic lupus erythematosus (SLE) pathogenesis have identified two major families of mediators: type I interferon (IFN-I) and autoantibodies to nucleic acids and their proteins, as the main factors contributing to the development of the disease. Against a background of genetic predisposition, a trigger stimulus, possibly microbial, induces the production of IFN-I, autoantibodies or, more likely, both, leading to inflammation. The interaction of cells of the innate and adaptive immune system are involved in the autoimmune response with the development of a variety of clinical manifestations of SLE. The aim of our study was to describe clinical and immunological characteristics of SLE depending on IFN gene signature (IFNGS).

Methods: This observational retrospective-prospective study included 76 patients (86% women, median aged 33 [25;43] years (median [interquartile range 25;75%]), with a definite diagnosis of SLE (SLICC 2012) attending a routine visit at our Clinic between February 2021 and June 2024. Baseline demographics, disease characteristic, organ system involvement/damage were analysed descriptively according to SLE Disease Activity Index-2000 (SLEDAI-2K), Systemic Lupus International Collaborating Clinics damage index (SDI) and IFNGS status (high/low). IFN status was assessed by the expression of IFN-inducible genes (MX1, RSAD2, EPSTI1) using real-time polymerase chain reaction. IFNGS was calculated as the average expression value of three selected genes. In patients, IFNGS was considered high when the average value of gene expression exceeded the average value of gene expression in donors. The control group consisted of 20 healthy donors comparable in sex and age with the SLE patients.

Results: The median disease duration was 2.3 [0.2;11.0] years, SLEDAI-2K 7 [4;11], SDI 0 [0;2] score. IFNGS-high was detected in 72% of SLE patients. IFNGS-high patients were younger at the time of inclusion (31 [25; 41] and 40 [32; 49] years), had less

frequent remission of SLE (SLEDAI-2K=0) (2% and 19%), and higher concentrations of anti-dsDNA (219.8 [120.3; 729.3] and 131.0 [46.6; 265.9] IU/ml, normal <100 IU/ml), ANF titre ≥1/1280 (84% and 52%), lower absolute count of blood leukocytes (4.2 [3.2; 5.6] and 6.6 [4.2; 8.8] x109/L) and lymphocytes (1.3 [0.8; 1.8] and 2.0 [1.2; 3.2] x109/L), p<0,05 in all cases. Of the criterion and non-criteria manifestations of SLE the greater proportions of IFNGS-high versus IFNGS-low patients had haematological (56% and 29%), primarily leukopenia (53% and 24%) and dermal (31% and 19%) involvement, p<0,05 in all cases.

Conclusions: Elevated type I IFN signalling is a marker of a certain type of SLE patients - young age with predominant skin, haematological and immunological disorders.

PV197 / #398

Poster Topic: ***AS22 - SLE Heterogeneity***

INCIDENT CARDIOVASCULAR AND VENOUS THROMBOEMBOLIC EVENTS IN AUTOANTIBODY DEFINED SLE CLUSTERS

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Background/Purpose: Patients with SLE are at high risk of cardiovascular (CV) and venous thromboembolic (VTE) events. Previously, we identified four autoantibody-defined SLE clusters (1), associated with different HLA-DRB1 genotypes, clinical manifestations and cytokine patterns. We aimed to compare incidence rates of CV and VTE events between the clusters and to compare each cluster to a general population control group.

Methods: Unsupervised clustering, based on 13 autoantibodies, clustered SLE patients into four clusters: Cluster 1 was dominated (>50% positive) by anti-SSA/SSB, Cluster 2 by anti-nucleosome/Sm/RNP/dsDNA, Cluster 3 by aPL and Cluster 4 by negativity to the 13 autoantibodies. Information on vascular outcomes was collected through ICD codes from the National Patient Register. Controls from the Total Population Register were matched 10:1 on birth year, sex and residence to each patient. Subjects with a vascular event before enrollment were excluded. Incidence rates (IR) were calculated for 1000 person-years and 95% CI were calculated using the Poisson distribution. Age adjusted Hazard Ratios (HR) and 95% CI from Cox proportional hazards models estimated relative risks of incident vascular events.

Results: 461 SLE patients were enrolled, mean follow-up of 12.24±5.6 years. SLE patients in cluster 2 were younger at inclusion and younger at first CV and VTE event. Cluster 3 had the highest crude IR for all the outcomes. The risk of major adverse CV events (MACE) in cluster 3 was almost twice as high compared to cluster 4 (Table 1). Moreover, cluster 3 had more than 2.5 higher risk of cerebrovascular events and VTE than cluster 1. Cluster 2 had similarly high HR for heart failure and VTE. Notably, HR for ischemic heart disease did not differ between cluster 4 and controls (Table 1). **Table 1. Incidence rates and Hazard ratios (HR) for vascular outcomes between SLE clusters and between each cluster and general population controls**

	Incidence Rate (95% CI)	HR (95%CI, versus Ref cluster*	HR and 95% CI, versus general population comparators*
MACE			
Cluster 1 (N=141)	19.05 (18.85-19.26)	1.16 (0.59-2.24)	2.89 (1.97-4.23)
Cluster 2 (N=105)	11.44 (11.26-11.63)	1.18 (0.55-2.55)	3.14 (1.77-5.58)
Cluster 3 (N=154)	28.55 (28.3-28.79)	1.91 (1.01-3.58)	5.03 (3.61-7.01)
Cluster 4 (N=61)	15.55 (15.28-15.83)	Ref	2.52 (1.34-4.73)
IHD			
Cluster 1	10.76 (10.6-10.91)	2.02 (0.68-5.98)	3.35 (1.99-5.58)
Cluster 2	6.03 (5.89-6.16)	1.92 (0.57-6.49)	2.58 (1.19-5.62)
Cluster 3	12.16 (12-12.32)	2.5 (0.86-7.27)	5.69 (3.42-9.47)
Cluster 4	5.07 (4.91-5.22)	Ref	1.85 (0.64-5.36)
Cerebrovascular events			
Cluster 1	4.86 (4.76-4.96)	Ref	2.26 (1.1-4.65)
Cluster 2	3.71 (3.61-3.81)	1.17 (0.38-3.57)	3.22 (1.19-8.7)
Cluster 3	11.55 (11.4-11.71)	2.68 (1.23-5.84)	5.27 (3.16-8.77)
Cluster 4	NP	NP	NP
Heart failure			
Cluster 1	7.46 (7.34-7.59)	0.9 (0.34-2.37)	3.77 (2.09-6.79)
Cluster 2	7.43 (7.29-7.58)	1.74 (0.62-4.86)	5.05 (1.73-14.7)
Cluster 3	12.67 (12.52-12.83)	1.73 (0.71-4.22)	4.92 (2.71-8.91)
Cluster 4	7.49 (7.3-7.68)	Ref	3.57 (1.55-10.11)
VTE			

Cluster 1	3.24 (3.15-3.32)	Ref	2.35 (0.97-5.71)
Cluster 2	6.91 (6.76-7.05)	2.57 (0.89-7.45)	NP
Cluster 3	8.24 (8.12-8.37)	2.69 (1.05-6.9)	8.35 (4.37-15.95)
Cluster 4	NP	NP	NP

MACE: major adverse cardiovascular events; IHD:ischemic heart disease; VTE:venous thromboembolism; NP:not performed. *Age-adjusted Cox-regression models. MACE= IHD+ischemic cerebrovascular events+peripheral arterial thrombosis/embolism+heart failure+death due to CV events; Cerebrovascular events=ischemic cerebrovascular events+cerebral hemorrhages; VTE=deep venous thrombosis+pulmonary embolism.

Conclusions: In SLE, incidence of MACE and VTE differs between autoantibody defined clusters, with the highest incidence observed in the aPL positive and the lowest incidence in the autoantibody negative patients. Reference: Diaz-Gallo LM et al. ACR Open Rheum (2022).

PV198 / #384

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

ANTI-HISTONE ANTIBODIES CLINICAL SIGNIFICANCE IN PATIENTS WITH SYSTEMIC LUPUS: A MOROCCAN COHORT OF 80 PATIENTS

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Background/Purpose: Objectives : Systemic lupus erythematosus (SLE) is a complex and heterogeneous autoimmune disease, presenting a number of significant challenges in both its understanding and management. While classic antibodies have been the focus, anti-histone antibodies are crucial markers warranting further exploration.The aim of our study was to examine a wide range of clinical and biological features and analyze their correlation with this antibody, providing valuable insights into the complexities of this multifaceted condition.

Methods: Methods : In this case-control study, carried out in the internal medicine department of the Cheikh Khalifa International University Hospital in Casablanca between January 2017 and July 2024, 80 patients with SLE were included, of which 30 were positive for anti-histone antibodies (37.5%) and 50 were negative (62.5%), along with 2 patients with induced lupus. Ethics committee approval was obtained.

Results: Results : The mean age of our patients was 38,5 years (± 15,2). A female predominance was observed at 90% (female-to-male ratio of 9 :1). By analyzing the two groups, positive and negative for the antibody, we highlighted significant differences in clinical presentation and biological profiles. Anti-histone antibodies correlated with fever(p-value=0,018) , weight loss(p-value=0,019), renal markers such as hematuria (p-value=0,003) and proteinuria (p-value=0,002) and the development of lupus nephropathy (p-value=0,003). Hematologically, their positivity correlated with anemia(p-value=0,0002) and lymphopenia(p-value=0,024). A more pronounced inflammatory profile and increased disease activity were observed among the positive patients.The SLEDAI(Systemic Lupus Erythematosus Disease Activity Index) score was significantly higher in the group positive for anti-histone antibodies(p-value=0,0001).Additionally, there was a strong association between anti-histone and anti-nucleosome antibodies (p-value<0,00001).Lupus patients with anti-histone antibodies would also be significantly more likely to have anti u1-snRNP(p-value=0,0005), anti ribosomal protein P (p-value=0,049) and anti DSF70 antibodies(p-value<0,0001). Among the two reported cases of induced lupus, one was linked to anti-TNF alpha treatment and was negative for anti-histone antibodies, while the other was

associated with an adenovirus vaccine for COVID-19 and tested positive for these antibodies.

Conclusions: . Conclusion : These data highlight the essential role of measuring these auto-antibodies in SLE and drug-induced lupus. These antibodies could be a valuable asset as a diagnostic tool and a marker of disease activity, helping to enhance follow-up and management.Their detection, along with anti-nucleosome and anti-DNA antibodies, reinforces the importance of triple positivity as a predictor of the severity of renal damage. Considering the tuberculosis-endemic situation in our country, isoniazid-induced lupus might be underdiagnosed among the Moroccan population, and assessing anti-histone antibodies could provide additional value for clinicians.

PV199 / #53

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

PROPOSALS FOR DEFINITIONS OF MODERATE AND SEVERE DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS. IMPACT ON FLARES, QUALITY OF LIFE, DAMAGE ACCRUAL, HOSPITALIZATIONS AND MORTALITY.

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Background/Purpose: To propose a definition for moderate disease activity state (MODAS) and severe disease activity state (SEDAS) in SLE and using the RELESSER-PROS cohort to describe the prevalence of both states of activity and to analyze the impact of this categorization on mortality, organ damage, flares, hospital admissions and health-related quality of life (HRQoL)

Methods: We used data from the prospective phase of RELESSER (RELESSER-PROS), the SLE register of the Spanish Society of Rheumatology. MODAS and SEDAS definitions are based on: cSLEDAI, presence of severe manifestations and PGA. MODAS was defined as the presence of at least one of the following conditions: <4 cSLEDAI < 8 or 1< PGA < 2 (without severe clinical manifestations); and SEDAS: SLEDAIc >8 or PGA > 2 or the presence of severe SLEDAI and Non-SLEDAI manifestations. We analyzed the impact of remaining in MODAS or SEDAS in terms of several robust outcomes.

Results: 1,463 patients were included, mean age (±SD): 56 (±13.5) years; mean disease duration (±SD): 14 (±8.5) years. Patients had a mean (±SD) of 4.2 (±1.2) visits and a mean (±SD) follow-up time of 3.6 (±1.4) years. Patients with at least one visit in MODAS or in SEDAS had significantly higher numbers of flares, worse HRQoL, more damage accrual and more hospital admissions. Both, damage accrual and hospital admissions were significantly higher in SEDAS than in MODAS. Table 1 and 2. When comparing MODAS and SEDAS vs low disease activity, worse were the outcomes in the moderate/severe activity states. Figure 1. Table 1. Outcomes, according to the number of visits in SEDAS.

	Number of visits in SEDAS						
	0 (n=1103)	1 (n=249)	2 (n=76)	3 (n=24)	p-value 0 vs 1	p-value 1 vs 2	p-value 2 vs 3
Deaths; n (%)	36 (3.26%)	5 (2.01%)	2 (2.63%)	0 (0%)	NS	NS	NS
Admissions; mean (SD)	0.72 (1.55)	1.31 (1.90)	2.09 (3.32)	3.63 (4.00)	<0.001*	1.000	0.281
D SDI (V5-V1); mean (SD)	0.41 (0.76)	0.69 (1.03)	1.30 (1.38)	1.57 (1.83)	0.003*	0.006*	1.000
Number of flares; mean (SD)	1.17 (1.92)	2.02 (2.53)	2.83 (2.80)	3.71 (2.20)	<0.001*	0.189	0.512

Quality of life (mean LIT); mean (SD)	28.2 (20.6)	33.3 (19.6)	37.2 (22.5)	38.3 (16.0)	0.001*	1.000	1.000

Table 2. Outcomes, according to the number of visits in MODAS.

	Number of visits in MODAS						
	0 (n=1103)	1 (n=249)	2 (n=76)	3 (n=24)	p-value 0 vs 1	p-value 1 vs 2	p-value 2 vs 3
Deaths; n (%)	26 (3.26%)	7 (3.27%)	3 (5.17%)	0 (0%)	NS	NS	NS
Admissions; mean (SD)	0.58 (1.35)	1.00 (1.73)	1.03 (1.83)	2.14 (3.94)	0.002*	1.000	1.000
D SDI (V5-V1); mean (SD)	0.33 (0.68)	0.56 (0.80)	0.61 (1.18)	0.85 (0.94)	0.001*	1.000	1.000
Number of flares; mean (SD)	0.79 (1.51)	1.77 (2.14)	3.26 (2.91)	3.57 (3.61)	<0.001*	<0.001*	1.000
Quality of life (mean LIT); mean (SD)	25.8 (20.2)	33.1 (20.6)	39.2 (18.0)	37.8 (21.2)	<0.001*	0.333	1.000

Figure 1. Comparison of risk of admissions, damage accrual, flares and quality of life between different states of activity with each other.

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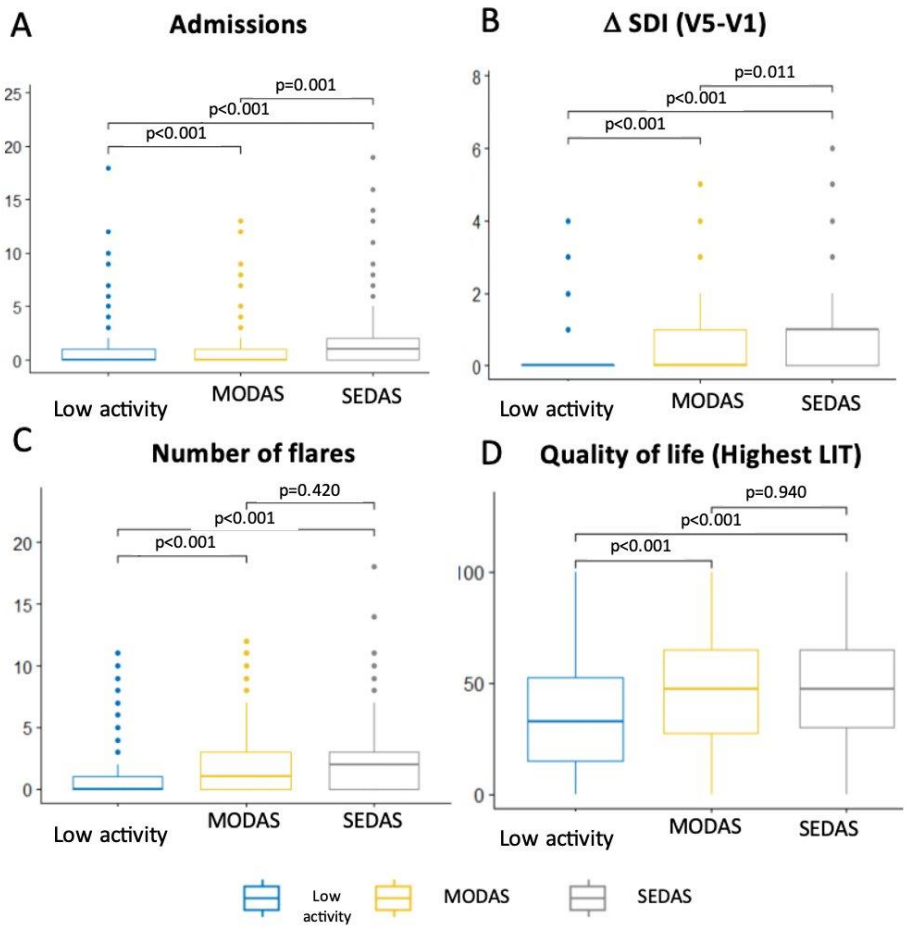

Conclusions: Patients who were in MODAS or SEDAS at least once had worse outcomes in terms of numbers of flares, HRQoL, damage accrual, and hospital admissions. Furthermore, the more time spent in these states entailed greater risks. These results emphasize the importance of an adequate stratification of disease activity in SLE patients.

PV200 / #278

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

SOCIODEMOGRAPHIC PROFILE AND INITIAL CLINICAL PRESENTATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AMONG BANGLADESHI POPULATION

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune multisystem disease characterized by a diverse range of organ involvement and clinical manifestations. The presentation of SLE has significant geographical variation, with the disease being more prevalent among Asian, Hispanic, and Afro-American populations. The incidence and prevalence of SLE vary widely across different regions. Alongside variations in epidemiological subgroups such as race/ethnicity, gender, and age of onset; other sociodemographic factors including socioeconomic status, education level, and access to medical care, can influence disease activity and outcomes. This study aimed to identify the sociodemographic profile and initial clinical presentation of SLE patients among Bangladeshi population.

Methods: This cross-sectional observational study was conducted at the Green Life Center for Rheumatic Care and Research and the Green Life Medical College Hospital from July 2022 to June 2024. Patients diagnosed with SLE who met the classification criteria of either 1997 American College of Rheumatology (ACR) or 2012 Systemic Lupus International Collaborating Clinics (SLICC), or 2019 EULAR/ACR were included. Patients with overlap, MCTD or unwilling to participate were excluded. A total of 252 consecutive SLE patients were enrolled. Investigators conducted face-to-face interviews and reviewed medical records to gather information on the sociodemographic profile and initial clinical presentations within the first three months of disease onset. Data were collected using a pre-formed data sheet and analyzed using SPSS version 25, calculating percentages and frequencies as appropriate.

Results: Among the 252 patients, the majority were female (92%), resulting in a female-to-male ratio of 11.6:1. The mean age was 29.5 ± 10.6 years, with men being younger on average than women (27.5 years vs. 29.6 years). Approximately two-thirds of the participants resided in urban areas, with 62% being married, 48% identified as homemakers, and 35% as students. Over 90% of the participants had at least a primary education, and 26% were graduates. Most participants (58%) belonged to the low to lower-middle socioeconomic class, with a monthly income ranging from 10,000 to 30000 BDT. None were smoker. The most common initial clinical presentations were alopecia (85%), followed by fatigue (82.5%) and arthralgia/arthritis (80%). Additionally,

68% reported a history of fever, 64% presented with oral ulcers, 60% had various rashes, and 47% had photosensitivity. Headaches were reported by 60% of the patients. The most common initial major organ involvement was renal (41% with proteinuria and 11% with elevated serum creatinine). Anemia was observed in 70% of patients, with 24% having autoimmune hemolytic anemia, 22% had thrombocytopenia, and 14% with leukopenia. Other notable features included a history of raynaud's phenomenon (35%), pleural effusion (15%), convulsions (12%), psychosis (8%), pericardial effusion (4%), and other manifestations (18%). Around 60% of patients presented with more than two features initially. Over 50% of patients experiencing a delay of more than six months, and 23% requiring more than two years from initial presentations to final diagnosis.

Conclusions: The sociodemographic profile of this cohort showed that lupus affects young females, most of them are married or students and belonged to low socioeconomic backgrounds. The initial presentations were largely nonspecific. High index of suspicion is required for early diagnosis. Alopecia, fatigue, and arthralgia/arthritis were identified as the most frequent initial symptoms. Other common presenting features included fever, headaches, and anemia. Some patients may present with major organ involvement, especially renal or neuropsychiatric. Recognition of these features in young females should prompt further evaluation for SLE.

PV201 / #334

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CLINICAL PROFILES AND OUTCOMES OF PURE VERSUS MIXED PROLIFERATIVE AND MEMBRANOUS LUPUS NEPHRITIS: A STUDY FROM A TERTIARY CENTER

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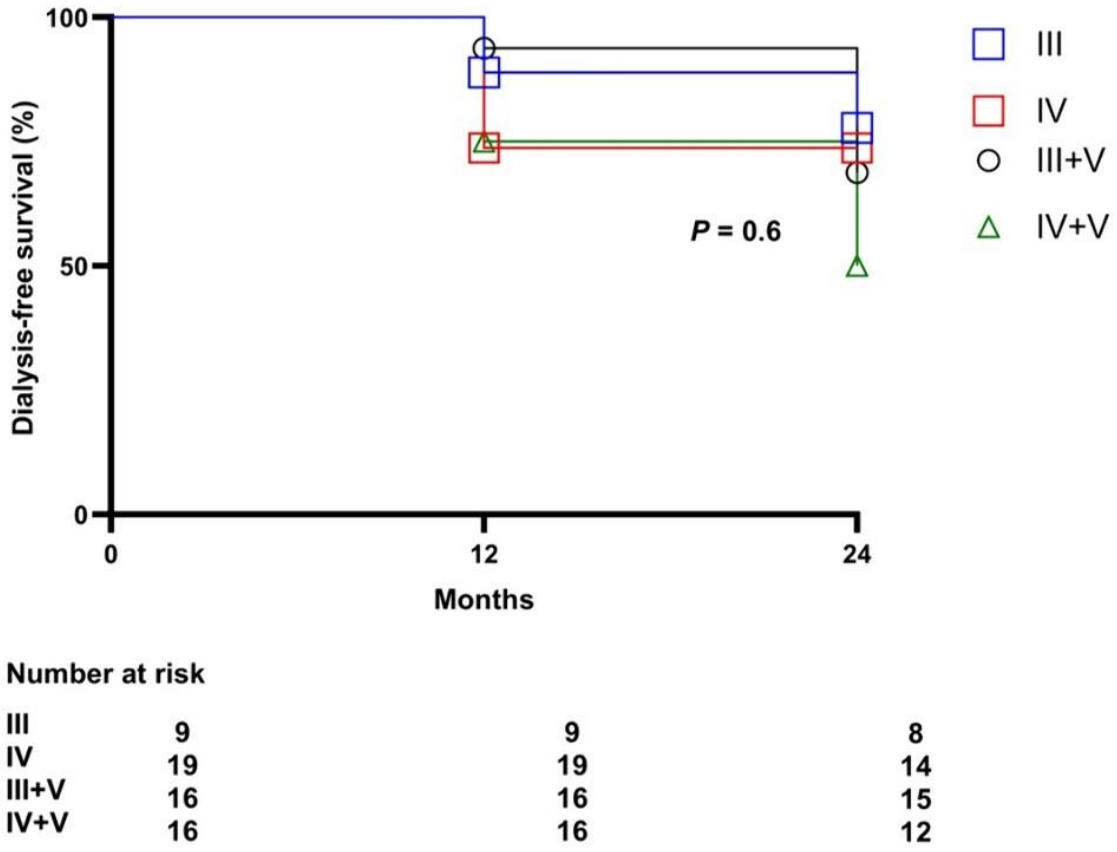
Background/Purpose: Lupus nephritis (LN) represents one of the most severe and complex complications of systemic lupus erythematous (SLE), affecting a substantial proportion of patients. This study aims to describe the clinical profiles and outcomes of four different classes of LN in a diverse patient cohort, with the goal of identifying potential demographic, laboratory and clinical characteristics associated with poorer outcomes.

Methods: We conducted a retrospective review of the medical records for 254 patients with LN confirmed by renal biopsy at Houston Methodist Hospital between 2016 and 2023. A subset of patients with pure and mixed proliferative and membranous LN (class III or IV + class V according to the 2003 ISN/RPS classification criteria) were included. Continuous variables are presented as means with standard deviations, and categorical variables as frequencies and percentages. Differences in continuous and categorical variables were analyzed using the chi-square, Fisher's exact test or analysis of variance (ANOVA), as appropriate. Kaplan-Meier analysis was applied to evaluate dialysis-free survival. Data processing and analysis were conducted using GraphPad Prism version 10.3.1.

Results: We identified 93 patients with LN across the four classes. The demographic and clinical characteristics are summarized by each class in Table 1. The mean age across all patients was 36.6 years, and 81.7% of the cohort were female. In terms of race, non-Hispanic Black patients represented the largest proportion, accounting for 44.1% of the cohort, with the highest representation in the class III+V group (50%). Laboratory testing revealed that patients with class IV+V were more likely to have higher serum creatinine (2.5 mg/dL), lower eGFR (42.5 ml/min), lower complement C3 level (61.4 mg/dL) and worse proteinuria (UPCR 4211.3 mg/g) compared to the other groups. Interestingly, six individuals in the cohort were found to have a negative antinuclear antibody (ANA) test. The mean SLEDAI-2K score was 13.0 in all the patients, indicating active SLE disease, with the highest score (21.9) observed in class III. The most used immunosuppressive therapies were glucocorticoids (89.9%) and mycophenolate mofetil (68.8%), followed by hydroxychloroquine (62.4%), cyclophosphamide (16.1%),

belimumab (5.4%), voclosporin (3.2%) and rituximab (2.2%). Overall, a greater proportion of patients were under the care of a nephrologist compared to a rheumatologist (89.2% vs 65.5%). In the total study population, the mean follow-up duration was 39.9 months. During the follow-up period, only 22.6% of the patients achieved complete remission, with the highest rate observed in class IV (28%) and the lowest in class IV+V (9.1%). A total of 23.7% of patients required dialysis, with the highest incidence found in class IV+V (36.4%); however, the time-dependent incidence did not show a statistically significant difference (p=0.6) [Figure 1]. The overall all-cause mortality rate was 5.4%.

Variable	Total n=93	Class III LN n=18	Class IV LN n=25	Class III+V LN n=28	Class IV+V LN n=22	p value
Demographic data						
Age (years)	36.6 (12.2)	35.8 (10.4)	40 (11.5)	34.3 (10.5)	38.4 (15.5)	0.197
Female	76 (81.7)	16 (88.9)	21 (84.0)	23 (82.1)	16 (72.8)	0.644
Race						
Non-Hispanic Whites	24 (25.8)	4 (22.2)	8 (32.0)	6 (21.4)	6 (27.3)	0.846
Non-Hispanic Black	41 (44.1)	11 (61.1)	11 (4.0)	14 (50.0)	5 (22.8)	0.088
Non-Hispanic Asian	12 (12.9)	0 (0.0)	2 (8.0)	7 (25.0)	3 (13.6)	0.083
Hispanic	14 (15.1)	3 (16.7)	4 (16.0)	1 (3.6)	6 (27.3)	0.113
Unknown	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.1)	0.096
BMI						
<18.5 Kg/m^2	5 (5.2)	1 (5.6)	0 (0.0)	2 (7.1)	0 (0.0)	0.679
18.5-24.9 Kg/m^2	33 (35.5)	6 (3.3)	9 (36.0)	9 (32.1)	9 (40.9)	0.705
25-29.9 Kg/m^2	27 (29.0)	5 (27.8)	9 (36.0)	9 (32.1)	4 (18.2)	0.574
>30 Kg/m^2	28 (30.1)	5 (27.8)	7 (28.0)	7 (25.0)	9 (40.9)	0.645
Smokers (current or former)	10 (10.8)	2 (11.1)	2 (8.0)	6 (21.4)	0 (0.0)	0.103
Laboratory data						
WBC (k/uL)	6.2 (3.6)	6.2 (3.8)	5.5 (2.6)	6.9 (4.3)	6.1 (3.5)	0.654
Neutrophils (%)	73.6 (15.1)	73 (15.9)	70.3 (12.5)	74.6 (18)	78.8 (15.4)	0.623
Lymphocytes (%)	16.1 (9.9)	16.6 (11.9)	19.6 (10.5)	14.0 (8.6)	12.1 (5.2)	0.027
Hemoglobin (g/dL)	10.0 (1.8)	10.2 (1.9)	9.5 (1.9)	10.4 (1.8)	9.8 (1.8)	0.589
Platelet count (k/uL)	288.4 (79.6)	255.9 (80.7)	215.8 (79.1)	254.7 (79.6)	309.0 (72.0)	0.166
Creatinine (mg/dL)	1.9 (1.4)	1.6 (1.2)	2.1 (1.0)	1.5 (1.0)	2.5 (2.0)	0.051
eGFR (mL/min/1.73 m2)	52.8 (32.0)	50.8 (22.6)	44.3 (31.5)	70.0 (35.3)	42.5 (26.2)	0.011
AST (IU/L)	48 (169.5)	32.8 (22.7)	97.5 (314.5)	29.9 (32.7)	22.6 (9.8)	0.443
ALT (IU/L)	60.7 (339.9)	22 (19.0)	158.2 (689.0)	20.0 (17.4)	23.5 (20.9)	0.459
Complement C3 (mg/dl)	64.9 (26.7)	68.7 (36.4)	62.0 (18.6)	69.1 (28.5)	61.4 (24.8)	0.423
Complement C4 (mg/dL)	11.4 (8.5)	12.5 (11.7)	10.5 (4.7)	12.4 (7.6)	10.9 (10.0)	0.848
ANA titer						
Negative	6 (6.5)	0 (0.0)	4 (16.0)	1 (3.7)	1 (4.5)	0.212
1:80-1:160	10 (10.8)	1 (5.6)	4 (16.0)	4 (14.8)	1 (4.5)	0.54
1:320-1:640	44 (47.3)	12 (66.7)	11 (44.0)	11 (39.3)	10 (45.5)	0.312
≥ 1:1280	11 (11.8)	1 (5.6)	2 (8.0)	6 (21.4)	2 (9.1)	0.405
Unknown	22 (25.7)	4 (22.2)	4 (16.0)	6 (21.4)	8 (36.4)	0.411
Anti-dsDNA titer						
Non detectable	15 (16.1)	3 (16.7)	6 (24.0)	4 (14.3)	2 (9.1)	0.563
1:80-1:160	25 (26.9)	5 (27.8)	4 (16.0)	10 (35.7)	6 (27.3)	0.453
1:320-1:640	16 (17.2)	1 (5.6)	6 (24.0)	5 (17.9)	4 (18.2)	0.456
≥ 1:1280	12 (12.9)	5 (27.8)	3 (12.0)	2 (7.1)	2 (9.1)	0.246
Unknown	25 (26.9)	4 (22.2)	6 (24.0)	7 (25.0)	8 (36.4)	0.715
Urinalysis data						
UPCR (mg/g)	3147.4 (2868.9)	1655.3 (1535.5)	2965.1 (3047.2)	3395.2 (2980.1)	4211.3 (3077.9)	0.126
RBC ≥ 5 HPF	53 (57.0)	11 (61.1)	18 (72.0)	8 (28.6)	16 (72.7)	0.003
WBC ≥ 5 HPF	46 (49.5)	12 (66.7)	9 (36.0)	10 (35.7)	15 (68.2)	0.009
Disease activity						
SLEDAI-2K	13.0 (7.9)	21.9 (12.4)	12.4 (4.1)	8.9 (4.8)	11.4 (4.1)	0.001
Follow-up, months	39.9 (27.1)	37.9 (29.2)	39.0 (26.7)	44.4 (28.6)	37.3 (25.6)	0.748
Induction therapy						
Glucocorticoid	79 (84.9)	17 (94.4)	24 (96.0)	22 (78.6)	16 (72.7)	0.066
Mycophenolate mofetil	64 (68.8)	14 (77.8)	18 (72.0)	21 (75.0)	11 (50.0)	0.105
Hydroxychloroquine	58 (62.4)	14 (77.8)	16 (64.0)	16 (57.1)	12 (54.5)	0.78
Cyclophosphamide	15 (16.1)	4 (22.2)	4 (16.0)	3 (10.7)	4 (18.2)	0.728
Belimumab	5 (5.4)	0 (0.0)	1 (4.0)	3 (10.7)	1 (4.5)	0.596
Voclosporin	3 (3.2)	1 (5.6)	1 (4.0)	1 (3.6)	0 (0.0)	0.881
Rituximab	2 (2.2)	0 (0.0)	0 (0.0)	1 (3.6)	1 (4.5)	0.836
Other agents						
ACEIs/ARBs	26 (28.0)	10 (55.6)	6 (24.0)	8 (28.6)	2 (9.1)	0.012
SGLT2i	1 (1.1)	0 (0.0)	1 (4.0)	0 (0.0)	0 (0.0)	0.699
Specialist						
Nephrology	83 (89.2)	15 (83.3)	25 (100.0)	23 (82.1)	20 (90.9)	0.107
Rheumatology	61 (65.6)	13 (72.2)	15 (60)	19 (67.9)	14 (65.6)	0.89
Outcomes						
Remission						
Complete	21 (22.6)	5 (27.8)	7 (28.0)	7 (25.0)	2 (9.1)	0.356
Partial	28 (30.1)	6 (55.5)	8 (32.0)	7 (25.0)	8 (36.4)	0.845
Orphors	22 (25.7)	3 (16.7)	5 (20.0)	6 (21.4)	8 (36.4)	0.488
All-cause mortality	5 (5.4)	0 (0.0)	1 (4.0)	3 (10.7)	1 (4.5)	0.596



Number at risk

III	9	9	8
IV	19	19	14
III+V	16	16	15
IV+V	16	16	12

Conclusions: In our study, patients diagnosed with class IV+V LN often presented with more severe disease characteristics, such as lower eGFR, lower remission rates and greater dialysis need. Therefore, aggressive treatment strategies are necessary, and dual or triple therapy should be considered for this higher-risk group. This is particularly crucial for younger, female, and non-Hispanic Black patients, who tend to have worse outcomes compared to their counterparts. Hydroxychloroquine was significantly underutilized in this cohort. Hence, our study underscores the importance of a collaborative treatment approach that integrates both nephrology and rheumatology.

PV202 / #141

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

MACROPHAGE ACTIVATION SYNDROME IN SYSTEMIC LUPUS ERYTHEMATOSUS: REPORT OF 8 CASES

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that is characterized by various clinical and biological manifestations. Among its rare but critical presentations, macrophage activation syndrome (MAS) is a severe complication involving the dysregulated activation of cytotoxic T lymphocytes and NK cells, leading to systemic inflammation and multiple organ damage. MAS is a secondary form of hemophagocytic lymphohistiocytosis (HLH). Diagnosis of MAS poses a real challenge, as its clinical manifestations closely resemble those of active SLE. We present a series of cases aimed at detailing the distinctive clinical features of MAS in SLE.

Methods: This was a retrospective and descriptive study involving eight cases collected from the internal medicine department over a period of 14 years, from January 2010 to May 2024. The diagnosis of systemic lupus erythematosus was established according to the SLICC or ACR/EULAR 2019 criteria, and patients presented with macrophage activation syndrome (MAS) according to the HLH 2004 criteria.

Results: Eight patients were included in the study. The average age of the patients was 26 years (range, 17–42 years). There were 7 women and 1 man, resulting in a sex ratio of 7/1. MAS was the initial manifestation of lupus in half of the patients (4 women), while it occurred after the diagnosis of lupus in the other 4 patients. A triggering factor was identified in all patients (infection in three patients, pregnancy in three patients, and a stressful event in the other two). Lupus was severe in all the patients. The systemic lupus erythematosus disease activity index (SLEDAI) was calculated for all 8 patients, with an average score of 61.38, a standard deviation of 19.29, a median of 60.5, and a range from 32 to 88. Hematological involvement was observed in 87.5% of the patients (7 cases), cutaneous involvement in 62.5% (5 cases), articular involvement in 50% (4 cases), severe renal involvement in 37.5% (3 cases), serositis in 25% (2 cases), and pancreatitis in 12.5% (1 case). Biologically, pancytopenia was found in 6 patients (75%), and bicytopenia was found in the other 2 patients. Lymphopenia and hyperferritinemia were constant in all patients, with an average lymphocyte count of 680 cells/mm^3 and average ferritin level of 4786 ng/mL, ranging from 800 to 11816 ng/mL. Hypofibrinogenemia was observed in 5 patients, with an average fibrinogen level of approximately 1.19 g/L, ranging from 0.3 g/L to 1.5 g/L. Hypertriglyceridemia was noted in 4 patients, with an average of approximately 4.865 g/L, ranging from 3.60 g/L to 6.42

g/L. The complement levels C3, C4, and CH50 were severely reduced in all patients. Antinuclear antibodies were more than 1/80 in all patients, and anti-DNA antibodies were positive in 75% of the patients. All patients received intravenous bolus corticosteroid therapy, antibiotic treatment in 3 patients, and immunosuppressants in 4 patients (2 patients received cyclophosphamide and 2 received mycophenolate mofetil). The outcome was favorable in 75% of the cases, with death recorded in 25%.

Conclusions: Macrophage activation syndrome is a severe and potentially fatal complication of systemic lupus erythematosus that requires heightened vigilance for early diagnosis and prompt management. Our study revealed that MAS is often triggered by infection, pregnancy, and stress. The clinical manifestations of MAS frequently overlap with those of active SLE, complicating diagnosis. This study highlights the necessity for early detection and appropriate therapeutic interventions to effectively manage MAS in SLE patients.

PV203 / #609

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

LATE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS : ABOUT 5 CASES.

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that usually affects young women in their third decade, but can occur at any age. SLE is said to have a late onset when the diagnosis is made at the age of 50 or over. Studies of this entity are few. The aim of our study was to investigate the clinico-biological, immunological, therapeutic and evolutionary features of late-onset SLE.

Methods: This is a monocentric, descriptive, retrospective study conducted in the internal medicine department of the university hospital center Ibn Rochd Casablanca including records of patients hospitalized for SLE (fulfilling SLICC 2012 and EULAR/ACR 2019 criteria) during the period between 2015 and 2024 and who were 50 years of age or older at the time of diagnosis.

Results: Our series included 5 lupus patients. They were 4 women and 1 man with a mean age at diagnosis of 58.6 years. The mean SLEDAI score was 17.8. The mean time to diagnosis was 10.4 months. Comorbidities were dominated by dyslipidemia (40%) and arterial hypertension (20%). Revealing manifestations of SLE were usually pure nephrotic syndrome, pericardial effusion and deep-vein thrombosis. Inflammatory polyarthralgia was the inaugural manifestation in 2 patients (40%), and Raynaud's phenomenon in 2 patients (40%). In our series, the most frequent pathologies were renal, hematological and serositis. As regards the biological work-up, all patients presented lymphopenia and proteinuria > 0.5 g/24h, a biological inflammatory syndrome and autoimmune hemolytic anemia (AIHA) were noted in 80% of cases, leukopenia in 60% and thrombocytopenia was observed in 40%. On the immunological front, antinuclear antibodies were positive in all patients. Anti-SSA and anti-SSB were positive in 40% and 20% of cases respectively. Anti-phospholipid and anti-nucleosome antibodies were positive in 40% of cases. Anti-DNAnative, anti-ribosome, anti-Sm and anti-histone antibodies were positive in 20% of cases, and complement consumption C3 and C4 was observed in a single patient. The association with another autoimmune disease (AID) was observed in 3 patients. One patient had an authentic Sjögren's syndrome, another an antiphospholipid syndrome (APS) and the 3rd a combination of the two. All our patients were treated with synthetic antimalarials and corticosteroids. Four of our patients were treated with immunosuppressants: cyclophosphamide was

prescribed for 2 patients and azathioprine (AZA) for 2 patients. All showed a favorable course of treatment.

Conclusions: Late-onset SLE is most often characterized by an insidious onset and unspecific inaugural signs. It is a diagnosis that should not be dismissed, even after the age of 50. In our context, severe symptoms are often observed, contrary to what is described in the literature. This is because our climate is very sunny, which partly explains the severity of the disease. The presence of other autoimmune diseases is frequent. Treatment differs little from that of younger patients, and must also take into account the patient's comorbidities. Early diagnosis and treatment guarantee a good outcome.

PV204 / #461

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

ANTI-C1Q ANTIBODIES AS INDICATORS OF DISEASE ACTIVITY, RENAL INVOLVEMENT, AND NON-SCARRING ALOPECIA IN PATIENTS WITH SLE

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Background/Purpose: Anti-C1q antibodies are found in various autoimmune diseases and are believed to be associated with lupus nephritis (LN) in patients with systemic lupus erythematosus (SLE). Animal models have shown that anti-C1q antibodies lead to renal inflammation and damage. However, in addition to the association with LN, whether anti-C1q antibodies were linked to other SLE-related complications remains unknown.

Methods: This retrospective study analyzed 883 SLE patients at a medical center in Taiwan from 2017 to 2020 who met the American College of Rheumatology (ACR) 1990 or SLICC 2012 classification criteria. C1q CIC levels were measured within one month before or after diagnosis. Correlations of C1q CIC with other clinical manifestations were explored.

Results: We found that C1q CIC-positive patients were younger, with an average age of 38.8. Clinically, SLE patients presenting with non-scarring alopecia, renal disorder, and leukopenia had a significantly higher prevalence of C1q CIC positivity ($p < 0.05$)(table1). Laboratory findings showed that C1q CIC-positive patients had elevated ESR, low complement levels, the presence of anti-dsDNA antibodies, and higher SLEDAI scores, suggesting that C1q antibodies are associated with active disease. Additionally, these patients had elevated UPCR and eGFR levels, indicating concurrent renal involvement.

Table 1. Demographic data of participants			
	C1q Antibody Negative	C1q Antibody Positive	*p* value
N	678	205	
Demography			
Sex			0.031*
Female	620 (91.4%)	177 (86.3%)	
Male	58 (8.6%)	28 (13.7%)	
Age	46.1 (37.5-55.7)	38.8 (30.2-50.6)	<0.001**
SLE Onset Age	32.0 (24.0-42.0)	27.0 (21.0-38.0)	0.002**
Smoking	36 (5.3%)	16 (7.8%)	0.184
SLICC Clinical Criteria			
Acute cutaneous lupus	299 (44.1%)	99 (48.3%)	0.290
Chronic cutaneous lupus	83 (12.2%)	15 (7.3%)	0.049*
Oral or nasal ulcers	75 (11.1%)	27 (13.2%)	0.408
Nonscarring alopecia	40 (5.9%)	24 (11.7%)	0.005**
Synovitis involving two or more joints	401 (59.1%)	113 (55.1%)	0.306
Serositis	80 (11.8%)	35 (17.1%)	0.049*
Renal disorder	298 (44.0%)	118 (57.6%)	<0.001**
Neurologic disorder	61 (9.0%)	10 (4.9%)	0.057
Hemolytic anemia	58 (8.6%)	19 (9.3%)	0.751
Leukopenia < 4,000/mm3, or Lymphopenia <1,000/mm3	257 (37.9%)	99 (48.3%)	0.008**
Thrombocytopenia< 100,000/mm3	128 (18.9%)	40 (19.5%)	0.847
Laboratory Examination			
WBC (/μL)	5920.0 (4570.0-7700.0)	5440.0 (4230.0-7855.0)	0.163
Hb (g/dL)	12.8 (11.6-13.8)	12.3 (11.1-13.4)	<0.001**
Platelet x10^3/μL	234.0 (188.8-284.0)	231.0 (186.0-287.3)	0.909
ESR (mm/hr)	15.0 (8.0-28.0)	19.0 (12.0-38.0)	<0.001**
Creatinine (umol/L)	0.7 (0.6-0.9)	0.7 (0.6-0.9)	0.445
eGFR (mL/min/1.73m2)	92.9 (74.0-108.1)	99.2 (78.8-117.4)	0.009**
UPCR (mg/g)	123.1 (66.7-298.2)	174.9 (94.7-638.7)	<0.001**
Urine cast			0.379
Hyalin cast 0-2	267 (44.8%)	80 (46.5%)	
Hyalin cast >2	57 (9.6%)	23 (13.4%)	
Granular Cast >1	94 (15.8%)	26 (15.1%)	
Urine cast unfound	178 (29.9%)	43 (25.0%)	
Immunology			
ANA	623 (91.9%)	193 (94.1%)	0.285
Low C3	449 (66.2%)	166 (81.0%)	<0.001**
Low C4	342 (50.4%)	143 (69.8%)	<0.001**
Anti-dsDNA Ab	237 (35.0%)	144 (70.2%)	<0.001**
SLEDAI score	2 (0-4)	4 (2-6)	<0.001**
Medication			
Prednisolone	537 (79.2%)	182 (88.8%)	0.002**
Hydroxychloroquine	622 (91.7%)	184 (89.8%)	0.378
Methotrexate	36 (5.3%)	10 (4.9%)	0.807
Azathioprine	211 (31.1%)	65 (31.7%)	0.874
Mycophenolate mofetil	25 (3.7%)	24 (11.7%)	<0.001**
Mycophenolic acid	94 (13.9%)	29 (14.1%)	0.919
Cyclosporin	48 (7.1%)	20 (9.8%)	0.208

Chi-Square test or Mann-Whitney U test, Median (IQR).

Conclusions: Our result suggests that C1q may be a biomarker for LN. The association of C1q with non-scarring alopecia warrants further investigation.

PV205 / #486

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CARDIAC LUPUS: A DISEASE NOT TO BE NEGLECTED .

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Background/Purpose: Introduction Systemic lupus erythematosus (SLE) is an autoimmune disease affecting several organs, including the heart. Cardiac involvement is variable, affecting all tunics. Echocardiography enables early diagnosis of cardiac manifestations of SLE.The aim of this study was to analyze the various cardiac abnormalities in patients with lupus.

Methods: Patients and methods This was a retrospective, descriptive study carried out in the internal medicine department of IBN ROCHD university hospital in Casablanca, covering the records of patients hospitalized between 2010 and 2023 for SLE (retained on ACR and SLICC criteria). We studied cases with cardiac manifestations.

Results: In a series of 360 cases of SLE, cardiac manifestations were found in 49 patients (13.61%), with an average age of 32 years and extremes between 18 and 63 years; 47 were women and 2 men, indicating a clear female predominance. Cardiac involvement revealed the disease in 34 cases.Lupus pericarditis was the most frequent cardiac manifestation (71.42%), followed by valve damage (10.2%) of mitral insufficiency (5 cases), Libmann-Sacks endocarditis (3 cases), PAH and myocarditis, There were 3 cases of tamponade.Clinically, the most frequent symptoms were chest pain in 20 cases (41%) and dyspnea in 13 cases (28.2%). Chest X-rays revealed cardiomegaly in 13 patients. ECG abnormalities were found in 20 patients, including rhythm and/or conduction disorders and microvoltage.Cardiac ultrasound confirmed the diagnosis of pericarditis and valvulopathy, and detected pulmonary hypertension (PH).Myocardial damage required MRI confirmation, showing focal sub-epicardial contrast and endomyocardial fibrosis.Treatment was based on corticosteroid therapy in 100% of cases, with cyclophosphamide indicated in 20 patients, followed by azathioprine in 13 and mycophenolate mofetil in the others, in addition to specific cardiac treatments in all patients. Progression was favourable in 18 patients (36.73), less so in cases of heart failure or severe rhythm disorders.

Conclusions: Conclusion Cardiac involvement in SLE is frequent and serious, and should be systematically investigated even in the absence of any clinical symptoms.Cardiac echocardiography remains an excellent non-invasive tool for detecting severe cardiac involvement in SLE.

PV206 / #35

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CHOROIDOPATHY OF SYSTEMIC LUPUS ERYTHEMATOSUS, ABOUT TWO CASES RECEIVED AT THE BRAZZAVILLE OPHTHALMOLOGICAL CENTER

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Background/Purpose: Lupus choroidopathy is a rare but potentially serious ocular complication of systemic lupus erythematosus (SLE), an autoimmune disease affecting multiple organs and systems. Although choroidopathy is less common than other ocular manifestations of SLE, it can cause significant visual loss if not diagnosed and treated promptly. The objective of this study is to describe two cases of lupus choroidopathy treated at the Ophthalmological Center of Brazzaville, in order to illustrate the clinical characteristics, treatment modalities and results obtained.

Methods: This study is based on the analysis of two clinical cases of patients diagnosed with choroidopathy associated with SLE, received at the Ophthalmological Center of Brazzaville. Clinical data were collected from medical records, including medical history, presenting symptoms, results of ophthalmological examinations (ophthalmoscopy, optical coherence tomography (OCT), fluorescein angiography), as well as treatments administered. The patients were followed over a specific period to assess the effectiveness of the treatment and the evolution of their condition.

Results: Both patients presented a decrease in visual acuity accompanied by scotomas, serous retinal detachments and subretinal exudates, confirmed by ophthalmological examinations. The patients were treated with systemic corticosteroid therapy combined with immunosuppressants, which led to a significant improvement in ocular condition and stabilization of visual function. The clinical course of both cases demonstrated a favorable response to treatment, with a reduction in retinal detachments and inflammatory signs

Conclusions: Lupus choroidopathy, although rare, should be considered in any patient with systemic lupus erythematosus presenting with visual symptoms. These two cases illustrate the importance of early diagnosis and adequate therapeutic management to improve visual outcomes and prevent serious complications. A multidisciplinary approach is crucial for the effective management of this pathology and to minimize the risk of irreversible visual loss in patients with SLE.

PV207 / #177

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CHARACTERISTICS OF PATIENTS WITH INTERMITTENT AND PERSISTENT TYPE 2 SLE

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Background/Purpose: Our prior qualitative work demonstrated there are at least two distinct subgroups of Type 2 SLE; one is related to active inflammation (Intermittent Type 2 SLE) and another can be present regardless of inflammation (Persistent Type 2 SLE). The objective of this study was to utilize longitudinal measures of Type 1 and Type 2 SLE activity to characterize these Type 2 SLE subgroups.

Methods: SLE patients meeting SLICC or ACR criteria were enrolled in a university lupus registry. At each clinic visit, participants completed the Polysymptomatic Distress Scale (PSD), and rheumatologists completed disease activity measures, including the SLEDAI and Physician Global Assessments (PGA) for both Type 1 and Type 2 SLE activity. Patients seen between May 2023 and April 2024 were invited to participate in a sub-study that included the FACIT fatigue scale; PROMIS measures for pain intensity, pain interference, self-efficacy, and psychological stress; and the Trauma History Screen. Only patients who participated in the sub-study and had ≥3 visits in the registry were included in the analysis. High Type 1 SLE activity was defined as clinical SLEDAI ≥4, SLEDAI ≥6, active lupus nephritis or PGA ≥1. High Type 2 SLE activity was defined as Type 2 PGA ≥1 or PSD ≥8. Patients who had high Type 1 SLE activity at <30% of visits and high Type 2 SLE activity at ≥50% of visits were classified as Persistent Type 2 SLE. Patients who had fluctuating Type 2 SLE activity were classified as Intermittent Type 2 SLE. Patients who never had high Type 2 SLE activity during follow-up (n=13) were excluded from the analysis. Differences in characteristics between the two groups were estimated by t-tests and Fisher's exact tests.

Results: The analysis included 183 patients (mean age 45 years, 92% female, 60% Black); 26% of patients had Persistent Type 2 SLE. Demographics were similar between the two groups (Table 1). Patients with Persistent Type 2 SLE were more likely to have experienced abusive trauma. While patients with Intermittent Type 2 SLE had higher Type 1 SLE activity over time, approximately half of patients in each group had a history of lupus nephritis, and there were no differences between groups in historical use of prednisone, DMARDs, or biologics. Patients in the Persistent Type 2 SLE group were more likely to have been prescribed a Type 2 SLE medication and to have been

prescribed more Type 2 SLE medications over time. By definition, patients with Persistent Type 2 SLE had higher PSD scores during follow-up, yet patients with Intermittent Type 2 SLE still had mild to moderate PSD scores, on average, during follow-up. There were similar self-efficacy scores for managing medications between groups, yet patients with Persistent Type 2 SLE had lower self-efficacy for managing symptoms; they also had worse scores for FACIT fatigue, PROMIS pain intensity, and pain interference.

Table 1. Cohort characteristics.

	Intermittent Type 2 SLE	Persistent Type 2 SLE	
	n=135	n=48	p-value
Demographics			
Age, years	44.0 (13.9)	46.8 (11.1)	0.2
Female	121 (90%)	47 (98%)	0.1
Black	80 (59%)	29 (60%)	1.0
Hispanic	12 (9%)	1 (2%)	0.2
College degree or more (n=180)	58 (44%)	18 (38%)	0.5
Individuals insured through Medicaid or Medicare or without insurance (n=179)	67 (51%)	26 (54%)	0.7
Annual Household Income <$50,000 (n=177)	78 (60%)	27 (57%)	0.9
Trauma History			
None	20 (15%)	2 (4%)	0.008
Non-Abusive Trauma	64 (47%)	16 (33%)	
Abusive Trauma	51 (38%)	30 (63%)	
Clinical History			
Duration of disease, years	15.0 (9.0)	15.8 (9.7)	0.6
2019 ACR/EULAR Criteria (n=135)	92 (96%)	39 (100%)	0.3
LN History (n=147)	51 (48%)	20 (49%)	1.0
Average Disease Activity During Follow-Up			
SLEDAI	3.1 (2.8)	1.0 (1.3)	<0.0001
Type 1 PGA	0.7 (0.5)	0.2 (0.2)	<0.0001
Type 2 PGA	0.7 (0.5)	1.1 (0.4)	<0.0001
Type 2 SLE Symptoms During Follow-Up			
Average During Follow-Up			
Polysymptomatic Distress Score (n=180)	8.5 (5.6)	12.9 (5.0)	<0.0001
Widespread Pain (n=180)	3.6 (3.5)	5.9 (3.4)	0.0002
Symptom Severity Score (n=180)	4.8 (2.8)	7.0 (2.5)	<0.0001
Moderate to Severe Symptoms During Follow-Up			
Depression (n=178)	69 (53%)	36 (77%)	0.005
Fatigue (n=177)	89 (68%)	42 (89%)	0.006
Brain Fog (n=178)	44 (34%)	31 (66%)	0.0001
Sleep Disturbance (n=178)	84 (64%)	40 (85%)	0.009
Medication History			
Prednisone	95 (70%)	29 (60%)	0.2
DMARD or biologic	117 (87%)	41 (85%)	0.8
Type 2 SLE medication	90 (67%)	44 (92%)	0.0005
Number of Type 2 SLE medications	2.5 (2.8)	3.9 (2.8)	0.004
Opioid or tramadol	35 (26%)	19 (40%)	0.1
Patient-Reported Measures			
PROMIS Pain Intensity, median (IQR)	54 (48-63)	59 (54-65)	0.01
PROMIS Pain Interference, median (IQR)	56 (52-64)	61 (56-67)	0.006
PROMIS Self-Efficacy: Manage Symptoms, median (IQR)	48 (43-55)	43 (40-50)	0.006
PROMIS Self-Efficacy: Manage Medications, median (IQR)	49 (41-58)	48 (41-58)	0.9
Psychological Stressful Experiences Score, median (IQR)	59 (52-64)	63 (57-69)	0.003
Resilience score	21.2 (5.2)	20.3 (5.3)	0.3
FACIT Fatigue score* (n=176)	33.4 (11.7)	25.8 (11.8)	0.0002
Constant fatigue	20 (15%)	18 (38%)	0.002

Numbers presented are mean (SD) or n (%), unless otherwise specified
*Higher FACIT Fatigue scores indicate less fatigue

Conclusions: One in four patients met our study definition for Persistent Type 2 SLE. Despite having taken on average four different medications to treat Type 2 SLE symptoms, patients with Persistent Type 2 SLE continued to have a high burden of pain, fatigue, depression, and brain fog, demonstrating a need for better treatment approaches. Several psychosocial stressors could predispose or perpetuate Persistent

Type 2, and future work will evaluate these triggers to better understand the etiology and target solutions for these symptoms.

PV208 / #631

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CHARACTERISTICS OF NEUROLOGICAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS AT A TERTIARY UNIVERSITY HOSPITAL

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Background/Purpose: Neurological manifestations in systemic lupus erythematosus (SLE) are diverse and often underdiagnosed. At our tertiary university hospital, we proactively assess neurological involvement in patients with SLE using a structured protocol. This study aims to characterize these manifestations in a cohort of SLE patients.

Methods: From a total of 229 SLE patients, 12 (5.24%) met criteria for neuro-lupus. Systematic assessment included brain MRI, electroencephalogram (EEG), and, in selected cases, lumbar puncture. Diagnoses were established collaboratively with the Neurology department.

Results: Among the 12 neuro-lupus patients:
• Peripheral neuropathy: 2 cases of axonal sensorimotor polyneuropathy were attributed to lupus.
• Acute psychosis: 1 case, fully attributed to SLE activity after exclusion of other causes.
• Lupus headache: 3 cases, classified based on current definitions.
• Cognitive impairment: 6 cases ranged from moderate to severe, all with pathological MRI findings (Fazekas-type lesions). Treatment:
• 2 patients received belimumab.
• 3 were treated with anifrolumab.
• 7 received rituximab.

Conclusions: Neurological manifestations in SLE are common (5.24% in our cohort) and likely underdiagnosed. A proactive clinical approach, combined with advanced imaging and collaboration with Neurology, facilitates timely identification and management of neuro-lupus.

PV209 / #633

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

SEVERE HEMATOLOGICAL MANIFESTATIONS IN SLE: TWO CASES OF THROMBOTIC THROMBOCYTOPENIC PURPURA

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Background/Purpose: Thrombotic thrombocytopenic purpura (TTP) is a rare but life-threatening hematological complication of systemic lupus erythematosus (SLE). In our cohort of 229 SLE patients, TTP was observed in 0.87% of cases. This report presents the clinical course and management of these patients.

Methods: We reviewed the medical records of two patients diagnosed with TTP secondary to SLE. Both cases were characterized by microangiopathic hemolytic anemia, thrombocytopenia, and multiorgan involvement. Treatment protocols, outcomes, and therapeutic responses were analyzed.

Results: • Case 1: Treated with intravenous methylprednisolone boluses (IVMP), intravenous immunoglobulin (IVIG), rituximab, and 12 cycles of eculizumab. The patient achieved remission with resolution of hematological and organ involvement.
• Case 2: Treated with IVMP boluses, IVIG, and rituximab, leading to normalization of blood parameters and recovery of organ function.

Conclusions: TTP in SLE was identified in 0.87% of our cohort. Prompt recognition and aggressive treatment with IVMP, IVIG, and rituximab proved effective, with eculizumab playing a crucial role in refractory cases. Multidisciplinary collaboration and individualized treatment strategies are essential to improve outcomes in this rare but severe complication.

PV210 / #497

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS (SLICC) FRAILTY INDEX (SLICC-FI) PREDICTS HOSPITALIZATIONS IN A PREVALENT LATIN AMERICAN LUPUS COHORT.

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Background/Purpose: Frailty, measured with the SLICC-FI, has been reported as a predictor of damage in several cohorts. The aim of this study is to evaluate the SLICC-FI as a predictor of hospitalization in systemic lupus erythematosus (SLE) patients.

Methods: Patients from a single-center prevalent cohort were included. The SLICC-FI was measured at baseline. Hospitalizations were reported during the first two years after the baseline visit as their number as well as their duration. Univariable and multivariable negative binomial regressions were performed to determine the association between the baseline SLICC-FI (per 0.05 increase) and hospitalizations during follow-up (number and length), adjusted for sex, age at diagnosis, socioeconomic status, educational level, disease duration, SLE Disease Activity Index 2000 (SLEDAI-2K), SLICC damage index (SDI), prednisone daily dose, antimalarial and immunosuppressive drug use at baseline.

Results: Of the 302 patients included 280 (92.7%) were female, with mean (SD) age at diagnosis of 34.6 (7.2) years. At baseline, the mean (SD) disease duration was 7.2 (6.4) years, and the mean (SD) SLICC-FI was 0.21 (0.05). The mean number of hospitalizations per patient was 0.5 (1.6) and the mean number of days hospitalized during the two-year period per patient was 5.3 (16.8) days; 58 (17.9%) of the patients were hospitalized at least once during the follow-up. The SLICC-FI predicted a higher probability of hospitalizations as well as with a higher number of hospitalizations; these data are depicted in table 1.

Table 1: Impact of the SLICC-FI on the number and length of hospitalizations. Univariable and multivariable analyses

	Univariable		Multivariable	
	IRR (95% CI)	*p* value	IRR (95% CI)	*p* value
Number of hospitalizations				
SLICC-FI per 0.05 increase	1.468 (1.174-1.836)	<0.001	1.552 (1.215-1.982)	<0.001
Length of hospitalizations, days				
SLICC-FI per 0.05 increase	1.348 (1.156-1.573)	<0.001	1.576 (1.319-1.884)	<0.001

Conclusions: The SLICC-FI predicts hospitalizations in SLE patients, independently of other well-known risk factors of hospitalizations. Further studies are needed to determine strategies to improve frailty in SLE patients.

PV211 / #363

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

A CASE-CONTROL STUDY ON AUTOIMMUNE POLYENDOCRINE SYNDROMES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that can impact multiple organs, including joints, kidneys, skin, heart, blood cells, lungs, and nervous system. SLE patients face a higher risk of various comorbidities and treatment-related complications, with an increased mortality rate compared to the general population. Studies on observational cohorts have identified cardiovascular diseases, diabetes mellitus type 2 (T2DM), osteoporosis, certain types of cancer, and autoimmune endocrine disease, such as Hashimoto's thyroiditis (HT), Graves' disease (GD), type 1 diabetes mellitus (T1DM) and hyperparathyroidism, as common cause of morbidity in SLE patients. However, to our knowledge, no data currently exist on the connection between SLE and Autoimmune Polyendocrine Syndromes (APS), which are rare diseases characterized by multiple autoimmune conditions affecting at least one endocrine organ. APS 1 is due to gene AIRE mutations; APS 2 is characterized by Addison's disease (AD) associated with HT or GD and/or T1DM; HT or GD with any other autoimmune diseases (excluding AD and hypoparathyroidism) fall under APS 3; APS 4 includes remaining combinations of autoimmune forms having an impact on endocrine organs. This study aimed to investigate the prevalence of Autoimmune Polyendocrine Syndromes (APS) in patients with Systemic Lupus Erythematosus (SLE) and to assess whether APS predicts higher disease activity or worse outcomes.

Methods: Clinical charts of 417 SLE patients referring to our Centre between 2021 and 2023 were analysed. APS cases were identified using ORPHA code definitions; 185 APS-free SLE patients, randomly enrolled, served as controls. Demographic, clinical and serological data were collected.

Results: Forty-seven (11%) SLE patients have another autoimmune disease affecting the glands that allows the diagnosis of APS: 39 were diagnosed with HT, 6 with GD, and 3 with T1DM. Forty-five patients were affected by APS type 3, and 2 by APS type 4; no patients were diagnosed with APS type 1 or 2. **Table 1** show the sequence in which

autoimmune diseases manifest. SLE was the first manifestation of APS in 22 patients (47%). HT was the first autoimmune manifestation for 21 (45%) patients, GD was the first for 2 (4%) patients and 2 women started with rheumatoid arthritis (2%) and autoimmune urticaria (2%), respectively. SLE was the second manifestation in 23 (49%) patients and the fourth for 2 (4%) patients. The comparison between APS+ and APS- patients, as shown in **Table 2**, revealed no significant differences in clinical or serological features, except for pulmonary hypertension (p=0.044) and renal microangiopathy (p=0.044). At the last evaluation, approximately 80% of both groups' patients were in clinical remission and approximately half of the patients were still on steroid therapy. APS+ patients had a slightly higher median damage index (SLICC-SDI), although this was not associated with increased disease activity.

Table 1: Sequence of autoimmune diseases presentation in patients with SLE and APS

First disease n(%)	Median age in years at first disease onset	Second disease n(%)	Median age in years at second disease onset	Third disease	Median age in years at third disease onset	Fourth disease	Age in years at fourth disease onset
HT 21 (45)	32	SLE 20 (43)	35	-	-	-	-
		Vitiligo 1 (2)	33	Atrophic gastritis	34	SLE	43
SLE 22 (47)	28	HT 15 (32)	35	-	-	-	-
		GD 4 (9)	51,5	-	-	-	-
		DM1 2 (4)	30	-	-	-	-
		Multiple sclerosis 1 (2)	26	HT	28	-	-
GD 2 (4)	42	SLE 2 (4)	50,5	-	-	-	-
AR 1 (2)	21	HT 1 (2)	27	DM1	27	SLE	28
AU 1 (2)	8	SLE 1 (2)	19	HT	24	-	-

LES= Sistemic Lupus Erythematosus; HT= Hashimoto thyroiditis; GD= Graves Disease; RA= Rheumatoid Arthritis; DM=Diabetes Mellitus; AU=Autoimmune Urticaria

Table 2: Comparison of data in SLE patients with and without APS

	SLE with APS	SLE without APS	P value
Total SLE patients n(%)	47	185	
Age in years (median [IQR])	54 (41-65)	52 (42-62)	0,930
Age in years at LES onset (median [IQR])	28 (23-43)	27 (20-34)	0,047
Female n (%)	45 (96)	179 (97)	0,734
Disease duration in years (median [IQR])	21 (11-24)	23 (15-32)	0,019
Tabacco exposure n(%)	15 (32)	53 (29)	0,660
BMI (median [IQR])	24 (22-28)	22 (21-26)	0,251
Constitutional symptoms n(%)	40 (85)	148 (81)	0,546
Fever n(%)	15 (32)	75 (41)	0,267
Asthenia n(%)	39 (83)	137 (75)	0,221
Cutaneus manifestations n(%)	37 (79)	158 (85)	0,264
Butterfly rash n(%)	24 (51)	108 (58)	0,366
SCLE n(%)	1 (2)	15 (8)	0,148
Discoid rash n(%)	16 (34)	76 (41)	0,378
Tumid Lupus n(%)	1 (2)	1 (0,5)	0,293
Alopecia n(%)	12 (25)	71 (38)	0,101
Photosensitivity n(%)	20 (43)	96 (52)	0,253
Oral ulcers n(%)	0	4 (2)	0,313
Cutaneus vasculitis n(%)	4 (9)	37 (20)	0,070
Sicca symptoms n(%)	15 (32)	49 (26)	0,457
Rayneud phenomenon n(%)	20 (43)	76 (41)	0,855
Muscoloskeletal involvement n(%)	40 (85)	171 (92)	0,118
Arthralgias n(%)	37 (79)	159 (86)	0,222
Arthritis n(%)	20 (49)	128 (69)	0,009
Jaccoud n(%)	3 (6)	14 (8)	0,781
Osteonecrosis n(%)	0	2 (1)	0,474
Myositis n(%)	0	5 (3)	0,255
Neurological involvement n(%)	15 (32)	52 (28)	0,607
Headache n(%)	3 (6)	32 (17)	0,062
Seizures n(%)	4 (8)	11 (6)	0,536
Psycosis n(%)	1 (2)	2 (1)	0,571
Depression n (%)	7 (15)	15 (8)	0,156
Confucion n(%)	1 (2)	1 (0,5)	0,293
Cerebral ischemia/stroke n(%)	1 (2)	5 (3)	0,624
Transient ischemic stroke n(%)	2 (4)	14 (8)	0,424
Cognitive impairment n(%)	1 (2)	10 (5)	0,345
Pheripheral mononeuropathy n(%)	0	4 (2)	0,309
Pheripheral polineuropathy n(%)	1 (2)	7 (4)	0,578
Cranial nerve neuropathy n(5%)	1 (2)	2 (1)	0,571

	SLE with APS	SLE without APS	P value
Total SLE patients n(%)	47	185	
Serositis n(%)	11 (23)	33 (18)	0,385
Pleuritis n(%)	5 (11)	19 (10)	0,941
Pericarditis n(%)	10 (21)	25 (13)	0,184
Hematological involvement n(%)	26 (55)	119 (64)	0,255
Hemolytic anemia n(%)	10 (21)	30 (16)	0,412
Leukopenia n(%)	18 (38)	96 (52)	0,096
Thrombocytopenia n(%)	12 (25)	28 (15)	0,092
Lymphocytopenia n(%)	11 (23)	63 (34)	0,162
Neutropenia n(%)	6 (13)	20 (11)	0,704
Renal involvement n(%)	12 (26)	71 (38)	0,120
Renal failure n(%)	2 (4)	4 (2)	0,419
Glomerulonephritis Class I n(%)	0	1 (0,5)	0,613
Glomerulonephritis Class II n(%)	2 (4)	8 (4)	0,983
Glomerulonephritis Class III n(%)	2 (4)	14 (8)	0,424
Glomerulonephritis Class IV n(%)	4 (8)	27 (15)	0,274
Glomerulonephritis Class V n(%)	3 (6)	14 (8)	0,781
Glomerulonephritis Class VI n(%)	1 (2)	0	0,047
Tubulointerstitial nephritis n(%)	0	1 (0,5)	0,613
Microangiopathy n(%)	2 (4)	1 (0,5)	0,044
Cardiac involvement n(%) (including pericarditis)	15 (32)	44 (24)	0,253
Mycarditis n(%)	1 (2)	2 (1)	0,571
Endocarditis n(%)	5 (11)	16 (9)	0,671
Myocardial infartion n(%)	2 (4)	7 (4)	0,881
Cardiac arrhythmias n(%)	0	6 (3)	0,211
Pulmonary involvement n(%)	6 (13)	27 (15)	0,749
Pulmonary hypertension n(%)	2 (4)	1 (0,5)	0,044
Lupus pneumonia n(%)	0	2 (1)	0,474
Interstitial Lung Disease n(%)	1 (2)	3 (2)	0,812
Shrinking lung n(%)	0	2 (1)	0,474
Gastroenterological involvement n(%)	0	6 (3)	0,211
Pancreatitis n(%)	0	1 (0,5)	0,613
Esophageal dyskinesia n(%)	0	3 (2)	0,380
Mesenteric vasculitis n(%)	0	2 (1)	0,454
Ocular involvement n(%)	12 (25)	31 (17)	0,167
Thrombosis n(%)	5 (11)	15 (8)	0,596

	SLE with APS	SLE without APS	P value
Total SLE patients n(%)	47	185	
ANA n(%)	47 (100)	185 (100)	-
Anti-dsDNA n(%)	42 (89)	177 (96)	0,093
Anti-ENA n(%)	29 (62)	113 (61)	0,938
Anti-Ro/SSA n(%)	18 (38)	80 (43)	0,540
Anti-La/SSB n(%)	4 (9)	15 (8)	0,928
Anti-Sm n(%)	8 (17)	38 (20)	0,589
Anti-ribosomal P protein n(%)	3 (6)	4 (2)	0,131
Anti-U1RNP n(%)	5 (11)	46 (25)	0,035
Anti-Ki n(%)	3 (6)	3 (2)	0,066
Anti-nucleosome n(%)	3 (6)	3 (2)	0,066
Anti-histone n(%)	2 (4)	3 (2)	0,267
Anti-Scl70 n(%)	1 (2)	2 (1)	0,571
Anti-CENP n(%)	0	2 (1)	0,474
Anti-Jo1 n(%)	0	2 (1)	0,474
AMA n(%)	1 (2)	2 (1)	0,571
aPL positivity n(%)	20 (43)	92 (50)	0,362
aCL IgG n(%)	11 (23)	49 (27)	0,653
aCL IgM n(%)	5 (11)	31 (17)	0,295
aB2GPI IgG n(%)	8 (17)	56 (30)	0,067
aB2GPI IgM n(%)	4 (9)	31 (17)	0,155
LA test n(%)	9 (19)	45 (25)	0,432
aPL single positivity n(%)	11 (23)	34 (18)	0,436
aPL double positivity n(%)	6 (13)	34 (18)	0,363
aPL triple positivity n(%)	3 (6)	25 (13)	0,180
RF n(%)	3 (6)	22 (16)	0,459
Anti-CCP n(%)	3 (6)	7 (9)	0,193
Coombs test n(%)	13 (28)	72 (51)	0,242
C3 consumption n(%)	31 (66)	159 (86)	0,001
C4 consumption n(%)	35 (75)	159 (86)	0,058

	SLE with APS	SLE without APS	P value
Total SLE patients n(%)	47	185	
SLEDAI (median (min-max))*	0 (0-8)	2 (0-10)	0,002
SLEDAS (median (min-max))*	0,37 (0-22,7)	1,12 (0-20,1)	0,038
SLICC-SDI (median (min-max))*	1 (0-5)	0 (0-6)	0,669
DORIS remission n(%)*	38 (81)	152 (83)	0,665
Corticosteroids n(%)*	23 (49)	85 (46)	0,714
Prednisone mg/wk (median (min-max))*	0 (0-75)	0 (0-70)	0,538
Hydroxychloroquine n(%)*	38 (81)	146 (80)	0,870
DMARDs n(%)*	21 (45)	102 (56)	0,175

*at the last evaluation
SLE= Sistemic Lupus Erythematosus, BMI=Body Mass Index;
ANA= antinuclear antibodies, dsDNA= anti-double stranded DNA, anti-ENA: anti-extractable nuclear antigen, aPL: antiphospholipid antibodies, aCL: anti-cardiolipin, aB2GPI=anti-B2glicoprotein I, LA: Lupus Anticoagulant, RF= rheumatoid factor aCCP= anti-cyclic citrullinated peptide, SLEDAI=Systemic Lupus Erythematosus Disease Activity Index; SLEDAS=Systemic Lupus Erythematosus Disease Activity State; SLICC=Systemic Lupus International Collaborating Clinics; DMARDs=Disease Modifying Antirheumatic Drugs

Conclusions: The prevalence of APS among SLE patients is significantly higher than in the general population (11% vs. 0,005%), confirming the well-known association between autoimmune thyroiditis and SLE. However, APS+ patients do not appear to have a more aggressive disease or develop more complications. The only clinical conditions statistically associated with APS (renal microangiopathy and pulmonary hypertension) are so rare that no definite conclusions can be drawn. Limitations of the study include a small sample size and single-time-point data, highlighting the need for larger multicenter studies to clarify the link between SLE and APS.

PV212 / #397

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

OUTCOMES OF ADULTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOUS: A SCOPING REVIEW

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Background/Purpose: Systemic Lupus Erythematous (SLE) is a chronic, multisystem autoimmune disorder with a highly variable presentation and course. Approximately 20% of SLE cases are diagnosed within childhood. As increasing numbers of childhood-onset SLE (cSLE) patients are now seen surviving into adulthood, understanding their adulthood outcomes has become increasingly important. This scoping review aims to summarize the outcomes of adults with cSLE.

Methods: A peer-reviewed search strategy of OVID MEDLINE and Embase for English articles between 1 January 1990 to 30 June 2023 was developed with an academic librarian. The main search included all systemic autoimmune rheumatic diseases (SARD) and systemic vasculitides. This abstract focuses on only SLE studies. Our search was tested against 26 known SARD articles to verify search coverage. Childhood-onset of disease was as defined by authors (< 14-18 years old). Studies were excluded if: i) > 50% of the sample were not adults at final assessment and / or adult outcomes were not separately reported, iii) not a full-length article. Results from the search were uploaded into the Covidence website for subsequent workflow. Studies were graded for risk-of-bias using the Quality in Prognosis Studies (QuiPS) tool. Two reviewers independently graded the studies before meeting to reach consensus. Any disputes were resolved by a third reviewer.

Results: The total search identified 4379 papers, of which 24 SLE studies were included for this study. No study was published before 2000, 2 (8%) between 2001-2010, 16 (67%) between 2011-2020, and 6 (25%) between 2021-2024. Most studies were conducted in the United States (25%), Brazil (21%), and the Europe (13%). The vast majority of publications were cross-sectional in design (67%), followed by prospective cohorts (21%). Mean disease duration ranged from 5.5-23.9 years (13 studies) and median duration was 8.1-20 years (6 studies). Mean follow-up duration of longitudinal studies ranged from 6.3-14.2 years (4 studies) and median was 4 years (1 study). The most common reported outcomes were damage (50%), disease activity (38%) and mortality (21%). Other outcomes studied were depression, cognitive dysfunction, cardiovascular disease, malignancy, and clinical features.Mean SLICC damage index was 1.3-3.2 (4 studies) and median damage was 1-6 (5 studies), respectively. Mean and median SLE disease activity index [MM2] was 6.0-16 (4 studies) and median was 0-6 (5

studies), respectively. Mortality ranged from 2.5%-18.3% (5 studies). QuiPS identified a moderate to high risk-of-bias in the following domains: 92% of study participation, 100% of study attrition (N = 8, non-cross-sectional studies), 25% of prognostic factors, 71% of outcomes, 96% of confounding, 75% of statistical analysis.

Conclusions: There is increasing interest in the outcomes of cSLE adults as seen in the increasing number of publications. Current literature primarily focuses on disease damage, disease activity, and mortality. However, the studies showed significant biases, which perhaps reflects the difficulty of studying such a population. A collaborative and integrated approach between pediatric and adult rheumatologists to follow cSLE patients into adulthood, augmented by additional information sources such as population health data, will be essential to better understand the outcomes of cSLE patients with a wide spectrum of disease severity. Understanding current outcomes will inform better care for cSLE adults.

PV213 / #662

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CHARACTERIZING SLE PATIENTS INTO TYPE 1 AND TYPE 2 DISEASE STATES: INSIGHTS FROM A SINGLE LUPUS COHORT

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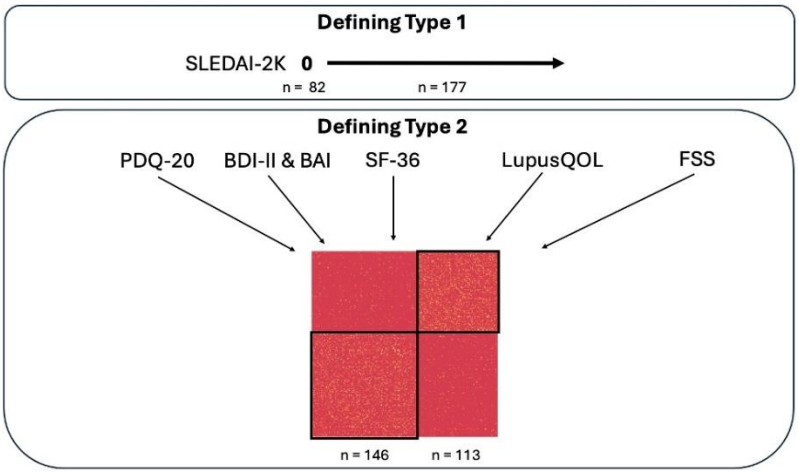
Background/Purpose: It has been proposed that SLE may be divided into Type 1 and Type 2 states. Type 1 manifestations are well captured in disease activity scores (e.g. SLEDAI-2K). Type 2 manifestations include fatigue, pain, depression, brain fog. These do not always correlate with conventional lupus disease activity, but can be pervasive and dominate in patient-reported outcomes (PROs). Patients may be classified into four disease states: Minimal (low type 1 activity, low type 2 activity), High Type 1 (high type 1 and low type 2), High Type 2 (low type 1, high type 2) and Mixed (high type 1 and high type 2). Our primary aim was to define the prevalence of patients who can be classified into the four states. Our secondary aim was to identify variables that predict each disease state.

Methods: This was a cross-sectional study of a single cohort of SLE patients who participated in a trial studying cognitive impairment and recruited prospectively since 2016. Type 1 activity was defined as a clinical SLEDAI-2K of >0 (excluding C3, C4 dsDNA levels). As there is no clear definition of Type 2 activity, we aimed to define this based on different PRO measures: Beck Depression and Anxiety Inventories (BDI-II and BAI), Lupus Quality of Life (Lupus QoL), Fatigue Severity Score (FSS), Perceived Deficits Questionnaire (PDQ-20) for subjective cognitive impairment, Short Form Health Survey (SF-36). We conducted a Similarity Network Fusion (SNF) analysis that used spectral clustering to generate participant subtypes and hypothesized that distinct groups would emerge (**Figure 1**). For our secondary aim, we included variables such as patient characteristics, SLICC/ACR damage index (SDI), antibodies, medications.



Results: 259 patients were included in the final analysis. Four distinct patient phenotypes emerged: Minimal (32 patients; 12.4%), High Type 1 (81 patients; 31.3%), High Type 2 (50 patients; 19.3%), and Mixed (96 patients; 37.1%). Patients with High Type 2 state had poorer median PRO scores in all measured outcomes (all p-values significant to <0.0001): PDQ20 (39.5 vs 20), BDI (20.2 vs 6.2), BAI (21 vs 6), SF-36 Mental Component Summary (36.5 vs 54.8) and SF-36 Physical Component Summary (32.2 vs 51.2), FSS (5.56 vs 3.11) and all Lupus QoL domains. Statistically significant variables ($p<0.05$ after Bonferroni correction) differentiating the four states included low C3/C4, elevated dsDNA, chromatin antibody presence, glucocorticoid dose and treatment with glucocorticoids within 3 months. The presence of these variables was associated with a High Type 1 and Mixed state **(Table 1)**.

Variables associated with Type 1 and Mixed State	P-value
Low C3	0.0005
Low C4	0.0005
Elevated double-stranded DNA	0.0005
Positive chromatin antibody	0.0005
Glucocorticoid dose	0.000002
Treatment with glucocorticoid within 3 months	0.0005

Conclusions: We identified that patients may be categorized into disease states based on Type 1 and Type 2 characteristics – Minimal 13%, High Type 1 31%, High Type 2 19% and Mixed 37%. High Type 2 patients uniformly scored poorly in all PRO domains. Multiple laboratory markers (low C3/4, elevated dsDNA, presence of chromatin antibody) as well as glucocorticoid use were found to predict High Type 1 or Mixed states.

PV214 / #533

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

A EULAR/ACR (2019) SLE CLASSIFICATION CRITERIA SCORE ≥20 IS A MARKER OF SEVERE DISEASE IN A PREVALENT SLE COHORT FROM THE PORTUGUESE REUMA.PT REGISTRY

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Background/Purpose: Recently, a EULAR/ACR 2019 systemic lupus erythematosus (SLE) classification criteria (EULAR/ACR 2019) score≥20 was identified in a SLE inception cohort with less than 2 years from diagnosis as a marker for more severe disease, including higher disease activity, more frequent flares, higher use of immunosuppressants, lower probability of achieving remission, and more damage accrual. However, this analysis has not been performed in SLE patients with longer disease duration.[1] The aim of our study was to assess a EULAR/ACR 2019 score ≥20 as a marker for severe disease in a prevalent SLE cohort.

Methods: We performed a cross-sectional multicenter study of patients fulfilling the EULAR/ACR 2019 classification criteria for SLE in the Portuguese registry of rheumatic diseases (Reuma.pt). Disease activity (SLE-DAS) and the EULAR/ACR score were assessed at the last visit, between June 2023 and March 2024. Groups of patients with EULAR/ACR 2019 score ≥20 or <20 were compared for demographic, clinical and treatment features, with parametric and non-parametric tests, as appropriate. Separate models were tested using different definitions of severe SLE (dependent variable), as present/absent:(1) cumulative SLE major organ involvement;(2) moderate/severe

disease activity, defined as SLE-DAS>7.64;(3) ongoing immunosuppressants;(4) ongoing systemic prednisolone>7.5 mg/day;(5) organ damage, defined as SLICC/ACR Damage Index (SDI)≥1. Predictors for each of these definitions were assessed in a two-step approach with logistic regression (LR) univariate analysis, followed by multivariate LR models including variables with p<0.10 in the first step, while excluding variables with multicollinearity. Multivariate analysis was used to identify independent predictors and estimate the respective adjusted odds ratios (OR) with 95% confidence intervals.

Results: There were 2459 patients registered in Reuma.pt, from 37 participating centers. A total of 709 patients, from 18 centers, who had data on and fulfilled the EULAR/ACR 2019 classification criteria and had a SLE-DAS scoring were included, 65.6% having an EULAR/ACR 2019 score≥20. These patients were younger at diagnosis (p<0.001), had longer disease duration (p<0.001), higher SLE-DAS score (p=0.001), received less frequently antimalarials (p=0.004), and were more frequently treated with synthetic and/or biologic immunosuppressants (p<0.001) and glucocorticoids (p<0.001). On univariate LR analysis, a EULAR/ACR 2019 score≥20 was associated with all definitions of severe disease (**table 1**). On multivariate LR analysis, a EULAR/ACR 2019 score≥20 was an independent predictor of cumulative major organ involvement (OR 7.30, 95%CI 4.86-10.95, p<0.001), moderate/severe disease activity (OR 7.36, 95%CI 2.18-24.82, p=0.001), ongoing immunosuppressants (OR 2.73, 95%CI 1.82-4.09, p<0.001), and ongoing systemic prednisolone>7.5 mg/day (OR 2.71, 95%CI 1.29-5.69, p=0.009), adjusted for significant covariates. In the multivariate LR, a EULAR/ACR score≥20 was not associated with organ damage, defined as SDI≥1.

Conclusions: A EULAR/ACR 2019 score ≥20 is associated with severe disease in a prevalent SLE cohort. Although this is not surprising, given the similarity and close relationship between items included in all instruments, this score may, in association with measures of disease activity, contribute to management in clinical practice, stratification of cases in observational studies and selection of patients for clinical trials. **References** Whittall Garcia LP et al. New EULAR/ACR 2019 SLE Classification Criteria: defining ominosity in SLE. Ann Rheum Dis. 2021;80(6):767-

Table 1 – Univariate and multivariate logistic regression analysis for severe SLE

MODEL 1 (dependent variable: cumulative major organ involvement†)				
	Unadjusted OR (90% CI)	p	Adjusted OR (95% CI)	p
Female	0.46 (0.31-0.70)	0.002	0.47 (0.26-0.84)	0.010
Age at diagnosis	0.97 (0.96-0.98)	<0.001	-	-
Early onset*	1.91 (1.46-2.51)	<0.001	1.61 (1.10-2.36)	0.015
Disease duration	1.05 (1.03-1.06)	<0.001	1.03 (1.01-1.05)	0.002
Score EULAR/ACR ≥20	8.80 (6.42-12.07)	<0.001	7.30 (4.86-10.95)	<0.001
MODEL 2 (dependent variable: SLE-DAS>7.64)				
	Unadjusted OR (90% CI)	p	Adjusted OR (95% CI)	p
Female	0.51 (0.26-1.01)	0.103	-	-
Age at diagnosis	0.97 (0.95-1.00)	0.040	0.97 (0.94-1.00)	0.034
Early onset*	1.24 (0.72-2.13)	0.509	-	-
Disease duration	0.97 (0.94-1.00)	0.065	0.94 (0.91-0.98)	0.003
Score EULAR/ACR ≥20	3.89 (1.75-8.64)	0.005	7.36 (2.18-24.82)	0.001
MODEL 3 (dependent variable: ongoing immunosuppressants)				
	Unadjusted OR (90% CI)	p	Adjusted OR (95% CI)	p
Female	0.71 (0.48-1.05)	0.152	-	-
Age at diagnosis	0.98 (0.97-0.99)	<0.001	-	-
Early onset*	1.51 (1.16-1.97)	0.010	1.51 (1.04-2.20)	0.030
Disease duration	0.98 (0.96-0.99)	0.001	0.95 (0.93-0.97)	<0.001
Score EULAR/ACR ≥20	2.78 (2.12-3.65)	<0.001	2.73 (1.82-4.09)	<0.001
Hydroxychloroquine	0.49 (0.33-0.71)	0.002	0.53 (0.30-0.93)	0.027
Oral corticosteroids	4.98 (3.86-6.41)	<0.001	4.47 (3.12-6.40)	<0.001
MODEL 4 (dependent variable: ongoing systemic prednisolone >7.5 mg/day)				
	Unadjusted OR (90% CI)	p	Adjusted OR (95% CI)	p
Female	0.68 (0.38-1.21)	0.268	-	-
Age at diagnosis	0.99 (0.98-1.01)	0.412	-	-
Early onset*	0.89 (0.57-1.37)	0.652	-	-
Disease duration	1.00 (0.98-1.02)	0.782	-	-
Score EULAR/ACR ≥20	3.72 (2.03-6.81)	<0.001	2.71 (1.29-5.69)	0.009
Hydroxychloroquine	0.43 (0.26-0.70)	0.004	0.46 (0.23-0.91)	0.026
Synthetic immunosuppressants and/or biologics	2.47 (1.62-3.77)	<0.001	1.40 (0.78-2.50)	0.255
SLE-DAS score	1.18 (1.12-1.23)	<0.001	1.17 (1.10-1.24)	<0.001
MODEL 5 (dependent variable: SDI score ≥1)				
	Unadjusted OR (90% CI)	p	Adjusted OR (95% CI)	p
Female	0.47 (0.31-0.69)	0.001	0.40 (0.24-0.67)	<0.001
Age at diagnosis	1.01 (1.00-1.02)	0.019	-	-
Early onset*	0.68 (0.52-0.90)	0.021	0.52 (0.36-0.75)	<0.001
Disease duration	1.05 (1.04-1.06)	<0.001	1.05 (1.03-1.07)	<0.001
Score EULAR/ACR ≥20	1.79 (1.35-2.37)	<0.001	1.43 (0.98-2.08)	0.063

*Diagnosis at age <16 years
†Presence of one or more of the following items: nephritis, neuropsychiatric lupus, hemolytic anemia, deforming or erosive arthritis and pulmonary items of SDI.
CI, Confidence Interval; EULAR/ACR, European League Against Rheumatism/American College of Rheumatology Systemic Lupus Erythematosus Classification Criteria; OR, Odds Ratio; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLE-DAS, Systemic Lupus Erythematosus Disease Activity Score

774. * Caroli
na Mazeda and Beatriz Mendes contributed equally and share first authorship.

PV215 / #526

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

TREAT-TO-TARGET ATTAINMENT IN PATIENTS WITH SLE FROM THE REUMA.PT SLE REGISTRY: A MULTICENTER PORTUGUESE CROSS-SECTIONAL STUDY OF 795 PATIENTS

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Background/Purpose: Treat-to-target (T2T) aiming for remission, or at least low disease activity (LDA), while tapering prednisone to ≤5mg/day is established as a pillar for management of systemic lupus erythematosus (SLE) in the 2023 updated EULAR recommendations for clinical practice. The aim of our study was to investigate the attainment of the T2T goal in the SLE population from the Rheumatic Diseases Portuguese Registry (Reuma.pt) and identify unmet treatment needs.

Methods: We performed a cross-sectional multicenter study of patients fulfilling the EULAR/ACR 2019 classification criteria for SLE in the Reuma.pt. The assessment was performed at the last visit occurring between June 2023 and March 2024. Disease activity and attainment of T2T were assessed with the SLE Disease Activity Score (SLE-DAS).[1] Patients with no SLE-DAS scoring were excluded. Patients were classified as in remission (clinical items of SLE-DAS =0 and prednisone ≤5 mg/day), low disease activity (LDA) (SLE-DAS ≤2.48 and prednisone ≤5 mg/day) and, for those not attaining T2T, in categories of disease activity (mild: 2.08<SLE-DAS≤7.64; moderate: 7.64<SLE-DAS≤9.90; severe: SLE-DAS>9.90). Descriptive analysis was performed, and a comparison between the remission vs. non-remission and LDA vs. non-LDA groups was

performed using Student's t-test, Fisher's exact test, Chi-square or Mann-Whitney U tests, as appropriate. IBM SPSS Statistics software version 27 was used. p≤0.05 was considered statistically significant.

Results: There were 2459 patients with SLE from 37 centers registered in Reuma.pt. Of these, 1664 (67.7%) were excluded due to: missing data on fulfilment (n=1257, 51.1%) or no fulfilment (n=83, 3.4%) of EULAR/ACR classification criteria; missing data for SLE-DAS (n=324, 13.2%). A total of 795 patients from 18 participating centers were included [89.6% female; mean age 49.9 (SD 14.2) years] (**table 1**). Main cumulative SLE clinical features included: mucocutaneous (72.5%), hematological (66.7%), arthritis (63.6%), nephritis (38.9%), serositis (19.4%) and neuropsychiatric lupus (6.8%). Remission was attained by 71.3% and an additional 3.0% were in LDA, meaning that the EULAR treatment target was achieved by 74.3%. The remaining patients presented active disease (mild 20%, moderate 2.6%, severe 3%). Hydroxychloroquine (HCQ) was prescribed to 88.3% of all patients. Patients not in LDA were more frequently treated with synthetic (69.1% vs 39.6%, p<0.001) and biologic (19.1% vs 8.5%, p<0.001) immunosuppressants. Of the patients with active SLE, 40.2% were receiving >7.5 mg/day of prednisolone-equivalent dose and 72.7% were treated with synthetic and/or biologic immunosuppressants.

Conclusions: This subgroup of patients with SLE registered in Reuma.pt present a high rate of attainment of the T2T, and most are treated with HCQ, in line with the EULAR recommendations. The high number of patients excluded preclude the generalization of these conclusions. This provides benchmarking indicators demonstrating high quality of care. Furthermore, unmet needs for new and improved therapies are demonstrated, with over a quarter of patients presenting active disease despite more intensive standard-of-care. Longitudinal studies are needed to assess if T2T goals are sustained over time. Optimized treatment regimens are needed to attain recommended T2T goals in many SLE patients. Improvement of registry in Reuma.pt is indispensable for a representative national appraisal. **References** Jesus D et al. Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS) enables accurate and user-friendly definitions of clinical remission and categories of disease activity. Ann Rheum Dis. 2021;80(12):1568-1574 * Carolina Mazeda and Beatriz Mendes contributed equally and share first authorship. **Table 1.** Characteristics of the patients included (n=795).

	Total (n=795)	Remission (n=567)	Non-remission (n=228)	p value	LDA (n=591)	Non-LDA (n=204)	p value
Demographic characteristics							
Female, n (%)	712/795 (89.6)	508/567 (89.6)	204/228 (89.5)	0.960	531/591 (89.8)	181/204 (88.7)	0.651
European, n (%)	645/720 (89.6)	476/519 (91.7)	169/201 (84.1)	**0.003**	496/540 (91.9)	149/180 (82.8)	**<0.001**
Age at symptom onset (years), mean±SD (n)	31.1±13.1 (713)	31.6±13.1 (509)	29.8±12.9 (204)	0.098	31.6±13.2 (532)	29.8±12.8 (181)	0.101
Age at diagnosis (years), mean±SD (n)	33.3±13.7 (721)	33.9±13.6 (511)	31.9±13.8 (210)	0.061	33.9±13.6 (534)	31.7±13.8 (187)	**0.047**
Age at study visit (years), mean±SD (n)	49.9±14.2 (795)	50.7±14.2 (567)	47.7±14.1 (228)	**0.006**	50.7±14.2 (591)	47.3±14.2 (204)	**0.003**
Disease duration (years), mean±SD (n)	16.7±10.0 (721)	17.1±10.1 (511)	15.7±9.5 (210)	0.145	17.1±10.0 (534)	15.5±9.8 (187)	0.095
Cumulative SLE clinical features							
Mucocutaneous, n (%)	569/785 (72.5)	382/561 (68.1)	187/224 (83.5)	**<0.001**	397/584 (68.0)	172/201 (85.6)	**<0.001**
Arthritis, n (%)	497/782 (63.6)	343/559 (61.4)	154/223 (69.1)	**0.043**	353/583 (60.5)	144/199 (72.4)	**0.003**
Serositis, n (%)	151/778 (19.4)	104/556 (18.7)	47/222 (21.1)	0.432	108/580 (18.6)	43/198 (21.7)	0.341
Renal, n (%)	299/768 (38.9)	203/552 (36.8)	96/216 (44.4)	0.050 (ns)	208/574 (36.2)	91/194 (46.9)	**0.008**
Neuropsychiatric, n (%)	52/760 (6.8)	34/549 (6.2)	18/211 (8.5)	0.253	39/573 (6.8)	13/187 (7.0)	0.945
Hematological, n (%)	518/777 (66.7)	358/556 (64.4)	160/221 (72.4)	**0.033**	378/579 (65.3)	140/198 (70.7)	0.162
Cumulative SLE immunological features							
ANA, n (%)	795/795 (100)	567/567 (100.0)	228/228 (100.0)	-	204/204 (100)	591/591 (100)	-
Anti-dsDNA, n (%)	677/782 (86.6)	475/559 (85.0)	202/223 (90.6)	**0.038**	497/582 (85.4)	180/200 (90.0)	0.099
Anti-Sm, n (%)	44/419 (10.5)	35/326 (10.7)	9/93 (9.7)	0.769	35/339 (10.3)	9/80 (11.3)	0.808
aPL, n (%)	305/685 (44.5)	218/503 (43.3)	87/182 (47.8)	0.299	233/525 (44.4)	72/160 (45.0)	0.890
Low C3/C4, n (%)	617/771 (80.0)	430/552 (77.9)	187/219 (85.4)	**0.019**	450/575 (78.3)	167/196 (85.2)	**0.036**
Disease activity scores							
SLE-DAS, median (range) (n)	1.12 (0.37-29.51) (795)	0.37 (0.37-2.08) (567)	2.99 (0.37-29.51) (228)	-	0.37 (0.37-2.47) (591)	3.50 (0.37-29.51) (204)	-
SLEDAI-2K, median (range) (n)	2 (0-20) (782)	0 (0-8) (559)	3 (0-20) (223)	**<0.001**	0 (0-8) (583)	4 (0-20) (199)	**<0.001**
PGA, median (range) (n)	0.1 (0.0-2.5) (670)	0.1 (0.0-1.0) (490)	0.5 (0.0-2.5) (180)	**<0.001**	0.1 (0.0-1.5) (508)	0.6 (0.0-2.5) (162)	**<0.001**
SLE-DAS disease activity category							
Remission, n (%)	567/795 (71.3)	567/567 (100.0)	0/228 (0.0)	-	567/591 (95.9)	0 (0)	-
Low disease activity, n (%)	591/795 (74.3)	567/567 (100.0)	24/228 (10.5)	-	591/591 (100.0)	0 (0)	-
Mild, n (%)	159/795 (20.0)	0/567 (0.0)	159/228 (69.7)	-	0 (0.0)	159/204 (77.9)	-
Moderate, n (%)	21/795 (2.6)	0/567 (0.0)	21/228 (9.2)	-	0 (0.0)	21/204 (10.3)	-
Severe, n (%)	24/795 (3.0)	0/567 (0.0)	24/228 (10.5)	-	0 (0.0)	24/204 (11.8)	-
Damage							
SDI score ≥1, n (%)	286/772 (37.0)	201/554 (36.3)	85/218 (39.0)	0.483	210/576 (36.5)	76/196 (38.8)	0.562

Ongoing SLE treatment							
Hydroxychloroquine, n (%)	693/785 (88.3)	510/567 (89.9)	183/218 (83.9)	**0.019**	528/591 (89.3)	165/194 (85.1)	0.107
Synthetic immunosuppressants, n (%)	368/785 (46.9)	219/567 (38.6)	149/218 (68.3)	**<0.001**	234/591 (39.6)	134/194 (69.1)	**<0.001**
Mycophenolate mofetil or Mycophenolic acid, n (%)	136/785 (17.3)	82/567 (14.5)	54/218 (24.8)	**<0.001**	85/591 (14.4)	51/194 (26.3)	**<0.001**
Azathioprine, n (%)	129/785 (16.4)	73/567 (12.9)	56/218 (25.7)	**<0.001**	84/591 (14.2)	45/194 (23.2)	**0.003**
Methotrexate, n (%)	96/785 (12.2)	59/567 (10.4)	37/218 (17.0)	**0.012**	61/591 (10.3)	35/194 (18.0)	**0.004**
Cyclosporine, n (%)	11/785 (1.4)	7/567 (1.2)	4/218 (1.8)	0.522	7/591 (1.2)	4/194 (2.1)	0.479
Tacrolimus, n (%)	8/785 (1.0)	5/567 (0.9)	3/218 (1.4)	0.692	5/591 (0.8)	3/194 (1.5)	0.416
Leflunomide, n (%)	6/785 (0.8)	4/567 (0.7)	2/218 (0.9)	0.672	4/591 (0.7)	2/194 (1.0)	0.641
Intravenous immunoglobulin, n (%)	3/785 (0.4)	1/567 (0.2)	2/218 (0.9)	0.188	1/591 (0.2)	2/194 (1.0)	0.153
Cyclophosphamide, n (%)	2/785 (0.3)	0/567 (0.0)	2/218 (0.9)	0.077	0/591 (0.0)	2/194 (1.0)	0.061
Dapsone, n (%)	1/785 (0.1)	0/567 (0.0)	1/218 (0.5)	0.278	0/591 (0.0)	1/194 (0.5)	0.247
Biologics, n (%)	87/785 (11.1)	49/567 (8.6)	38/218 (17.4)	**<0.001**	50/591 (8.5)	37/194 (19.1)	**<0.001**
Belimumab, n (%)	52/785 (6.6)	33/567 (5.8)	19/218 (8.7)	0.144	33/591 (5.6)	19/194 (9.8)	**0.041**
Rituximab*, n (%)	33/785 (4.2)	16/567 (2.8)	17/218 (7.8)	**0.002**	17/591 (2.9)	16/194 (8.2)	**0.001**
Anifrolumab, n (%)	3/785 (0.4)	0/567 (0.0)	3/218 (1.4)	**0.021**	0/591 (0.0)	3/194 (1.5)	**0.015**
Synthetic immunosuppressants and/or biologics, n (%)	391/785 (49.8)	235/567 (41.4)	156/218 (71.6)	**<0.001**	250/591 (42.3)	141/194 (72.7)	**<0.001**
Oral corticosteroids, n (%)	390/785 (49.7)	217/567 (38.3)	173/218 (79.4)	**<0.001**	229/591 (38.7)	161/194 (83.0)	**<0.001**
Dose of PDN (mg/day), mean±SD (n)	3.5 ±6.5 (785)	1.6±2.1 (567)	8.6±10.3 (218)	**<0.001**	1.6±2.1 (591)	9.4±10.6 (194)	**<0.001**
Dose >0 and ≤5 mg/day of PDN, n (%)	280/785 (35.7)	217/567 (38.3)	63/218 (28.9)	**0.014**	229/591 (38.7)	51/194 (26.3)	**0.002**
Dose >5 and ≤7.5 mg/day of PDN, n (%)	32/785 (4.1)	0/567 (0.0)	32/218 (14.7)	-	0/591 (0.0)	32/194 (16.5)	-
Dose >7.5 mg/day of PDN, n (%)	78/785 (9.9)	0/567 (0.0)	78/218 (35.8)	-	0/591 (0.0)	78/194 (40.2)	-

*Ongoing or in the last 6 months.
ANA, antinuclear antibodies; Anti-dsDNA, anti-double stranded DNA antibodies; aPL, antiphospholipid antibodies; Anti-Sm, anti-Smith antibodies; LDA, low disease activity; Low C3/C4, low serum levels of complement fractions C3 and/or C4; PDN, prednisolone-equivalent; PGA, physician global assessment; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SLE-DAS, Systemic Lupus Erythematosus Disease Activity Score.

PV216 / #355

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

SLE CLASSIFICATION CRITERIA ITEM RELATIONSHIPS: IMPLICATIONS ON SLE AS A DISEASE ENTITY

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Background/Purpose: To investigate for clusters and associations between the European Alliance of Associations for Rheumatology (EULAR)/American College for Rheumatology (ACR) classification criteria items.

Methods: Multiple Correspondence Analysis (MCA) was performed on the 10 classification criteria domains, using R (version 4.3.2) and FactoMineR (version 2.11) package in an international cohort of 1,197 SLE patients. Consensus clustering was performed using the ConsensusClusterPlus package (Version 1.66.0). Associations between individual criteria items were analyzed in the full 23x23 table (Graph Pad prism), and, by Bonferroni's correction, statistical significance was defined as $p<9.45e-5$.

Results: SLE patients fulfilled a minimum of zero (n=1) and a maximum of 15 of the 23 items (median 6) within 0 to 9 of the 10 domains (median 4). More than 2/3 of the patients (presently and/or historically) had criteria items within the domain SLE-specific antibodies (79.8%), the mucocutaneous (72.0%) and musculoskeletal (71.9%) domains, and complements (71.6%). In MCA, constitutional, musculoskeletal, and serosal domains clustered together, separating from the renal domain, complements, and SLE-specific antibodies (Figure 1A). However, the distribution of individual patients based on the first two dimensions (Figure 1B) was not reflective of a relevant separation of the cohort within those two dimensions. Consensus clustering, set at 10 clusters according to the cumulative distribution function (CDF, Figure 2A and 2B), revealed clusters with various combinations of domains (Figure 2C, proportion of patients with items in the respective domain indicated), but without a clear, mutually exclusive pattern. Among the 529 pairwise comparisons of items, 27 pairs showed a positive association, with r-values ranging from 0.11 to 0.58, and 4 pairs a negative association (r-values from -0.13 to -0.16). All r-values of 0.3 or higher were within an organ domain.

An r-value of ≥2.0 was found for anti-dsDNA, proteinuria, and proliferative (class III or IV) nephritis, each with low complements, in addition to associations between domains. **Figure 1.** MCA.

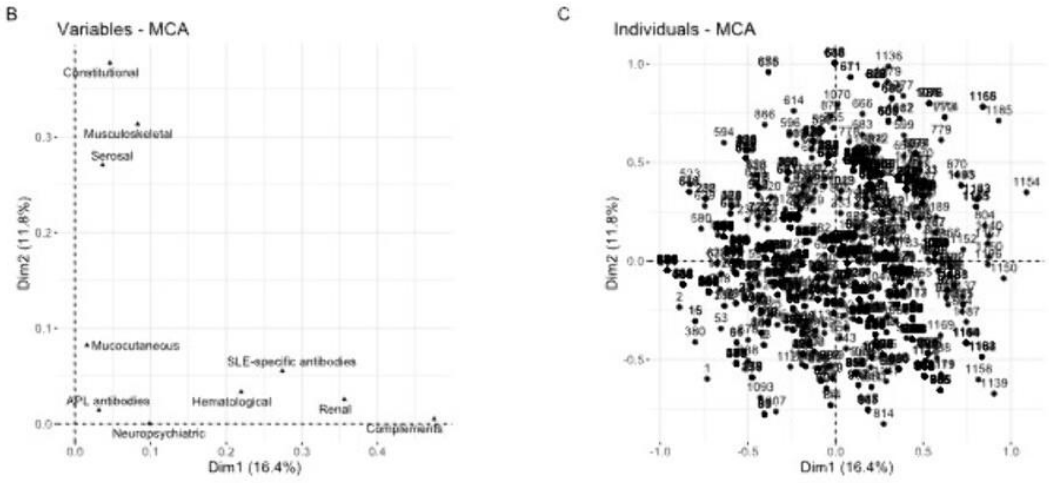
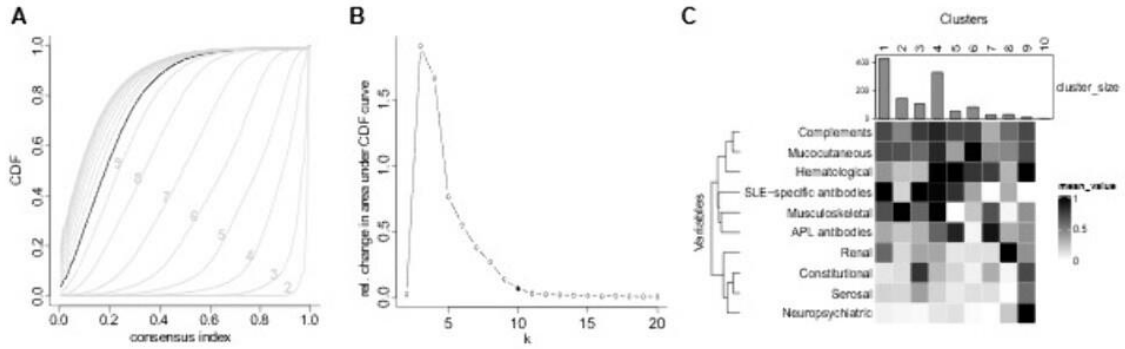


Figure 2. Consensus Clustering.



Conclusions: We found distributions more compatible with chance associations of domains and items than with true SLE subsets. The associations between items within domains support the decision to use domains in the EULAR/ACR classification criteria structure.

PV217 / #472

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

EXPEDITING LUPUS CLASSIFICATION OF AT RISK INDIVIDUALS USING NOVEL TECHNOLOGY: OUTCOMES OF A PILOT STUDY

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Background/Purpose: Individuals at risk of developing systemic lupus erythematosus (SLE) often go through a difficult diagnostic journey and may receive conflicting diagnoses from multiple medical providers over time. This study seeks to utilize a novel technology-based program employing virtual and digital care models to determine if the time taken for accurate SLE classification of at-risk individuals could be shortened from the current five to seven years.

Methods: Study participants were digitally recruited through a publicly available web portal designed for visitors to evaluate their risk of developing rheumatic connective tissue diseases with the Connective Tissue Disease Screening Questionnaire (CSQ). Individuals identified as “possible” (SLE-CSQ=3) or “probable” (SLE-CSQ≥4) risk of SLE were recruited to consent and participate in the study. Medical records (MRs) were obtained and reviewed for a stated SLE diagnosis and/or ICD-10 code M32.9 or related codes. Participants without an apparent diagnosis were eligible to move forward in the study in a sequential digital/virtual diagnostic protocol. They first completed a telehealth evaluation by a primary care physician (PCP) and mobile phlebotomy sample procurement for a predetermined panel of standard and lupus-associated laboratory tests. Laboratory test results, MRs, and PCP evaluation findings were made available to a community rheumatologist (CR) who completed a rheumatology-focused telehealth session. Finally, a tertiary care rheumatologist (TCR) specializing in SLE reviewed all study information and completed a telehealth session. The CR and TCR completed a classification form for each participant that included ACR 1997 or EULAR/ACR 2019 SLE classification criteria.

Results: The study target was 100 consented participants. In the first 60 days of the study, 108 participants that qualified by the CSQ and signed the informed consent were enrolled. The study population consisted of 95% females with mean age (SD) of 36 (6) years with 85% white, 7% black and 8% other races/ethnicities. MRs were requested for 102 that provided physician contacts; 81 were received. MRs review identified 67 with no previous SLE diagnosis and 14 with SLE diagnosis. Of the 67 who qualified, 39 completed the entire process and were evaluated by their PCP, CR, and TCR. Seven of 39 (18%) met SLE classification (ACR 1997 score range 4-6; EULAR/ACR 2019 score =13), 18 (46%) were classified as incomplete SLE, and 14 (36%) had no current indication of SLE. For those that met SLE classification, the time from date of consent to classification was mean (SD) 371 (43) days, with a range of 326 to 463 days.

Conclusions: A major goal of this virtual/digital study program was to shorten time to accurately diagnose SLE classification from the typical five to seven years. For the 18% who met classification, the mean time to accurate diagnosis was one year and six days. For the 46% with incomplete SLE and the 36% with no current indication of SLE, the program may have the potential to shorten time to accurate classification as these participants are prospectively followed. The digital and virtual care technologies applied in this study program combined with currently available laboratory tests demonstrate the potential to effectively classify SLE in a remote care model. Acknowledgements: This study was sponsored by Progentec and funding was provided by GSK (GSK 219884). GSK was provided with the opportunity to review a preliminary version of this abstract for factual accuracy, but the authors are solely responsible for final content and interpretation.

PV218 / #452

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

DRUG-INDUCED LUPUS: CLINICAL AND SEROLOGICAL FEATURES IN A TERTIARY HOSPITAL

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Background/Purpose: Several drugs have been implicated in the development of *de novo* systemic lupus erythematosus (SLE), unmasking of quiescent SLE or causing an exacerbation of previously diagnosed SLE. Our aim is to describe the causative drugs, clinical and serological features of patients diagnosed of Drug-Induced lupus (DIL) in our Rheumatology Department

Methods: A total of 445 patients diagnosed with SLE treated in our Rheumatology Department from 2012 to 2023 were retrospectively screened for the fulfilment of DIL criteria through the search of medical electronic records. Demographic, clinical and laboratory data were summarised using descriptive statistics.

Results: We identified 18 patients diagnosed with DIL, representing a prevalence of 4% among all SLE patients in our Department. There was a female preponderance and a young age at disease onset. Patients' clinical and serological characteristics are shown in Table 1. Only three drugs (infliximab, adalimumab and sulfasalazine) were identified as causative agents of DIL, anti-TNF being the most common. Most patients were treated for a condition different from a rheumatic disease, mainly inflammatory bowel disease (IBD). Median time to symptom onset after drug initiation ranged from 3 to 194 weeks (median 50.4). Peripheral arthritis and skin rash were the most frequent symptoms, with 4 patients (22%) presenting both at onset. Serologically, only 2 patients were ANA negative, but tested positive for anti-dsDNA. After drug withdrawal, ANA titre showed a slow decreasing trend over time, as well as anti-dsDNA antibodies. However, only 2 patients lost ANA-positivity through follow-up. Remarkably, more than half of the patients tested positive for antiphospholipid antibodies.

Conclusions: DIL showed a prevalence of 4% in our Rheumatology Department. Anti-TNF agents were the most common drugs causing DIL. ANA tend to decrease over time, but only become undetectable in a few patients. Antiphospholipid antibodies are common in our DIL patients. Age at onset is earlier than previously reported, probably because causative drugs are being used in younger populations.

PV219 / #613

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CLINICAL ASSOCIATIONS AND OUTCOMES OF PERICARDITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Pericarditis is an important feature in the classification criteria and disease activity assessments in Systemic Lupus Erythematosus (SLE). We aimed to study the prevalence, outcomes, and associations of pericarditis.

Methods: This is an observational cohort study of patients with pericarditis identified from a single-center SLE prospective database from July 1970 to Mar 2024. The diagnosis of pericarditis was based on SLEDAI-2K. The prevalence of pericarditis was determined in both inception (enrolled within one year of diagnosis) and prevalent cohorts. The remaining analysis focused on the inception cohort. Demographic and clinical variables were retrieved. The outcomes of pericarditis were defined as acute (resolution < 3 months), chronic (lasting ≥ 3 months), and relapsing (recurrence after complete resolution). Variables associated with pericarditis as compared to the rest of the cohort were analysed using Cox proportional hazards modelling. Factors associated with the outcome of pericarditis (acute vs. chronic, relapse vs. no relapse) were examined within the pericarditis subgroup.

Results: Pericarditis was identified in 428 of 2122 patients (20.16%), 205 of 900 (22.8%) in the inception, and 223 of 1222 (18.2%) in the prevalent cohorts. The median age at SLE diagnosis was 30.31 years (IQR 13.72-41.06) (**Table 1**). Pericarditis typically developed early in the disease course, with a median disease duration of 0.51 years (IQR 0.11-2.11) at the first event. In 170 patients, the severity of chest pain was 6.5 of 10 (IQR 4.25-8). Associated myocarditis was observed in 5.3%, endocarditis in 1.9%, and cardiac tamponade in 1.4%. SLEDAI-2K at the time of pericarditis was 6 (2-14), with commonly affected organ systems being hematologic (81%) and skin (76.1%). The majority had low complements and/or elevated anti-dsDNA (79.5%). Treatment included oral glucocorticoids (79%), and antimalarials (54.6%), with the most common immunosuppressant being azathioprine (20.9%). In comparison with patients without pericarditis, pericarditis was associated with younger age [0.98 (0.97-0.99)], higher average mean SLEDAI 2K [1.05 (1.02-1.09)], more constitutional symptoms [1.6 (1.19-2.19)], and less skin involvement [0.41 (0.27-0.62)]. The pericarditis outcomes were favourable for most, with 79.5% achieving complete resolution within 3 months. Chronic pericarditis was observed in 15.6% and lasted for 4.59 (3.3-16.78 months).

Relapses occurred in 22.9% of patients, with a median of two relapses (IQR 2-3). No associations with age at diagnosis, anti-dsDNA, low complements, or organ involvement were found for those with chronic pericarditis and relapses.

Conclusions: Conclusion Pericarditis was observed in one in five patients and was typically seen early in the disease course. The majority resolved within 3 months, with chronic pericarditis in 15.6%, and relapsing course in 22.9%. No associations were observed with chronic pericarditis and relapse

Table 1: Demographics, clinical features, and serology of the inception cohort with pericarditis

Variables	**Inception cohort, 205 of 900 (22.8%)**		
Age at diagnosis of SLE in years	30.31 [23.72- 41.06]		
Sex, Male (%)	32 (15.6)		
Race (%)			
Black	36 (17.7)		
White	126 (62.1)		
Chinese	20 (9.9)		
Other	21 (10.3)		
Antibodies and complements ever (%)			
Anti- Smith	94 (45.9)	Anti-Ribosomal P	19 (9.3)
Anti-RNP	106 (51.7)	Anti- Cardiolipin	66 (32.2)
Anti-Ro	111 (54.1)	Anti-dsDNA	70 (58)
Anti-La	74 (36.1)	Low C3 and/or C4	183 (89.3)
Variables at the time of pericarditis			
Age at the first episode of pericarditis	32.81 [25.20, 43.24] years		
Duration of SLE from diagnosis to the first episode of pericarditis	0.51 [0.11, 2.11] years		
Development of pericarditis within one year of diagnosis (%)	139 (67.8)		
Development of pericarditis within three years of diagnosis (%)	164 (80.0)		
Clinical Features of pericarditis			
The severity of chest pain on a scale from 0-10*	6.00 [4.50, 7.00]		
Associated myocarditis	11 (5.3)		
Associated endocarditis	4 (1.9)		
SLEDAI-2K	6.00 [2.00, 14.00]		
Other organ involvement at the time of pericarditis by SLEDAI-2K organ-systems			
Cutaneous	156 (76.1)	Pleurisy	60 (29.3)
Nervous	59 (28.8)	Hematologic	166 (81.0)
Vasculitis	33 (16.1)	Constitutional	54 (26.3)
Musculoskeletal	118 (57.6)	Serology	163 (79.5)
Renal	85 (41.5)		
Treatment received for pericarditis-1st episode(%)			
Glucocorticoids	162 (79)	Immunosuppressants	79 (38.5%)
Dose of prednisone in mg	20 [12.5-35]	Azathioprine	43 (20.9)
Antimalarials	112 (54.6)	Mycophenolate Mofetil	24 (11.7)
NSAIDs	47 (22.9)	Methotrexate	6 (2.9)
		Cyclophosphamide	10 (4.8)

*Available in 170 patients, pain scale of 0-10 with 0 being no pain
C- complements, dsDNA- double-stranded Deoxy Ribonucleic Acid, mg-milligram, NSAIDs- Non-Steroidal Anti-Inflammatory Drugs SLE- Systemic Lupus Erythematosus, SLEDAI 2K- Systemic Lupus Erythematosus Disease Activity Index 2000

PV220 / #517

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

THE STUDY OF CARDIOVASCULAR RISK ATTAINMENT AMONGST PATIENTS WITH LUPUS AND RHEUMATOID ARTHRITIS

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Background/Purpose: It has been well studied that patients with rheumatologic disease have an increased risk for cardiovascular (CV) events and those who are underserved are at especially high risk. Rheumatoid arthritis (RA and lupus (SLE) are the most common rheumatologic conditions. Therefore, goal of this project is to identify the prevalence of cardiovascular risk factors in patients with SLE or RA within the Yale rheumatology and to evaluate the success of current efforts to minimize CV risk.

Methods: In this one center, cross-sectional study, cardiovascular risk factor data, which include hyperlipidemia (HLD), hypertension (HTN), smoking, obesity, and diabetes (DM), were extracted from Yale health system from 2010-2023 with related ICD codes to investigate the prevalence and target attainment of traditional risk factors in patients with SLE and RA. A survey of knowledge gap of managing CV risk factors in rheumatological diseases was performed in Yale primary care residents who are primary providers serving the underserved patient population including those with rheumatological diseases.

Results: Cardiovascular disease (CVD) in this study includes coronary artery disease, cerebral vascular disease and peripheral vascular disease. Of total 295 patients with SLE, 138 (46.8%) had CVD and 157 (53.2%) had no CVD. Of those SLE with CVD vs. without, we found HLD (69.9% vs. 47.8%), HTN (76.8% vs.56.1%), smoking (52.9% vs. 41.1%), obesity (64.2% vs. 24.2%) and DM (20% vs. 14.2%). Of total 1680 patients with RA, 607 (36.1%) had CVD and 1073 (63.9%) had no CVD. Of those RA with CVD vs. without, we found HLD (88.8% vs. 56.6%), HTN (82.3% vs.54.9%), smoking (17.1% vs. 11.2%), obesity (51.9% vs. 45.2%) and DM (48.6% vs. 25.1%). 55 patients with SLE and 32 patients with RA were assessed the attainment of traditional risk factors for CVD. We found there were 68.1% with LDL <100, 78.7% with TG <150, 72.7% HTN <130/80, 90.1% non /former smoker, 30.9% of patients with BMI less than 30, 100% with HbA1c <7 in SLE patients, and 59.4% with LDL <100, 78.1% TG, 59.4% HTN <130/80, 75.0% non /former smoker, 21.9% with BMI less than 30, 61.3% with HbA1c <7 in RA patients. Of the total 31 medical residents completed the survey for the knowledge evaluation in CV risk management. Approximately 25.80% acknowledged all rheumatological diseases associated with increased risk for CVD, 58.06% identified appropriate CV risk factors,

25.8% can identify all appropriate orders for patients at risk, and 58.84% expressed lack of experience in working directly with patients with rheumatological conditions.

Conclusions: This study showed a strong prevalence for traditional risk factors amongst rheumatic patients with inadequate control. We also found an education gap in medical training regarding CV screening and management in patients with rheumatological diseases, namely SLE and RA in this study. For future studies, further investigation into improving knowledge in medical residency training as well as patient awareness should be investigated.

PV221 / #530

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

IS THERE A ROLE FOR ULTRA-HIGH FREQUENCY ULTRASOUND IN THE ASSESSMENT OF SKIN INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS? PRELIMINARY INSIGHTS FROM A MONOCENTRIC COHORT.

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Background/Purpose: The assessment of skin involvement in Systemic Lupus Erythematosus (SLE) can represent a challenge for clinicians, not only in the differential diagnosis with other dermatological conditions but also in discerning SLE cutaneous disease activity from damage. This results in a need to optimise the management of SLE patients with mucocutaneous involvement, as the development of skin damage may be early during disease course. Ultra-high frequency ultrasound (UHFUS), with sub-millimeter resolution, is a promising tool for evaluating superficial structures, finding increasing application in the field of dermatology in recent years. The aim of the study was to explore a possible role of UHFUS assessment in the evaluation of skin involvement in a monocentric cohort of SLE patients.

Methods: Consecutive adult SLE patients (2019 EULAR/ACR criteria) regularly followed at our Lupus Clinic were prospectively enrolled during a scheduled outpatient visit in presence of skin lesions. Demographical, clinical, serological and treatment data were collected at enrolment. Disease activity and organ damage were evaluated with the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and SLICC/ACR Damage Index (SDI), respectively. Clinical assessment of skin lesions was done by an experienced rheumatologist using the Cutaneous LE Disease Area and Severity Index (CLASI); at the same time, UHFUS evaluation of skin lesions was performed with a 70 MHz probe by an experienced dermatologist. The Skindex-16 questionnaire was used to assess the impact of skin involvement on patients' quality of life.

Results: We included 94 assessments in 59 SLE patients with skin lesions. Cutaneous disease subtypes were distributed as follows: 18/59 acute (30.5%), 8/59 subacute (13.6%), 27/59 chronic (45.8%); a minority of patients had non-specific skin lesions (10.2%). The characteristics of the cohort are detailed in Table 1. At the clinical evaluation, concomitant presence of active lesions and skin damage was observed in 52/94 cases (55.3%), presence of active skin lesions without damage in 40/94 cases

(42.6%), while only skin damage in 2/94 cases (2.1%). The most frequent UHFUS alteration was the presence of power Doppler (68/94, 72.3%), followed by dermal oedema (43/94, 45.7%), dermal inhomogeneity (41/94, 43.6%), follicular plugging (37/94, 39.4%), vascular ectasia (30/94, 31.9%), thinning (11/94, 11.7%) and thickening (9/94, 9.6%) of the epidermis. The CLASI activity score was significantly higher in cutaneous areas with power Doppler signal ($p = 0.005$). Dermal oedema was also found to be associated with higher CLASI activity scores, considered both globally ($p = 0.004$) and at the level of the US-evaluated area ($p < 0.001$). Skindex-16 symptoms subscale scores were significantly higher in patients with UHFUS findings of power Doppler ($p = 0.01$) and thinning of the epidermis ($p = 0.04$). Moreover, we found a positive correlation between CLASI activity and the scores of all Skindex-16 subscales (Rho 0.324, $p = 0.002$ for symptoms; Rho 0.312, $p = 0.003$ for emotions; Rho 0.378, $p < 0.001$ for functioning), also present but weaker between CLASI damage and the symptoms (Rho 0.228, $p = 0.032$) and functioning (Rho 0.275, $p = 0.009$) domains.

Table 1: characteristics of the cohort

N° of patients	59
Female	52 (88.1%)
Age[1] [years]	46 (35-55)
Disease duration[1] [years]	12 (7-20)
Ethnicity: Caucasian / Asian / African-American	55 (93.2%) / 3 (5.1%) / 1 (1.7%)
Organ involvement *[cumulative / ongoing*]*	
Mucocutaneous	59 (100%) / 92 (97.9%)
Articular	37 (62.7%) / 12 (12.8%)
Haematological	31 (52.5%) / 10 (10.6%)
Renal	7 (11.9%) / 4 (4.3%)
Serositis	4 (6.8%) / 0
Neuropsychiatric	4 (6.8%) / 0
SLEDAI-2K[1*]	4 (2-6)
SDI[1*]	0 (0-1)
CLASI activity[1*] *[global / UHFUS area]*	5 (3-8) / 2 (1-3)
CLASI damage[1*] *[global / UHFUS area]*	2 (0-5) / 0 (0-2)
Skindex-16 symptoms[1*]	50.0 (16.7-81.3)
Skindex-16 emotions[1*]	61.9 (33.3-95.2)
Skindex-16 functioning[1*]	33.3 (10.0-80.0)

[1] Median (IQR)

* data on 94 assessments

Conclusions: Our preliminary data demonstrate that UHFUS presence of power Doppler and dermal oedema is associated with skin activity clinically assessed by CLASI. These findings suggest that UHFUS may play a role in supporting the clinician in the differential diagnosis between active skin lesions and damage, to optimise the management of skin involvement in SLE.

PV222 / #475

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

DIFFERENT PHENOTYPES OF SEVERE FLARES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RESULTS OF A CLUSTERING ANALYSIS IN A MONOCENTRIC COHORT.

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Background/Purpose: to identify and compare different phenotypes of severe flares in a monocentric cohort of SLE patients.

Methods: This is a retrospective study of prospectively collected data from a monocentric cohort of adult SLE patients (2019 EULAR-ACR classification criteria), hospitalised in the last five years, due to a severe flare (SELENA-SLEDAI flare index definition). Patients with concomitant infections, oncologic and onco-hematologic conditions were excluded. Hospitalisation was defined as baseline (t0). At t0 demographics, clinical, laboratory and treatment data were collected. Disease activity was assessed with SLEDAI-2K and BILAG-2004. Disease outcomes (Lupus Low Disease Activity State (LLDAS) and DORIS remission) and treatment were evaluated at 3, 6, 12-months (t3, t6, t12) after the flare. Organ damage (SLICC-Damage Index (SLICC-DI)) was assessed at baseline and t12. A clustering analysis was performed on SLE flares, with a hierarchical method. Post-hoc elaborations (1-way analysis of variance with Bonferroni test for quantitative variables, and Chi square test for qualitative variables) were performed to estimate any statistically significant differences between the clusters.

Results: 122 severe flares in 110 patients (female 83%, Caucasian 89%) were included. 3 clusters were identified, composed of 40, 34 and 48 flares respectively. *Cluster 1* included flares that occurred in younger patients (mean age 38.2±12 vs 46.3±13.9 and 43.2±11.1 in *clusters 2 and 3* respectively; p=0.007) with a shorter disease duration (9.1±6 years vs 17.5±11.5 and 15±8.7; p=0.0001), characterized by a higher frequency of BILAG A manifestations in the constitutional, cardiopulmonary and musculoskeletal domains (p= 0.0001). These flares presented *hyper-inflammatory* stigmata (higher C-reactive protein, more severe lymphopenia, a tendency for higher ferritin values) and a richer autoantibody profile (anti-dsDNA, anti-Smith, anti-nucleosome, anti-hystone), compared to the other clusters. *Cluster 2* included less severe flares with more BILAG B scores (59% vs 28% and 19%; p=0.0001) and mainly joint and skin

manifestations. *Cluster 3* was characterized by a clear predominance of renal flares (96%) (p=0.0001). 85% of flares in each cluster required adding/changing the immunsuppressant, mainly Mycophenolate in c*lusters 1* and *3* (30% and 47% vs 9%; p=0.001). Glucocorticoid pulses were less frequently used in c*luster 2*, accordingly to a milder flare phenotype (15% vs 50% and 83%; p= 0.0001). Belimumab was added in 25% and 30% of flares in cl*uster 1* and *2* respectively, only in 8.5% in c*luster 3* (p=0.02), as the majority of flares occurred before the approval of Belimumab for lupus nephritis. At t6 and t12, flares in *clusters 1* and *3* presented a significantly higher cumulative glucocorticoid dose, compared to *cluster 2*. At the different timepoints, c*luster 1* and *3* presented a comparable and quite low percentage of patients that achieved LLDAS and remission (Table 1). No differences emerged among the clusters for SLICC-DI at t12. Table 1.

	Cluster 1	Cluster 2	Cluster 3	p value
LLDAS t3	28%	64%	11%	0.0001*
Remission t3	17%	30%	16.5%	0.019*
LLDAS t6	43%	67%	36%	0.026*
Remission t6	29%	37%	20%	ns
LLDAS t12	47%	71%	48%	ns
Remission t12	29%	50%	36%	ns

*Cluster 2 vs 1 and 3

Conclusions: different phenotypes of severe SLE flares exist. We identified a “hyper-inflammatory” phenotype presenting with fever, arthritis and serositis, deserving similar aggressive therapeutic strategies as renal flares and burdened by a comparable proportion of unsatisfying response to treatment.

PV223 / #525

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

GENERATING CANDIDATE DOMAINS FOR THE OMERACT SYSTEMIC LUPUS ERYTHEMATOSUS CORE OUTCOME SET

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic multisystemic heterogenous auto-immune disease that can present in patients through a myriad of different clinical symptoms. The complexity of SLE makes the impact on patients multi-faceted through numerous domains hindering the standardization of the important domains to measure in clinical trials and longitudinal research. A Core Outcome Set (COS) can standardize the important domains of SLE and their measurement. In 1998,

the first Outcome Measures in Rheumatology (OMERACT) SLE COS was developed, though it never progressed to instrument selection nor achieved patient representation. In 2018 we re-established the OMERACT SLE Working Group gathering collaborators (patients, clinicians, researchers, pharmaceutical representatives, and more representing 6 continents and over 260 members from over 35 countries) to develop a new SLE COS to address the unmet need of identifying the most important domains of SLE and standardizing their measurement.

Methods: Domain Generation We endeavored on 3 projects to identify candidate domains for the SLE COS. The first project was a survey of domains revisiting known SLE domains and identifying novel domains. The survey was administered to 100 SLE patients from the University of Toronto Lupus Clinic and 145 OMERACT SLE Working Group members. The second project was a scoping literature review of SLE systematic reviews and clinical trials since 2010 capturing domains, definitions, and measurement instruments. The third project was focus groups with SLE patients from around the world identifying the impactful and important domains to SLE patients. Domain Winnowing and Binning Preliminary domains identified from domain generation were reviewed by the OMERACT SLE Advisory Group. Domains deemed too contextual, narrow, broad, or unspecific were winnowed out and the remainder were binned into appropriate domains. Domain Definition Candidate definitions were identified from the scoping literature review and additional searches of literature looking at published definitions. The OMERACT SLE Advisory Group reviewed candidate definitions, modified definitions if required, and selected suitable definitions for each candidate domain.

Results: Domain generation, winnowing, and binning identified 25 candidate domains and definitions for each candidate domains were established (Table1).

Table 1. Candidate Domains and Definitions

Domain	Definition
Adverse Events	Any untoward medical occurrence in a participant, which does not necessarily have a causal relationship with the trial intervention.
Anxiety	Fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness).
Cognition Impact	The extent to which cognitive function is perceived (by the patient and their support network and immediate circle, as well as the healthcare team) to interfere with daily functioning and a patient's life.
Cognitive Function	Mental acuity, concentration, verbal and nonverbal memory, verbal fluency, and other cognitive domains and their noted changes (this includes subjective and objective assessments).
Depression	Negative mood (sadness, guilt), views of self (self-criticism, worthlessness), and social cognition (loneliness, interpersonal alienation), as well as decreased positive affect and engagement (loss of interest, meaning, and purpose).
Economic Cost Impact	The resources that are expended or forgone as a result of a health problem. It includes health sector costs (direct costs), the value of decreased or lost productivity by the patient (indirect costs), and the cost of pain and suffering (intangible costs)
Emotional Health (living with and managing SLE)	A construct consisting of multiple domains that describes one's expression, perception, and conceptualization of emotions which includes knowledge, reactivity, and regulation of emotions. It is your ability to cope with both positive and negative emotions
Fatigue	Range of symptoms from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles.
Flares	An increase in disease activity in one or more organ systems involving new or worse clinical signs and symptoms and/or lab measurements. The increase must be considered clinically significant and in most cases, should prompt the consideration of a change or an increase in treatment.
Frailty	A clinically recognizable state in which the ability of people to cope with everyday or acute stressors is compromised by an increased vulnerability brought by declines in physiological reserve and function across multiple organ systems.
Health-Related Quality of Life	A term referring to the health aspects of quality of life, generally considered to reflect the impact of disease and treatment on disability and daily functioning. It has also been considered to reflect the impact of perceived health on an individual's ability to live a fulfilling life.
Pain Intensity	The intensity of the sensation of pain, encompassing the entire spectrum from a complete absence of pain to the most extreme levels of discomfort.
Pain Interference	Consequences of pain on relevant aspects of one's life. This includes the extent to which pain hinders engagement with social, cognitive, emotional, physical and recreational activities
Participation in all aspects of life (family, social, educational, work, and leisure activities)	The involvement of people in all areas of life, and the participation restrictions they experience (functioning of a person as a member of society).
Patient Global Assessment of Disease Activity	A patient's self perception of the degree of SLE disease activity.
Physical Function	One's ability to carry out various activities that require physical capability, ranging from self-care (activities of daily living) to more vigorous activities that require increasing degrees of mobility, strength or endurance.
Physician Global Assessment of Disease Activity	The physician's judgement of the degree of SLE disease activity
Reproductive Health	Refers to the state of complete physical, mental, and social well-being in all matters relating to the reproductive system and implies that people can have a satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when, and how often to do so.
Sexuality	A person's behaviors, desires, and attitudes related to sex and intimacy.
SLE Disease Activity	Reversible manifestations (global as well as organ specific) of the underlying inflammatory process and is a reflection of the type and severity of organ involvement at each point in time.
Sleep	Perceptions of sleep quality, sleep depth, and restoration associated with sleep.
Stress	A state of worry or mental tension caused by a difficult situation.
Tissue/Organ Damage	Damage is a health state related to tissue/organ structure and function. The degree of reduced tissue/organ function relates to physiologic impairment. Damage can occur before a diagnosis of SLE but should be attributable to SLE. Damage to a tissue/organ is irreversible, but the functional consequences on that tissue/organ may improve over time through physiological adaptation or treatment.
Treatment Satisfaction	The individual's rating of attributes of the process and outcomes of their therapeutic plan.
Use of Glucocorticoids including Tapering	The use of any form of administration of glucocorticoids including tapering and stopping.

Conclusions: Candidate domains with definitions have been prepared for the SLE COS. The proceeding stage of COS development will be a Delphi consensus exercise beginning in January, 20225, where patients and other collaborators from around the world will participate to vote on the most important domains of SLE to capture in all SLE clinical trials and longitudinal research. The Delphi will identify the core domains that will make up the SLE COS. Measurement instruments for each core domain will be

identified and appraised on their measurement properties, and the most suitable will be selected to capture each core domain. The work to modify or develop a novel instrument should no suitable one be identified will be recommended if required. The final product will be a new SLE COS able to standardize the measurement and reporting of important domains of SLE in clinical trials and longitudinal research. The SLE COS will provide standardized methodology and terminology to capture and report domains, prevent duplicate and waste research, create a trove of more accessible and interpretable data to advance research, and support regulatory bodies with endorsing pharmaceutical interventions assessed using the OMERACT SLE COS.

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Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

INITIAL CLINICAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS IN THE GUATEMALAN POPULATION: ISLA COHORT

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that affects multiple organ systems and exhibits a diverse range of clinical manifestations, predominantly in young women. The characteristics of the initial presentation may vary significantly based on the demographic and geographic context of the affected population. This study seeks to elucidate SLE's clinical behavior in patients from the Guatemalan lupus cohort.

Methods: The records of 268 patients diagnosed with SLE and followed up from December 2008 to June 2024 were analyzed in a retrospective cross-sectional study. These patients constituted a cohort from a single rheumatology center in Guatemala, specifically the Lupus cohort of the Guatemalan Social Security Institute in the Autonomous Unit (ISLA). The clinical manifestations observed during diagnosis were assessed utilizing the ACR/EULAR 2019 and SLICC 2012 classification criteria. The data characterization was systematically organized by gender.

Results: Our findings indicate that 91.42% of patients diagnosed with SLE were women, with a mean age of 30.56 years for females and 26.6 years for males, and predominantly came from the metropolitan area. Notably, 93.5% of females and 87% of males fulfilled the ACR/EULAR 2019 classification criteria, while all patients fulfilled the SLICC criteria **(Table 1).** The most common clinical manifestation was renal involvement, present in 46.9% of females and 69.9 % of males, primarily types III and IV nephropathy. Arthritis affected 55.5% of females and 39.1% of males. Regarding immunological conditions, ANA positivity was observed in 93.5% of females and 87% of males, while anti-dsDNA positivity was noted in 80.4% and 60.9%, respectively. Males predominantly exhibited renal involvement and a higher frequency of aPL with a higher frequency of thrombotic APS, whereas females exhibited mucocutaneous, renal, and neurological manifestations **(Table 2).**

	Female N: 245	Male N: 23	P valor
Mean Age (+/- SD) *	41.91 (11.54)	34.91 (8.62)	0.069
Mean Age of Diagnosis	30.56 (9.34)	26.26 (7.74)	0.15
Area of Residence n (%)			0.77
Metropolitan	170 (69.4)	20 (87)	----
Rural	75 (30.6)	3 (13)	----
Classification criteria			
EULAR/ACR criteria n (%)	229 (93.5)	20 (87)	0.25
Mean score (+/- SD)	22.18 (8.83)	22.48 (9.04)	0.53
SLICC criteria n (%)	245 (100)	23 (100)	------
Mean Clinical SLICC score (+/- SD)	3.05 (1.52)	2.96 (1.43)	1
Mean Immunological SLICC score (+/- SD)	3 (1.28)	3 (1.38)	0.58

*** Time in Years**

	Female N: 245	Male N: 23	P valor
Clinical criteria n (%)			
Constitutional disorder	34 (13.9)	5 (31.7)	0.31
Mucocutaneous disorder n (%)			
acLE	102 (41.6)	6 (26.1)	0.15
cdcLE	6 (2.4)	2 (8.6)	0.59
Photosensitivity	103 (9.8)	7 (30.4)	0.27
Mucosal ulcers	24 (9.8)	3 (13)	0.62
Non-scarring alopecia	86 (35.1)	2 (8.7)	0.010
Musculoskeletal disorder n (%)			
Arthritis n	136 (55.5)	9 (39.1)	0.13
Serositis n (%)			
Pleural or pericardial effusion	8 (3.3)	1 (4.3)	0.78
Acute pericarditis	6 (2.5)	0 (0)	0.45
Renal disorder n (%)			
Proteinuria	115 (46.9)	16 (69.6)	0.038
ISN/RPS III/IV *	56 (22.9)	9 (39.1)	0.082
ISN/RPS II/V	17 (6.9)	2 (8.7)	0.75
No Biopsy	35 (14.3)	3 (13)	0.87
Others	7 (2.85)	2 (8.69)	0.002
Neurologic disorder n (%)			
Seizure	10 (4.1)	2 (8.7)	0.3
Psychosis	2 (0.8)	0 (0)	0.66
Delirium	5 (2)	0 (0)	0.48
Others	25 (19.59)	2 (8.69)	0.21
Hematologic disorder n (%)			
Hemolytic anemia	69 (28.2)	7 (30.4)	0.82
Leukopenia	52 (21.2)	5 (21.7)	0.95
Thrombocytopenia	35 (14.3)	4 (17.4)	0.68
Immunological criteria n (%)			
Anti-dsDNA	197 (80.4)	14 (60.9)	0.029
Anti-Sm	50 (20.4)	14 (21.7)	0.88
Ro/SSA	69 (28.2)	4 (17.4)	0.27
Anti-phospholipid antibodies	80 (32.7)	13 (56.5)	0.021
LA	61 (24.9)	12 (52.2)	0.005
aCL	65 (26.5)	11 (47.8)	0.030
β2GPI	13 (5.3)	4 (17.4)	0.023
Triple aPL positivity	13 (5.3)	4 (17.4)	0.023
Low C3 and C4	110 (44.9)	10 (43.5)	0.89
Low C4	19 (7.8)	3 (13)	0.38
Low C3	8 (3.3)	0 (0)	0.38
Antinuclear antibody	229 (93.5)	20 (87)	0.25
Other Disorders n (%)			
Thrombotic APS	26 (10.6)	6 (26.1)	0.029
Obstetric APS	19 (7.8)	----	----

*** ISN/RPS International Society of Nephrology/Renal Pathology Society classes.**

Conclusions: Our study's findings emphasize the importance of recognizing the main clinical manifestations of SLE in our population, particularly the renal, joint, and mucocutaneous involvement, and their association with immunological phenomena and the presence of antiphospholipid antibodies in men. This understanding should motivate healthcare professionals, as it equips them with the knowledge to suspect SLE

when these clinical characteristics are present, thereby improving patient care and outcomes.

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Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A STUDY OF THE GUATEMALAN ISLA COHORT

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by periods of exacerbation and remission. Despite significant advancements in treatment strategies in recent years, patients may experience variable episodes of disease activity throughout their lives. Comorbidities and the accessibility of therapeutic interventions can influence the progression of SLE. Consequently, this study aims to elucidate the current disease activity among patients with SLE in a Guatemalan cohort.

Methods: This study employs a cross-sectional design and involves reviewing 268 patient records diagnosed with SLE from a single rheumatology center in Guatemala, specifically the Lupus cohort of the Guatemalan Social Security Institute in the Autonomous Unit (ISLA). The analysis focused on disease activity data from the most recent clinical follow-up evaluation conducted in 2024. The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) was employed to assess disease activity. The study systematically described activity domains, categorized by current disease status; the activity was defined as SLEDAI-2K > 4 points and included an overview of treatment regimens and comorbidities.

Results: The study identified that 48.88% of patients were active cases, predominantly women at 92.4%. The mean SLEDAI-2K score was 6.51, indicating significant disease activity, especially in renal aspects, with proteinuria in 28.2% and pyuria in 31.3%, with a mean proteinuria value over 24 hours amounting to 560.83 mg. Hypocomplementemia was found in 49.6% of cases, and 55.7% had anti-DNA levels elevated. Among inactive patients, 11.7% had low C3-C4 levels, and 26.3% had anti-DNA elevated. **(Table 1)** Corticosteroids were the most common treatment used by 79.6% of inactive and 82.4% of active patients, with average dosages of 5.63 mg and 9.96 mg, respectively. Hydroxychloroquine (HCQ) and azathioprine (AZA) were also used, with cyclophosphamide (CYC) as the primary rescue therapy during follow-up. Kidney transplantation occurred in 2.92% of inactive and 2.29% of active patients. **(Table 2)** Concerning comorbidities, the cardiovascular system was identified as the most affected, with arterial hypertension being the most prevalent condition, affecting 33.58% of the total patient sample. Moreover, 17 cases overlapped with other autoimmune diseases, the most common being systemic sclerosis. **(Table 2)**

	Inactive N: 137	Active N: 131	P valor
Mean SLE disease duration (+/- SD) *	11.57 (8.14)	10.46 (7.72)	0.42
Mean follow-up (+/- SD) *	7.72 (6.01)	7.47 (6.22)	0.55
Female n (%)	124 (90.5)	131 (92.4)	0.59
Mean Sledai-2K score (+/- SD)	0.84 (1.01)	6.51 (3.35)	0.0005
Activity Domains n (%)			
Recent onset seizure	0 (0)	2 (1.5)	0.15
Psychosis	0 (0)	0 (0)	----
Organic brain syndrome	0 (0)	0 (0)	----
Visual disturbance	0 (0)	1 (0.8)	0.31
Neuropathy	0 (0)	5 (3.8)	0.021
Lupus headache	0 (0)	2 (1.5)	0.15
New onset stroke	0 (0)	2 (1.5)	0.15
Vasculitis	0 (0)	3 (2.3)	0.075
Arthritis	0 (0)	6 (4.6)	0.011
Myositis	0 (0)	0 (0)	----
Heme-granular or RBC urinary cast	0 (0)	2 (1.5)	0.15
Hematuria	0 (0)	23 (17.6)	0.002
Proteinuria	0 (0)	37 (28.2)	0.002
Mean proteinuria in 24 hours (+/- SD) **	111.88 (103.93)	560.83 (969.08)	0.0021
Pyuria	0 (0)	41 (31.3)	0.0001
Inflammatory-type rash	0 (0)	2 (1.5)	0.15
Alopecia	0 (0)	1 (3.1)	0.039
Oral or nasal mucosal ulcers	0 (0)	2 (1.5)	0.15
Pleuritic involvement	0 (0)	1 (0.8)	0.30
Pericarditis	0 (0)	0 (0)	----
Low complement	16 (11.7)	65 (49.6)	0.00013
Mean C3 (+/- SD) ***	115.66 (26.84)	98.31 (27.93)	0.45
Mean C4 (+/- SD) ***	19.83 (8.08)	15.84 (9.38)	0.047
High DNA binding	36 (26.3)	73 (55.7)	0.009
Mean Anti-DNA (+/- SD) ****	24.9 (19.41)	85.03 (153.50)	0.0007
Fever	0 (0)	0 (0)	----
Thrombocytopenia	3 (2.2)	3 (2.3)	0.96
Mean platelets (+/- SD) †	296.74 (102.39)	284.67 (97.89)	0.69
Leukopenia	8 (5.8)	16 (12.2)	0.068
Mean WBC (+/- SD) †	6.71 (2.14)	6.40 (2.69)	0.040
Other manifestations n (%)			
Anemia	14 (10.2)	19 (14.5)	0.29
Mean hemoglobin (+/- SD) ††	12.88 (1.72)	12.5 (2.00)	0.48
Mean ESR (+/- SD) †††	9.23 (10.25)	10.34 (9.87)	0.74
Media CRP (+/- SD) ‡	4.75 (6.40)	4.85 (7.83)	0.75
Other conditions n (%)			
Pregnancy	2 (1.5)	2 (1.5)	0.96

*** Time in Years, ** mg/24 hrs.*** mg/dL, **** U/mL, † x10^3/ul, †† g/dL, ††† mm/h, ‡ mg/L**

	Inactive N: 137	Active N: 131	P valor
Current therapy n (%)			
Corticosteroid	109 (79.6)	108 (82.4)	0.54
Corticosteroid means doses (+/- SD) *	5.63 (6.78)	9.96 (10.39)	0.00012
AZA	71 (51.8)	65 (49.6)	0.72
MMF	57 (41.6)	60 (45.8)	0.49
HCQ	100 (73)	98 (74.8)	0.74
Tacrolimus	5 (3.6)	11 (8.4)	0.10
MTX	7 (5.1)	4 (3.1)	0.39
CYC	1 (0.7)	6 (4.6)	0.048
Rituximab	15 (10.9)	18 (13.7)	0.49
Anifrolumab	1 (0.7)	0 (0)	0.33
Rescue therapies used during follow-up n (%)			
IVIG	19 (13.9)	41 (31.3)	0.001
CYC	63 (46)	82 (62.6)	0.006
Rituximab	23 (16.8)	30 (22.9)	0.21
Other therapies n (%)			
ASA	44 (32.1)	53 (40.5)	0.15
Warfarin	8 (5.8)	6 (4.6)	0.64
Rivaroxaban	15 (10.9)	14 (10.7)	0.94
LMWHs	0 (0)	3 (2.3)	0.075
Clinical trials	0 (0)	3 (2.29)	0.029
Surgical procedures performed during follow-up n (%)			
Kidney transplant	4 (2.92)	3 (2.29)	----
Splenectomy	0 (0)	2 (1.53)	----

*** mg**

	Inactive N: 137	Active N: 131
Overlap syndromes n (%)		
Systemic scleroderma	7 (5.11)	1 (0.8)
Sjögren´s syndrome	2 (1.5)	2 (1.5)
Inflammatory myopathy	2 (1.5)	1 (0.8)
Rheumatoid arthritis	1 (0.7)	1 (0.8)
Associated comorbidities n (%)		
Cardiovascular disorders	82 (59.85)	56 (42.75)
Metabolic disorders	33 (34.09)	29 (22.14)
Pulmonary disorders	29 (21.16)	19 (14.50)
Thyroid disorders	25 (18.25)	17 (1.98)
Neurological disorders	22 (16.05)	19 (14.50)
Osteodegenerative disorders	19 (13.87)	22 (16.79)
Renal and genitourinary disorders	19 (13.87)	12 (9.16)
Psychiatric disorders	12 (8.76)	9 (6.87)
Fibromyalgia	10 (7.29)	11 (8.39)
Neoplasia	7 (5.11)	2 (1.5)
Liver disorders	5 (3.64)	5 (3.81)
Hematological disorders	3 (2.19)	6 (4.58)
Cutaneous disorders	2 (1.46)	3 (2.29)
Drug-associated disorders	2 (1.46)	3 (2.29)
Gastrointestinal disorders	1 (0.73)	5 (3.81)
Ocular disorders	1 (0.73)	1 (0.8)

Conclusions: This study describes the current activity characteristics of the patient cohort observed. It is essential to emphasize our population's high percentage of activity, particularly regarding significant renal involvement associated with immunological phenomena. Furthermore, the study underscores the presence of the serologically active clinically quiescent phenomenon, which is pertinent as it may predict future clinical activity. In light of the crucial role that access to medications and related comorbidities play in the manifestation of disease activity, this observation prompts a critical inquiry into whether we possess the necessary tools to address the challenges posed by Lupus adequately.

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Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

NEW IGG AND IGA AUTOANTIBODY SPECIFICITIES TARGETING DNA- AND RNA-BINDING PROTEINS DIFFERENTIATE SYSTEMIC LUPUS ERYTHEMATOSUS FROM HEALTHY INDIVIDUALS AND OTHER AUTOIMMUNE DISEASES

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Background/Purpose: Systemic lupus erythematosus (SLE) is characterised by the production of autoantibodies (AAbs), the specificities of which remain largely unknown and their contribution to disease pathogenesis remains poorly understood. Currently used AAbs either demonstrate high sensitivity across connective tissue diseases (e.g., ANA) or high specificity yet low sensitivity (e.g., anti-dsDNA). To address the urgent unmet needs of heterogeneity, unpredictability, and diagnostic delay in patients with SLE, we screened for circulating IgG and IgA autoantibodies against 1,609 proteins.

Methods: Plasma samples from patients with SLE, Sjögren's disease (SjD) and systemic sclerosis (SSc), and healthy controls (HC) were obtained from two independent cohorts (discovery and validation) within the European PRECISESADS consortium (NTC02890121). The discovery cohort comprised 199 patients with SLE, 115 patients with SjD, 115 patients with SSc, and 111 HC. The validation cohort included 30 patients with SLE, 31 patients with SjD, 24 patients with SSc, and 84 HC from an independent inception cohort. Plasma samples were analysed for IgG and IgA autoantibody specificities against a comprehensive panel of 1,609 human proteins, utilising the i-Ome Discovery protein microarray (Sengenics). Conventional autoantibodies (IgG anti-dsDNA, IgG anti-Smith, IgG and IgM anti-cardiolipin, IgG and IgM anti-b2GPI) were measured using an automated chemiluminescent immunoanalyser. Differentially abundant AAb (daAAb) analysis was performed with the limma R package after

adjustments for age, recruiting centre, batch, and polyspecific antibody reactivity (PSA) following diagnostic performance.

Results: In two independent cohorts, we identified and validated five IgG (anti-LIN28A, anti-HNRNPA2B1, anti-HMG20B, anti-HMGB2, and anti-TFCP2) and four IgA (anti-LIN28A, anti-HMG20B, anti-SUB1, and anti-TFCP2) autoantibodies that demonstrated high specificity for SLE, along with consistent and robust positivity frequencies. Levels of some, notably anti-LIN28A, varied over time and exhibited metrics that outperformed those of traditional autoantibody markers such as anti-dsDNA. We identified five patient subgroups based on SLE-specific IgG autoantibodies and five based on IgA autoantibodies. One subgroup exhibited broad reactivity against numerous antigens, three subgroups showed varying reactivity patterns, and one was completely seronegative for the specificities screened for. SLE patients with positive autoantibody levels for conventional autoantibody markers were similarly distributed across the clusters. Differentially abundant autoantibody targets pointed to RNA- and DNA-binding and transcription functions, with considerable overlap across patient subgroups stratified by IgG and IgA reactivity patterns.

Conclusions: We described and validated novel IgG and IgA autoantibody specificities. The observation of IgA seroreactivity is novel and provides implications for the importance of mucosal immunity in SLE pathogenesis. Certain autoantibodies were significantly more abundant in SLE compared to healthy controls and other autoimmune disease comparators, showing promise for improved diagnostics and aiding in the molecular characterisation of individuals with SLE. These findings could support more informed and personalised therapeutic strategies. Both IgG and IgA anti-LIN28A demonstrated high specificity and sensitivity in distinguishing SLE from healthy individuals and other autoimmune diseases, outperforming conventional autoantibodies in diagnostic metrics.

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Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

THE OUTCOMES AND VALUE OF EARLY DIAGNOSIS IN ACHIEVING REMISSION FOR SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS (OVERSLEEP STUDY): AN INTERIM REPORT.

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Background/Purpose: The definition of "early systemic lupus erythematosus (SLE)" is evolving as we recognize the importance of identifying symptoms and initiating treatment earlier to prevent organ damage and improve both short- and long-term outcomes (1). Several definitions of early SLE have been proposed concerning the time elapsed since symptom onset, ranging from <6 months to <36 months, with no general agreement. The OVERSLEEP study was designed to investigate whether there is a critical window of opportunity to establish an early diagnosis to improve the chances of achieving remission in SLE and prevent further damage once treatment begins.

Methods: OVERSLEEP is a multicenter (23 centers), prospective, observational study ideated by the Italian Society of Rheumatology's study group on early SLE. Eligible individuals are newly diagnosed SLE patients, fulfilling at least one of the validated sets of classification criteria. Diagnostic delay is defined as the time when symptoms are first presented to a healthcare provider (e.g., general practitioner, lab, specialist, emergency room) until a diagnosis is made. Visits at 6-month intervals, or earlier if needed, assess clinical and laboratory features. The primary endpoint is the achievement of remission after 6 months. Secondary endpoints are LLDAS, organ damage according to the SLICC/ACR damage index, flares, patient-reported outcomes, hospitalizations, and death. Primary statistical analysis will be performed by logistic regression with the primary endpoint as the dependent variable, including diagnostic delay as the exposure variable and several adjustment variables. This abstract reports on the selection process for the adjustment variables associated with delayed diagnosis calculated as the “diagnostic delay ratio” between groups with or without the reference variable (i.e.; Mean delay-time interest group/Mean delay-time reference group).

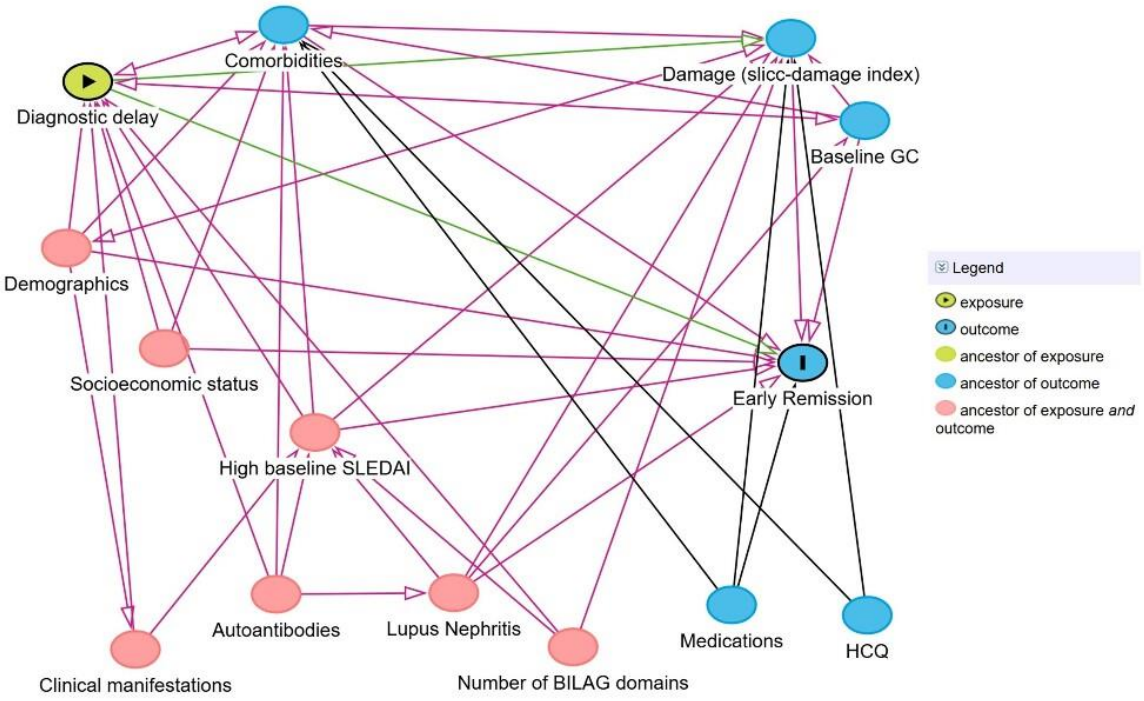
Results: Enrolment started in September 2020 and aims at a sample size of 420 patients. In October 2024, the study included 221 patients (84.1% female); the median

age is 38.0 (IQR 25.0 – 48.0) years, and 90% are Caucasians. The primary endpoint of remission at 6 months since diagnosis is achieved by 45 patients (25.6%). Univariate analysis identified factors associated with delayed diagnosis (Table 1), which, if confirmed in the whole study sample, will be used as adjustment variables, including baseline treatment with the daily and cumulative dose of glucocorticoids.

Table 1. Baseline variables and diagnostic delay ratio between the reference group and the interest group. F variable sex, the reference class is "female," and the interest class is male; the diagnostic delay ratio is 1.46, means that males have a 46% mean time delay in diagnosis compared to females.

Baseline variables	Mean time delay for reference group (months)	Mean time delay for group of interest (months)	Time delay ratio	P value
DEMOGRAPHICS				
Sex (ref. F)	7.38	10.8	1.46 (0.94-2.3)	0.090
Caucasian (ref. "no")	4.73	8.31	1.75 (1-3.1)	0.046
Smoking (ref."no")	7.24	10.03	1.39 (0.95-2)	0.091
Family history of SLE (ref."no")	8.24	5.78	0.7 (0.41-1.2)	0.190
BILAG DOMAIN OR ITEMS AT ONSET				
Constitutional (ref. "no")				
Fever (> 37.5°)	9.86	5.3	0.54 (0.39-0.74)	0.0002
Mucocutaneous (ref. "no")	8.21	7.42	0.9 (0.65-1.3)	0.54
Neuro (ref. "no")	7.78	8.74	1.13 (0.57-2.2)	0.74
Muscolosckeletal (ref. "no")	8.6	7.24	0.84 (0.61-1.2)	0.3
Severe arthritis	7.85	7.67	0.98 (0.52-1.9)	0.94
Moderate arthritis/tendonitis	8.68	5	0.58 (0.38-0.87)	0.009
Mild arthritis/Arthralgia /Myalgia	8.1	7.51	0.93 (0.38-0.87)	0.65
Cardio-respiratory (ref. "no")	8.44	5.41	0.64 (0.42-0.99)	0.044
Gastrointestinal (ref. "no")	7.93	4.71	0.59 (0.2-1.7)	0.34
Eye (ref. "no")	8.09	1.4	0.17 (0.053-0.56)	0.0038
Blood (ref. "no")	9.57	5.29	0.55 (0.4-0.77)	0.0006
Kidney (ref. "no")	8.75	4.33	0.5 (0.32-0.77)	0.0017
SEROLOGIC ABNORMALITIES				
anti, dsDNA (ref."Absent")	10.18	6.95	0.68 (0.48-0.97)	0.031
antiRo (ref."Absent")	8.73	6.8	0.78 (0.56-1.1)	0.14
antiLa (ref."Absent")	8.16	6.04	0.74 (0.46-1.2)	0.22
anti-RNP (ref."Absent")	7.7	8.55	1.11 (0.72-1.7)	0.63
antiSm (ref."Absent")	8.6	5.78	0.67 (0.46-0.99)	0.045
anti-Cardiolipin (ref."Absent")	7.3	10.24	1.4 (0.94-2.1)	0.098
anti-beta2GPI (ref."Absent")	7.1	10.07	1.42 (0.98-2.1)	0.065
Lupus Anticoagulant (ref."Absent")	7.61	8.71	1.14 (0.78-1.7)	0.5

The directed acyclic graph in Figure 1 shows the potential causal relationship between variables, identifying variables that will be included in the final model for primary statistical analysis of the OVERSLEEP study. The ancestor of exposure and outcome are confounders and will be included in the final model as adjustment factors.



Conclusions: The OVERSLEEP study targets a population in which remission is observable within 6 months of diagnosis. The enrolled population showed factors associated with delayed diagnosis, which are of interest for modeling the analysis of the OVERSLEEP study and further investigation aiming at developing red flags for early SLE diagnosis. *Listed authors have enrolled at least 10 patients with completed primary endpoint.

References: 1. Piga M, Tselios K, Viveiros L, Chessa E, Neves A, Urowitz MB, Isenberg D. Clinical patterns of disease: From early systemic lupus erythematosus to late-onset disease. Best Pract Res Clin Rheumatol. 2023 Dec;37(4):101938. doi: 10.1016/j.berh.2024.101938.

PV228 / #365

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

A NOVEL MODELING APPROACH TO ELUCIDATE THE ROLE OF AUTOANTIBODIES IN COMPLEMENT ACTIVATION IN SLE

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Background/Purpose: In SLE, autoantibodies (ANAs) can promote pathogenesis by forming immune complexes (ICs) that activate complement. While antibodies to DNA (anti-DNA) are known to be associated with complement levels, the role of other ANAs in activating complement is less clear. To elucidate better serological biomarkers in the context of novel therapies to decrease immunoglobulin levels or B-cells, we modeled the relationship between autoantibodies (anti-DNA, other ANAs, anti-C1q) and complement.

Methods: Adult SLE patients (SLICC or ACR/EULAR criteria) were enrolled during routine clinic visits from June 2020 to June 2024. At each visit, treating rheumatologists scored the PGA and SLEDAI, medications were recorded, and autoantibodies were measured. Autoantibodies including anti-DNA, anti-RNA-binding proteins (RBPs), and anti-C1q were measured by ELISA. Complement activation was defined as (1) low C3, (2) low C4, (3) low C3 and low C4, and (4) low C3 or low C4. Potential predictors of complement activation were modeled in 4 steps: (1) anti-DNA; (2) anti-DNA, anti-RBPs (Ro-52, Ro-60, Sm, La, U1RNP, RNP-70), and anti-C1q; (3) anti-DNA, anti-RBPs, anti-C1q, and medications; and (4) anti-DNA, anti-RBPs, anti-C1q, and disease activity. To identify linear and possible nonlinear relationships between predictors and complement activation, we considered both generalized linear models (GLMs; specifically, logistic regression with LASSO regularization) and decision tree models, each with continuous predictors. Models were trained and tuned on 80% of patients and evaluated on the remaining 20%.

Results: The study included 526 visits in 257 patients (mean age 42 years; mean disease duration 13 years; 88% female; 58% Black, 29% White; 6% Hispanic). Almost one-quarter of visits had low C3 or C4; anti-DNA was positive at 40% of visits. In Lasso regression models, the presence of anti-DNA accurately predicted complement levels (AUC: 0.71-0.79; Table 1); model performance improved with the inclusion of anti-RBPs and anti-C1q (AUC: 0.73-0.84). The inclusion of medications or disease activity led to

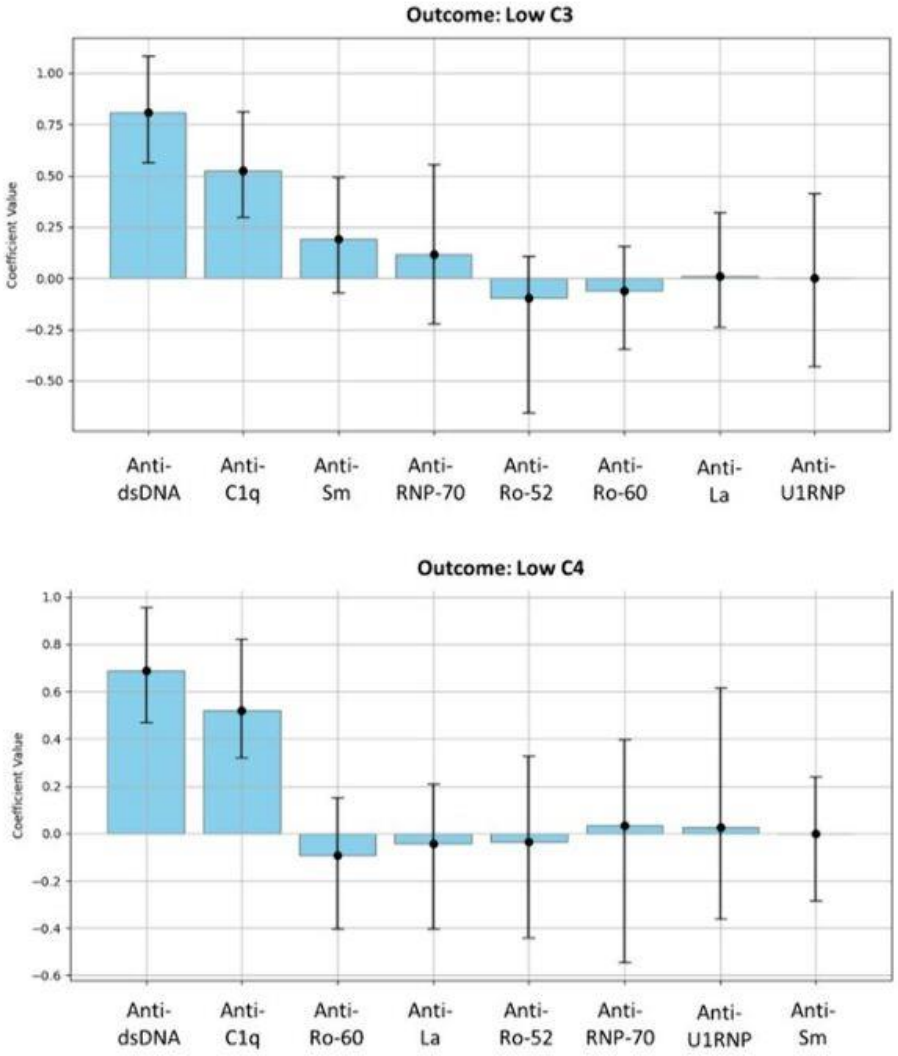
limited improvement in model performance. Across outcomes of complement activation, anti-DNA and anti-C1q were consistently associated with low complement (Figure 1). For the outcome of low C3, a one standard deviation increase in anti-DNA levels increased the odds of having low C3 by approximately 123%; a one standard deviation increase in anti-C1q levels was associated with an 82% increase in the odds of having low C3. Results were similar for low C4. The results of the decision tree models (Table 1) align with the findings from Lasso logistic regression models. For both low C3 and low C4, the decision tree consistently selected anti-DNA and anti-C1q as the primary splitting variables, further affirming their predictive power.

Table 1. Model performance of serologies, medications, and disease activity to predict low complement.

	Low C3	Low C4	Low C3 and C4	Low C3 or C4
LASSO LOGISTIC REGRESSION MODELS				
Anti-DNA only	0.76 (0.64, 0.86)	0.71 (0.61, 0.82)	0.79 (0.72, 0.85)	0.72 (0.60, 0.84)
Anti-DNA, anti-RBPs, and anti-C1q	0.79 (0.67, 0.88)	0.73 (0.65, 0.81)	0.84 (0.78, 0.90)	0.74 (0.64, 0.82)
Anti-DNA, anti-RBPs, anti-C1q, and Medications	0.80 (0.67, 0.87)	0.73 (0.66, 0.80)	0.85 (0.74, 0.95)	0.76 (0.70, 0.83)
Anti-DNA, anti-RBPs, anti-C1q, and Disease Activity	0.80 (0.67, 0.84)	0.74 (0.64, 0.84)	0.85 (0.76, 0.96)	0.76 (0.64, 0.85)
DECISION TREE MODELS	**Low C3**	**Low C4**	**Low C3 and C4**	**Low C3 or C4**
Anti-DNA only	0.67 (0.59, 0.79)	0.68 (0.62, 0.75)	0.70 (0.57, 0.79)	0.66 (0.55, 0.77)
Anti-DNA, anti-RBPs, and anti-C1q	0.72 (0.70, 0.76)	0.69 (0.63, 0.74)	0.72 (0.57, 0.81)	0.67 (0.56, 0.76)
Anti-DNA, anti-RBPs, anti-C1q, and Medications	0.75 (0.68, 0.79)	0.69 (0.63, 0.74)	0.72 (0.57, 0.81)	0.67 (0.56, 0.76)
Anti-DNA, anti-RBPs, anti-C1q, and Disease Activity	0.72 (0.63, 0.79)	0.71 (0.63, 0.77)	0.72 (0.57, 0.79)	0.68 (0.56, 0.80)

Values represent mean AUC (95% CI)

Figure 1. Coefficients of anti-DNA, anti-RBPs and anti-C1q on low C3 and low C4. Error bars indicate 95% confidence intervals obtained via bootstrapping (1000 resamples) the development set.



Conclusions: These results support the important role of anti-DNA antibodies in complement activation as reflected in levels of C3 and/or C4; the effects of other ANAs in the model were less marked, perhaps reflecting a more limited ability of these antibodies to form ICs that activate complement. The association of anti-C1q with low C3 and/or C4 is consistent with a role of this antibody in activating complement and suggests the value of assaying anti-C1q in studies on therapies that can impact autoantibody levels.

PV229 / #359

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

EVALUATION OF ACCRUAL DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARISON OF DATA FROM THE NATIONAL CROSS-SECTIONAL AND PROSPECTIVE LUPUS REGISTRY

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Background/Purpose: Adequate control of disease activity and early therapeutic interventions can minimize damage in Systemic Lupus Erythematosus (SLE). The objetive of this study was to describe and compare damage in patients with SLE from the national cross-sectional (CS)and prospective (P)
registries of the Argentine Society of Rheumatology (RELESSAR) and to assess associated factors.

Methods: A cross- sectional study was performing using two national lupus registries: the cross-sectional (RELESSARCS)
and the prospective (RELESSAR-P) ones. Data from 1648 patients across 67 centers were analyzed, with 9-year difference between both initiatives. Sociodemographic data, clinical manifestations, hospitalizations, activity and damage scores in patients with less than 5 years of SLE evolution were analysed. Statistical analysis: Descriptive statistics, Chi2, Fisher, Student's t, or Wilcoxon tests as appropriate.
Univariate/multivariate logistic regression identified factors associated with accrual damage.

Results: Data were collected from RELESSAR-CS (n=1515) and the baseline visit of RELESSAR-P (n=133). Cumulative damage was assessed by domain, with the musculoskeletal and renal domains being the most affected, the first in RELESSAR-CS and the second in RELESSAR-P. Patients with disease duration of less than 5 years from both registries were compared. It was observed that patients in RELESSAR-CS were younger (p=0.002), had a longer diagnostic delay (p<0.001), and had lower use of rituximab (p<0.001). No differences were found in cumulative damage. Comparisons were made between patients with (n=311) and without cumulative damage (n=428) from both registries. Patients with a SLICC/SDI score ≥1 were older (36[26-47] vs 31[25-41], p<0.001) and had a higher frequency of male sex (14% vs 9%, p=0.046), mestizos (58% vs 44%, p<0.001), and lower educational level (12[10-15] vs 12[11-15], p=0.019). Additionally, they exhibited higher SLEDAI disease activity (2 [0-6] vs 1 [0-4], p=0.008) and greater use of methotrexate (26% vs 18%, p=0.021), cyclophosphamide (38% vs 21%, p<0.001), and mycophenolate mofetil (27% vs 19%, p=0.021). They also had higher rates of hospitalizations (64% vs 44%, p<0.001) and infections (18% vs 9%, p<0.001). Age, mestizo ethnicity, SLEDAI score, and the use of methotrexate and cyclophosphamide were independently associated with cumulative damage.

Conclusions: Musculoskeletal domain was affected less frequently in the prospective registry, which could be associated
with lower frequency of avascular necrosis and lower use of corticosteroids. Age, mestizo ethnicity, SLEDAI, and the use
of methotrexate and cyclophosphamide were significantly associated with damage

PV230 / #447

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

VALIDATION OF A SCORE FOR THE PREDICTION OF SERIOUS INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM A LATIN AMERICAN LUPUS COHORT

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Background/Purpose: Patients with systemic lupus erythematosus (SLE) are at increased risk of serious infections, which in turn, are associated with morbidity and mortality. The Systemic Lupus Erythematosus Registry of the Spanish Society of Rheumatology (RELESSER) group has developed and internally validated a tool for prediction of severe infections in SLE, with a recently improved version (SLE Severe Infection Score-Revised or SLESIS-R)[1], being an accurate and reliable instrument. SLESIS-R includes age, previous SLE-related hospitalization, previous serious infection, and glucocorticoid dose. This study aimed to validate SLESIS-R in a multi-ethnic, multi-national Latin-American (LA) SLE cohort.

Methods: GLADEL 2.0 is an observational cohort from 10 LA countries of patients ≥ 18 years of age who fulfilled the 1982/1997 American College of Rheumatology (ACR) and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria. Patients with sufficient data at baseline and first annual visits were included. The outcome variable was any serious infection during the first year of

follow-up that led to hospitalization. Baseline demographics and clinical manifestations, disease activity (SLEDAI-2k), SLICC/ACR Damage Index (SDI) and treatments were examined. Logistic regression was used to examine the predictive effect of baseline variables on the development of serious infection in the first year of follow-up. Receiver operator characteristics (ROC) analysis was used to define the area under the curve (AUC) for SLESIS-R. The cut-off point with the best validity parameters (sensitivity and specificity) was identified.

Results: Of the 1016 patients who completed one-year follow-up, 208 (20.4%) had serious infections. Patients with serious infections were older, predominantly male, and had a longer disease duration (Table 1). This group had more frequent general, cardiac, pulmonary, hematological and gastrointestinal involvement at baseline and had a higher SDI and higher proportion of previous hospitalization. Univariate and multivariate analyses show variables associated with serious infection: disease duration, pulmonary and gastrointestinal involvements, and baseline glucocorticoid use (Table 2). The AUC for the SLESIS-R score was 0.922 (0.903-0.940). A score of 7 was chosen as the optimal cut-off point, demonstrating a sensitivity of 87% and specificity of 82%.

Table 1. Comparison between groups according to their baseline clinical characteristics, disease activity, damage index, and treatments				
Variable	**Serious Infection: No (N = 808)**	**Serious Infection: Yes (N = 208)**	***p*-value**	**Total (N = 1016)**
Age (years), Median (Q1, Q3)	34.7 (27.1, 44.2)	37.0 (28.2, 45.6)	**0.068**	35.3 (27.2, 44.3)
Female gender, n (%)	733 (90.7)	177 (85.1)	**0.025**	910 (89.6)
Disease duration (years), Median (Q1, Q3)	4.9 (1.3, 10.9)	9.3 (3.0, 15.2)	**< 0.001**	5.6 (1.6, 11.7)
Ethnic Group, n (%)				
Afro-Latin American	68 (8.4)	15 (7.2)	0.621	83 (8.1)
Indigenous	5 (0.6)	3 (1.4)		8 (0.7)
Mestizo	537 (66.5)	133 (63.9)		670 (65.9)
Other	2 (0.2)	0 (0)		2 (0.1)
Caucasian	193 (23.9)	56 (26.9)		249 (24.5)
Baseline clinical features, n (%)				
General involvement	602 (75.1)	181 (87.0)	**< 0.001**	783 (77.5)
Cutaneous involvement	726 (90.1)	194 (93.3)	0.200	920 (90.7)
Articular involvement	671 (83.4)	173 (83.2)	1	844 (83.3)
Hematological involvement	644 (80.1)	180 (86.5)	**0.042**	824 (81.4)
Renal involvement	479 (59.4)	131 (63.0)	0.383	610 (60.1)
Cardiac involvement	88 (10.9)	41 (19.8)	**< 0.001**	129 (12.7)
Pulmonary involvement	56 (6.9)	34 (16.4)	**< 0.001**	90 (8.8)
Gastrointestinal involvement	94 (11.7)	39 (18.8)	**0.009**	133 (13.1)
Neurological involvement	11 (1.3)	2 (0.9)	1	13 (1.28)
Serosal involvement	254 (31.6)	69 (33.2)	0.724	323 (31.9)
Hypocomplementemia*	649 (80.3)	178 (85.6)	0.102	827 (81.4)
SLEDAI, Median (Q1, Q3)	4.0 (1.0, 10.0)	6.0 (2.0, 12.0)	0.274	5.0 (1.0, 11.0)
SDI, Median (Q1, Q3)	0 (0, 1.0)	1.0 (0, 2.0)	**< 0.001**	0 (0, 1.0)
Previous SLE-related hospitalization, n (%)	486 (60.4)	208 (100)	**< 0.001**	694 (68.6)
Previous serious infection, n (%)	359 (44.4)	187 (89.9)	**< 0.001**	546 (53.7)
Baseline treatments, n (%)				
GC†			0.216	
≤ 5 mg	193 (34.8)	44 (27.3)		237 (33.1)
> 5 mg and < 10 mg	99 (17.9)	37 (23.0)		136 (19.0)
≥ 10 mg and < 30 mg	146 (26.4)	48 (29.8)		194 (27.1)
≥ 30 mg	116 (20.9)	32 (19.9)		148 (20.7)
Antimalarials	780 (97.6)	199 (95.7)	0.198	979 (97.2)
Cyclophosphamide-IV	76 (11.6)	24 (13.0)	0.094	100 (11.9)
Mycophenolate	269 (40.6)	79 (42.2)	0.074	348 (40.9)
Azathioprine	117 (17.8)	26 (14.0)	**0.0001**	143 (16.9)
Rituximab	29 (4.4)	9 (4.8)	0.205	38 (4.5)
Belimumab	14 (2.1)	5 (2.6)	0.809	19 (2.2)

*At least one of the following C3 or C4 or CH50; †GC: glucocorticoids expressed as mg of prednisone per day. GC, glucocorticoids; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Disease Index.

Table 2. Univariate and multivariate analyses of serious infection in SLE GLADEL patients				
Variable	**Univariate OR (95% CI)**	***p* value**	**Multivariate OR (95% CI)**	***p* value**
Age (years) ≥ 60	1.1 (0.5-2.2)	0.600		
Male gender	1.7 (1.1-2.6)	0.019		
Disease duration	1.0 (1.1-1.2)	< 0.001	1.1 (1.1-1.2)	< 0.001
Hematological involvement	1.6 (1.0-2.5)	0.035		
Cardiac involvement	2.0 (1.3-3.0)	< 0.001		
Pulmonary involvement	2.6 (1.6-4.1)	< 0.001	2.3 (1.4-3.7)	< 0.001
Gastrointestinal involvement	1.7 (1.1-2.6)	< 0.007	1.5 (1.0-2.4)	0.033
General involvement	2.2 (1.4-3.5)	< 0.001		
Hypocomplementemia	1.4 (0.9-2.2)	0.084		
SDI	1.4 (1.2-1.6)	< 0.001		
GC ≥ 30 mg at baseline	1.3 (0.8-2.0)	0.200	1.5 (1.1-2.4)	0.038
Azathioprine	1.1 (0.6-1.7)	0.700		
Cyclophosphamide-IV	1.1 (0.6-1.9)	0.600		
OR, odd ratio; CI, confidence interval; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Disease Index; GC, glucocorticoids expressed as mg of prednisone/day.				

Conclusions: Almost a third of patients had serious infections during the first year of follow-up. The score performed well in predicting serious infections, similar to the original score. **Reference** [1.] Rua-Figueroa I. Lupus Sci Med. 2024;11:e001096. doi:10.1136/lupus-2023-001096.

PV231 / #297

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

THE TYPE I IFN SIGNATURE BETWEEN PATIENTS WITH RA AND SLE.

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Background/Purpose: The purpose of the research was to evaluate IFN signature in patients (pts) with SLE and RA; and the relationship between IFN signature and disease activity

Methods: The analysis included 20 pts with Rheumatoid Arthritis (RA) (18-woman (90%) and 2-man (10%), Me (IQR) age 61.5 (54-66.5) years; 113pts with SLE (99-woman (87%) and 14 men (13%), age 34 (26-41) years. The control group consisted of 20 healthy donors, comparable in sex and age with the examined patients. We selected 3 genes whose expression was studied (MX1, EPSTI1, RSAD2) to evaluate the “IFN signature”. ‘IFN signature» was calculated as the average expression value of the three selected genes (IFN score). The level of matrix metalloproteinase 3 (MMP3) in blood serum the upper limit of normal values did not exceed 19.4 ng/ml (n=30) when sera of healthy donors were examined.

Results: The baseline expression of MX1, RSAD2, EPST1, IFN score in pts with SLE and RA were significantly higher compared to healthy donors, p<0.05 (table1). RSAD 2 in pts with SLE was also significantly higher compared to RA. Table1. The baseline expression between pts with RA, SLE and healthy donors

Parametres	**Results (Pts with RA) N=20**	**Results (Pts with SLE) N=113**	**Healthy donors (N=20)**
MX 1	11.4 (5.45-19.38) *	11.3 (3.7-33.9) *	1.25 (0.8-1.6) *
RSAD 2	**5.16 (2.73-10.4) *$**	**24.3 (5.9-46.1) *$**	1 (0.69-1.79) *
EPST 1	12.8 (5.62-19.64) *	13.1 (4.7-24.5) *	1.08 (0.74-2.11) *
IFN score	10.3 (5.18-17.12) *	17.4 (3.9-37.4) *	1.13 (0.8-1.55) *

*p<0.05 between pts and healthy donors, $ p<0.05 between pts with SLE and RA
Correlations between disease activity and IFN-stimulated gene expression levels

presented in Table 2. In pts with RA, a negative correlation between INF score and IFN stimulated genes with disease activity indices (DAS28), ESR, CRP, MMP3. A positive correlation between IFN score and IFN stimulated genes with autoantibodies (ds DNA, ANA hep-2) was found in SLE pts., table2. **Table 2.**

	pts with RA (n=20)			
Parametres	MX1	EPSTI1	RSAD2	ИФН score
DAS28	r=-0,4, p=0,06	r=-0,46*		r=-0,5*
ESR	r=-0,62*	r=-0,59*		r=-0,61*
CRP	r=-0,62*	r=-0,54*		r=-0,6*
MMP-3	r=-0,58*	r=-0,5*		r=-0,58*
Parametres	**pts with SLE (n=113)**			
ds DNA		r=0,28*		r=0,28*
ANA hep-2		r=0,34*	r=0,36*	r=0,34*

*p<0,05

Conclusions: Thus, the presented results indicate increased expression of IFN stimulated genes in patients with RA and SLE compared to healthy donors. A positive correlation “IFN signature” with laboratory parameters was found in pts with SLE. The obtained negative correlation of INF signature in patients with RA is probably related to the predominance of IFN β, but this requires clarification due to the limited sampling.

PV232 / #222

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

THE RELATIONSHIP OF THE LEVEL OF ANTINUCLEAR ANTIBODIES WITH CLINICAL AND IMMUNOLOGICAL SUBTYPES OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Antinuclear antibodies (ANA) are a specific marker related to the classification criteria of systemic lupus erythematosus (SLE). The purpose of our study was evaluating ANA levels in relation to clinical and immunological subtypes of SLE.

Methods: Sera from 94 patients (pts) diagnosed with SLE (SLICC criteria, 2012), including 80 women and 14 men, age (Median, [25th;75th percentile] 31 [27;47] years, disease duration 84.0 [24.0;168.0] months were studied. The following clinical manifestations were investigated: skin/mucous membrane lesions, kidney, central nervous system, constitutional manifestations, serositis, and haematological abnormalities. ANA were determined by multiplex immunoassay (MIA) based on magnetic microspheres using BioPlex® 2200 ANA Screen test system (Laboratories Inc. Hercules, CA, USA). Positive ANA measurements corresponded to the following values: for antibodies to double-stranded (anti-ds) DNA≥10.0 IU/ml; for other ANAs (aSm, aSS-A/Ro, aSS-B/La, antibodies to nucleosomes, RibP, RNP-70) ≥1.0 AI (Antibody Index).

Results: Elevated levels of antibodies to dsDNA, nucleosomes, and RibP were detected in SLE pts with kidney damage, serositis, haematological disorders, and skin and/or mucous membrane lesions: anti-dsDNA in the group of pts with kidney damage (14.5 [7.0;68.0]), serositis (45.0 [9.0;70.0]) and haematological disorders (22.0 [9.0;70.0]); antibodies to nucleosomes in the group of pts with kidney damage (3.7 [0.5;8.0]), serositis (5.7 [0.7;8.0]) and haematological disorders (8.0 [0.7;8.0]); anti-RibP in the group of pts with skin and/or mucous membrane damage (0.3 [0.2;0.8]) and haematological disorders (0.3 [0.2;0.6]). Pts without these clinical manifestations had lower antibody levels (Table 1). For all groups, $p<0.05$.

Table 1. Correlation of ANA levels with disease activity and presence or absence of clinical manifestations

ANA/clinical manifestations	manifestations are present / no manifestations	Median [25th percentile;75th percentile]

anti-dsDNA (IU/ml)/kidney damage	n=50 / n=44	14.5 [7.0;68.0] / 7.0 [2.0; 22.0]
anti-dsDNA (IU/ml)/serositis	n=35 / n=59	45.0 [9.0;70.0] / 7.0 [2.0;15.0]
anti-dsDNA (IU/ml)/haematological disorders	n=37 / n=57	22.0 [9.0;70.0] / 8.0 [2.0; 21.0]
antibodies to nucleosomes (AI)/kidney damage	n=50 / n=44	3.7 [0.5;8.0] / 0.7 [0.2;5.35]
antibodies to nucleosomes (AI)/serositis	n=35 / n=59	5.7 [0.7;8.0] / 0.7 [0.2;7.3]
antibodies to nucleosomes (AI)/haematological disorders	n=37 / n=57	8.0 [0.7;8.0] / 0.7 [0.2;3.3]
anti-RibP (AI)/skin and/or mucous membrane lesions	n=47 / n=47	0.3 [0.2;0.8] / 0.2 [0.2;0.3]
anti-RibP (AI)/haematological disorders	n=37 / n=57	0.3 [0.2;0.6] / 0.2 [0.2;0.3]

$p<0.05$ for all cases

Conclusions: The development of the pathological process in SLE is accompanied by the formation of a wide range of autoantibodies. The presence of certain ANA is associated with different clinical and immunological subtypes of SLE and may be useful for personalisation of therapy.

PV232a / #824

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***
Late-Breaking Abstract

CAUSES OF HOSPITALIZATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AT A TERTIARY CARE CENTRE IN NEPAL

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with multisystem involvement, primarily affecting the mucocutaneous, musculoskeletal, and renal systems. Patients with SLE often require hospitalization due to disease flares, infections, or complications related to organ involvement. While extensive data exist on SLE-related hospitalizations in Western countries, similar studies from developing regions are limited. This study aims to identify the most common reasons for hospital admissions and clinical outcomes of SLE patients in a tertiary care center in Nepal.

Methods: This descriptive cross-sectional study was conducted in the Department of Internal Medicine at B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal, from November 7, 2023, to November 6, 2024. Ethical approval was obtained from the Institutional Review Committee (Reference number: 223/080/081). Patients diagnosed with SLE for at least three months, based on the Systemic Lupus International Collaborating Clinics (SLICC) criteria, were included.

Results: A total of 64 patients were analyzed, with a female predominance (96.9%) and a mean age of 32.37 ± 11.10 years. Hypertension (15.6%) and hypothyroidism (12.5%) were the most common comorbidities. The mean duration of SLE diagnosis was 61.78 ± 57.63 months. The leading causes of hospitalization were renal flare (39.1%) and infection (20.3%), followed by volume overload (9.4%), evaluation (7.8%), and hematological and neurological flares (4.7% each). The average hospital stay was 5.34 ± 3.03 days

Conclusions: Renal flares and infections were the most frequent causes of hospitalization among SLE patients. These findings align with data from developed countries, emphasizing the need for early recognition and management of these complications to reduce hospital admissions.

PV233 / #350

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

THE ASSOCIATION BETWEEN TRAUMA AND QUALITY OF LIFE IN SLE.

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Background/Purpose: In SLE, early childhood trauma and adverse childhood experiences have been associated with chronic pain, fatigue, depression, self-reported flares and incident SLE. In this study we evaluated the frequency and impact of abusive and non-abusive trauma on quality of life in SLE.

Methods: This study involved adult SLE patients (2012 SLICC or 2019 ACR/EULAR criteria) from August 2023 to April 2024. Patients completed the LupusPRO; FACIT fatigue scale; PROMIS measures for pain intensity, pain interference, self-efficacy, and psychological stress; and the Trauma History Screen. Additional trauma questions regarding emotional abuse and pregnancy loss or abortion were added. Abusive trauma was defined as physical, sexual, and emotional trauma as an adult or child. Patients were divided into 3 groups: abusive trauma, non-abusive trauma, and no trauma. Differences across groups were analyzed by Fisher's exact test or ANOVA.

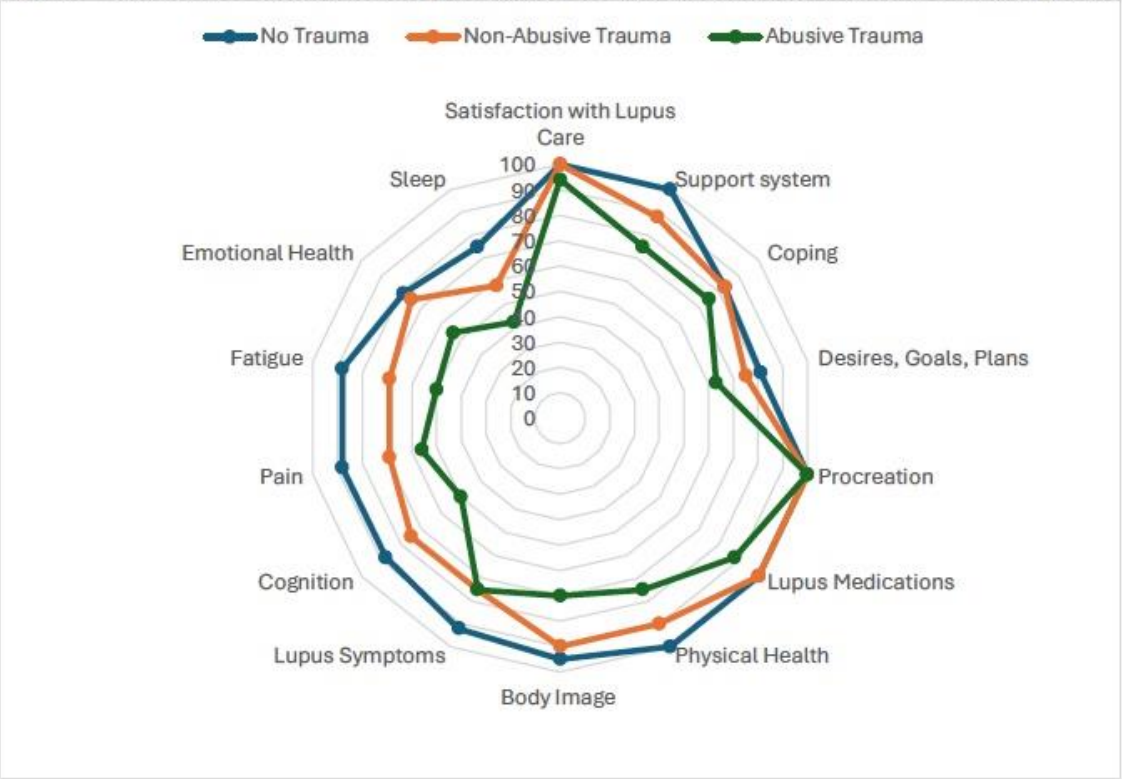
Results: In this cohort of 262 SLE patients (92% female, mean age 44 years, mean disease duration 15 years, 60% self-reported Black), the vast majority experienced at least one traumatic event (85%) with almost half suffering abusive trauma. Trauma was more common among women, with abusive trauma occurring almost exclusively in women. Education attainment was similar across groups, however a greater number of patients with abusive trauma had an annual income less than $50,000. There was a progressive increase in fatigue, pain intensity, and pain interference across the 3 groups with the highest scores in those with abusive trauma (Table 1). More than half of patients with abusive trauma reported moderate to severe levels of fatigue, pain intensity and interference in social and daily activities. Likewise, patients with trauma reported significantly more psychological stress and lower self-efficacy for managing symptoms and medications than those without trauma. When evaluating the relationship of trauma across LupusPRO, patients with abusive trauma had lower scores for sleep, physical and emotional health, pain, fatigue, cognition, body image, effects from lupus medications indicating worse health related quality of life in these

domains (Figure 1). Finally, scores for coping, desires and goals, and support system were worse in patients with abusive trauma.

Table 1. Influence of trauma on pain, fatigue, self-efficacy and stress

	No Trauma n=39	Non-Abusive Trauma n=113	Abusive Trauma n=110	p-value
FACIT Fatigue score (n=251)	38(12)	35 (11)	28 (13)	<0.0001
Fatigue (mod-severe) (n=251)	7 (19%)	38 (36%)	59 (55%)	0.0001
PROMIS Pain Intensity Score	48 (36-57)	54 (43-63)	59 (50-66)	<0.0001
Pain intensity at worst (mod-severe)	13 (33%)	69 (61%)	75 (68%)	0.0007
Pain intensity on average (mod-severe) (n=261)	10 (26%)	50 (45%)	61 (55%)	0.005
Pain intensity now (mod-severe) (n=260)	7 (18%)	25 (22%)	41 (38%)	0.01
PROMIS Pain Interference Score	50 (42-57)	57 (50-62)	61 (56-67)	<0.0001
Pain interference day-to-day activities (mod-severe)	7 (18%)	47 (42%)	66 (60%)	<0.0001
Pain interference around the home (mod-severe) (n=261)	7 (18%)	49 (44%)	65 (59%)	<0.0001
Pain interference social activities (mod-severe)	9 (23%)	42 (37%)	61 (55%)	0.0006
Pain interference household chores (mod-severe) (n=261)	10 (26%)	52 (46%)	62 (56%)	0.004
PROMIS Self-Efficacy				
Manage symptoms scores	51 (47-62)	48 (44-55)	45 (41-51)	0.0002
Manage medications scores	58 (43-58)	52 (41-58)	47 (41-58)	0.02
PROMIS psychological stress score	55 (46-63)	56 (50-62)	62 (57-68)	<0.0001

Figure 1. Influence of trauma on LupusPRO health and non-health related quality of life



Conclusions: Many patients with lupus have suffered trauma, including abusive trauma, throughout their lives and experience reduced quality of life across multiple health and non-health domains. Further, the data suggest that abusive trauma can impact the burden and severity of lupus symptoms as well the ability to manage symptoms and medications. Incorporating a trauma-informed approach to care may therefore be important in developing and delivering treatment to improve quality of life in SLE.

PV234 / #107

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

SYSTEMIC LUPUS ERYTHEMATOSUS IN A RUSSIAN COHORT: TRIGGERS AND DISEASE SEVERITY AT ONSET

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic heterogenic autoimmune disease affected by several genetic and environmental factors, whose incidence has been shown to vary with sex, ethnicity and global region. The aim of this study was to describe any provoking factors and disease severity in a Caucasian SLE cohort at the Russian rheumatology center.

Methods: This observational retrospective-prospective study included 140 patients (88% women, median aged 34 [26;41] years (median [interquartile range 25;75%]), with SLE (SLICC 2012criteria) attending a routine visit at our Clinic between February 2021 and June 2024. Disease at diagnosis was categorized as Mild, Moderate or Severe, based on SLE Disease activity index (SLEDAI-2K): SLEDAI-2K≤4 – Mild, SLEDAI-2K=5–10 - Moderate, SLEDAI-2K≥11 - High activity (Severe disease).

Results: SLE was diagnosed at median age 26[19;34] years, and the age of the first SLE manifestations was 23 [17;31] years, the period duration between the first symptoms and SLE diagnosis was 12[5;48]months. The median of SLE duration was 3 [0,3;12] years, the median of SLEDAI-2K score at the time of inclusion – 8 [4;11] score, Systemic Lupus International Collaborating Clinics damage index (SDI) – 0 [0;1] score. Positive family history of immune-inflammatory rheumatic diseases (IIRD) among the first-line relatives was found in 11% of SLE patients. In the most patients, there were no connection with any provoking factors and SLE onset - 56%, in 15% of patients - with ultraviolet radiation/insolation, in 14% - with infection, in 10% - with pregnancy, in a few patients (1-2%) - with combined oral contraceptives use, stress, vaccination and trauma. At the time of SLE diagnosis the most patients had Moderate (SLEDAI-2K=5-10 points) and Severe/high (SLEDAI-2K≥11 points) activity: 41% and 35%, respectively. Mild disease (SLEDAI-2K=0-4 points) was identified in 24% of SLE patients.

Conclusions: In the Russian cohort, as in the general population, young women predominated. SLE was diagnosed about a year after the first manifestations. In the

majority of cases, there was no specific trigger factor, the most frequently identified were: positive family history of IIRD, ultraviolet radiation/insolation, infections and pregnancy. In 76% of SLE patients the disease onset was characterized by moderate and high severity.

PV235 / #105

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

CLINICAL MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A RUSSIAN COHORT: FROM THE FIRST SYMPTOM TO FOLLOW-UP

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Background/Purpose: The aim of this study was to analyze the phenotype of systemic lupus erythematosus (SLE) starting from the first manifestation and during follow-up since the diagnosis of SLE in a Caucasian cohort at the Russian rheumatology center

Methods: This observational retrospective-prospective study included 140 patients (88% women, median aged 34 [26;41] years (median [interquartile range 25;75%]), with SLE (SLICC 2012) attending a routine visit at our Clinic between February 2021 and June 2024.

Results: SLE was diagnosed at median age 26 [19;34] years, and the age of the first SLE manifestations was 23 [17;31] years, the period duration between the first symptoms and SLE diagnosis was 12 [5;48] months. The median disease duration at last follow-up was 3 [0,3;12] years, SLEDAI-2K at the time of inclusion – 8 [4;11] score, Systemic Lupus International Collaborating Clinics damage index (SDI) – 0 [0;1] score. The first symptoms of SLE were: inflammatory arthritis - 40%, cutaneous lupus-34%, hematological disorders - 6%, nephritis - 5%, serositis -1%, nervous system involvement-1%, mucosal ulcers - 1%. Among 'non-criteria' symptoms the most common were: unexplained fever - 6%, interstitial lung disease - 3%, lymphadenopathy - 2%, Raynaud's phenomenon - 1%. During the period of follow-up of patients with diagnosed SLE, the frequency of clinical manifestations changed cumulatively: inflammatory arthritis - 92%, hematological disorders - 81%, cutaneous lupus - 77%, serositis - 46%, alopecia - 45%, nephritis - 44%, mucosal ulcers - 35%, nervous system involvement - 14%. Among 'non-criteria' symptoms the most common were: unexplained fever - 67%, lymphadenopathy - 42%, Raynaud's phenomenon - 26%, interstitial lung disease - 13%, ulcerative necrotising vasculitis - 11%, myocarditis - 2%.

Conclusions: The first SLE symptoms can be either criterion or "non-criterion" in accordance with SLICC 2012, the most common being arthritis/arthralgia, skin lesions and cytopenias. Nephritis, serositis and unmotivated fever were more common in the follow-up SLE period in our cohort, in contrast to other Caucasians.

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Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A META-ANALYSIS OF OVERALL AND CAUSE-SPECIFIC EFFECTS

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Background/Purpose: While therapeutic advancements have markedly refined the management of systemic lupus erythematosus (SLE), SLE patients persistently face mortality rates significantly higher—by two to fivefold—than the general population. Persistent concerns about mortality rates necessitate a thorough appraisal of mortality trends within this complex patient cohort. The objective of this study was to assess the overall and cause-specific standardized mortality ratios (SMRs) among patients with SLE.

Methods: An exhaustive systematic review was undertaken, encompassing studies that scrutinized SMRs, both overall and for specific causes, in patients diagnosed with SLE compared to the general populace. The databases of PUBMED, EMBASE, and Cochrane were meticulously searched to collate relevant literature. Following this comprehensive search, a meta-analysis was executed to methodically assess all-cause, sex-specific, ethnicity-specific, and cause-specific SMRs in patients with SLE.

Results: The inclusion criteria were met by twenty-nine studies encompassing 72,342 patients with SLE and documenting 7,352 deaths. The meta-analysis disclosed a pronounced 2.87-fold elevation in the SMR for all-cause mortality in SLE patients relative to the general population (SMR, 2.866; 95% confidence interval [CI], 2.490–3.242; $p < 0.001$). Region-specific assessments showed variable all-cause SMRs, with Europe reporting 2.607 (95% CI, 1.939–3.275; $p < 0.001$), Asia revealing 3.043 (95% CI, 2.082–4.004; $p < 0.001$), and particularly high SMRs noted in North America and Oceania. Gender-focused analyses presented a pooled SMR of 3.261 (95% CI, 2.674–3.848; $p < 0.001$) for females, and 2.747 (95% CI, 2.190–3.304; $p < 0.001$) for males. Evaluations specific to cause of death illustrated notably elevated SMRs for renal disease (SMR, 4.486; 95% CI, 3.024–5.948; $p < 0.001$), infections (SMR, 4.946; 95% CI, 4.253–5.639; $p < 0.001$), cardiovascular diseases (CVD) (SMR, 2.931; 95% CI, 1.802–4.061; $p < 0.001$), cerebrovascular accidents (CVA) (SMR, 1.588; 95% CI, 0.647–2.528; $p = 0.001$), and cancer (SMR, 1.698; 95% CI, 0.871–2.525; $p < 0.001$).

Conclusions: This meta-analysis shows a significant 2.87-fold elevation in the SMR among patients with SLE compared to the general population, transcending differences in sex or geographical regions. Moreover, an appreciable increase in mortality due to specific causes, including renal disease, infection, CVD, CVA, malignancy, and

neuropsychiatric SLE, accentuates the imperative for targeted interventions to mitigate these elevated risks in SLE patients.

PV237 / #247

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

QUALITATIVE PATIENT INTERVIEW STUDY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS TO ASSESS PATIENT PERCEPTION OF FATIGUE AND SKIN-RELATED SYMPTOMS

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder that disproportionately impacts women of childbearing age. Although the incidence varies widely based on ethnic and geographic differences, approximately 204,000 persons in the US had SLE in 2018. To understand the nature and relative importance of skin symptoms, evaluate the content validity of the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale in SLE, and assess what constitutes meaningful change in SLE-related fatigue and skin symptoms, this qualitative study interviewed individuals with SLE.

Methods: In August 2023, individual interviews were conducted in the US in adults who reported receiving a diagnosis of SLE at least 6 months prior to screening and who experienced SLE-related fatigue, fever, joint pain, and/or skin rash/redness in the 30 days prior to their interview. Each 60-minute virtual interview was conducted in English in a semistructured format, using an interview guide to encourage response spontaneity and to ensure consistent, systematic data collection. Study participants described their experience of SLE-related fatigue and skin symptoms and what constituted minimal meaningful improvement in each symptom, using the Patient Global Impression of Severity (PGIS) and Patient Global Impression of Change (PGIC) scales. Cognitive debriefing and content validity of SLE-related fatigue were elicited using the 13-item FACIT-Fatigue scale. All diagnoses were self-reported.

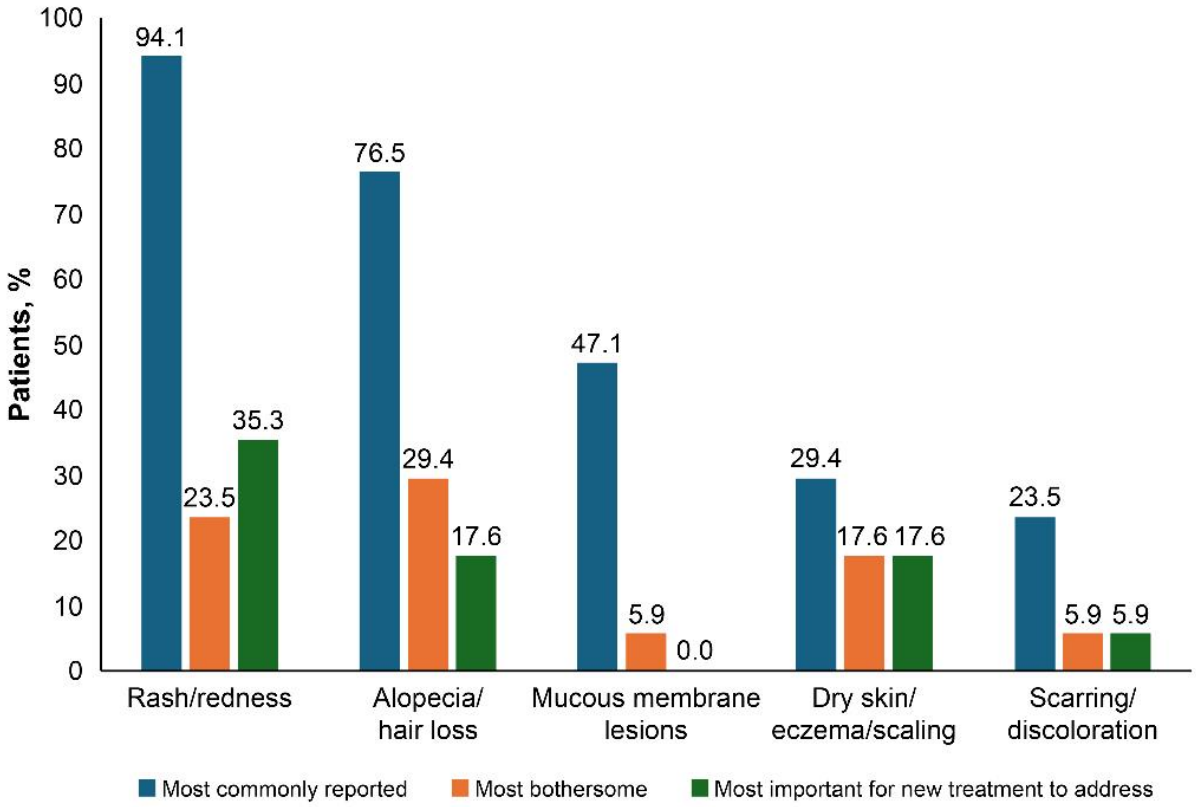
Results:

Table. Self-reported demographics and clinical characteristics

Parameter	Total (N=18)
Age, years	
Mean (SD)	51.7 (10.6)
Range	33–67
Female, n (%)	17 (94.4)
Race, n (%)	
White	9 (50.0)
Black	5 (27.8)
Hispanic	3 (16.7)
Alaskan Native or American Indian/Native American	1 (5.6)
Time since SLE diagnosis, years	
Mean (SD)	12.2 (10.1)
Range	1–37

SD, standard deviation; SLE, systemic lupus erythematosus.

Figure. Percentage of patients with systemic lupus erythematosus who reported experiencing skin symptoms (n=17)



The 18 participants interviewed had a mean age of 51.7 years (range, 33–67), 94.4% (n = 17) were female, and 50.0% (n = 9) were White (Table). Mean time since the clinical diagnosis of SLE was 12.2 years (range, 1–37). All but 1 participant reported

experiencing SLE-related fatigue prior to or near the time of SLE diagnosis. This SLE-related fatigue was described as tiredness/exhaustion that sleeping does not help, lack of energy, feeling sluggish/heavy, and/or needing to rest/sleep during the day. Most participants (94.4%; n = 17) were able to understand and answer all items without difficulty. Most participants (72.2%; n = 13) also indicated that even a 1-point improvement in fatigue on the PGIS would be meaningful. Among participants reporting SLE-associated skin symptoms (n = 17), rash/redness and alopecia/hair loss were the most frequently reported, most bothersome, and/or most important symptoms to be addressed by a new treatment (Figure). All participants understood the skin-specific PGIS and PGIC items without difficulty. Overall, 82.4% (n = 14) indicated that a 1-point improvement on the PGIS would be meaningful, while 70.6% (n = 12) indicated that "a little better" on the PGIC would represent meaningful improvement in skin symptoms.

Conclusions: These results support the content validity of the FACIT-Fatigue scale in SLE and suggest that even minimal improvement in fatigue and skin symptoms are meaningful to patients. New treatment options that can alleviate fatigue and skin symptoms are needed for patients with SLE.

PV238 / #532

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

SLE AT THE TURN OF THE THIRD MILLENNIUM: HOW DISEASE MANAGEMENT HAS CHANGED IN CLINICAL PRACTICE

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Background/Purpose: Background With the new millennium major changes have occurred in the management of lupus, these encompass the optimization of the use of old drugs, the identification of therapeutic targets such as LLDAS and remission and the introduction of new drugs such as biologics. The aim of the present study was to analyse how the new treatment paradigm impacted on the management of SLE over time in the real life setting.

Methods: This is a retrospective observational study on SLE patients regularly followed at our unit and with a follow-up of at least 1 year; patients were divided in two groups: group 1 including patients diagnosed between 1980 and 2000 and group 2 those diagnosed after 2000. Ddemographic characteristics, clinical manifestations at disease onset and cumulative organ involvement, disease activity, organ damage and disease state over time and treatments received were compared.

Results: 428 SLE patients were included in the study, 377 females (88%), 143 patients in Group 1 (33.4%) and 285 (66.6%) in group 2. Presenting symptoms were similar between the two groups, while over the entire disease course we found a higher frequency of renal involvement (54% vs 40%) and neuropsychiatric involvement (17% vs 6%) in patients diagnosed before 2000. As far as therapy is concerned, almost all patients received GC during their disease course although in group 2 we found 11 patients who did never take GC (4%, p=0.02). Longitudinal analysis of the GC cumulative dose showed similar doses during the first year of the disease; however, at 5 and 10 years after diagnosis group 1 received significantly higher dosages (median 8.7 g vs 7.6g and 15.35g vs 14g respectively, p<0.001 in both analyses). Interestingly, a higher percentage of patients was GC-free at 5 years from diagnosis in the group diagnosed after 2000 (29.4% vs 6.6%). 394 patients received HCQ during the disease course (93.5%), a higher proportion of patients in group 2 although not statistically different (95% vs 90%). The proportion of patients who received at least one IS drug within the first year of follow-up was significantly higher in patients diagnosed after 2000 (60.7% vs 39%, p<0.001) Overall, 129 patients received at least on biological drug (30%), with a significantly higher proportion in group 2 (34% vs 22%, p=0.01). In group 2, 22 (8%) patients received a biological treatment within the first year since diagnosis. At 1 year

from diagnosis remission resulted more frequently achieved in patients diagnosed after 2000 (57% vs 46% respectively, p=0.03). Overall 9.7% of patients developed at least one item of the SLICC/DI within the first year from diagnosis (median SDI=1, range 1-3); 17.7% within 5 years (median SDI= 1, range 1-5) and 32.6% within 10 years (median SDI=1, range 1-6). The median damage score over time was similarly very low in both groups. The occurrence of renal damage (RD), cardiovascular events (CVE) and osteoporotic fractures did not show statistically significant differences between the two groups.

Conclusions: The study highlights how the clinical management of SLE patients has changed in recent years by incorporating the new treatment paradigm based on the early use of immunosuppressive drugs and steroid sparing strategies, resulting in more effective disease control.

PV239 / #27

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) DIAGNOSTIC CHALLENGES, CLINICAL MANIFESTATIONS, AND PATIENT OUTCOMES.

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Background/Purpose: The purpose of this study is to research the diagnostic difficulties, different clinical manifestations, and patient results related with Systemic Lupus Erythematosus (SLE). The study aims to provide insights for enhancing patient quality of life and disease management by thoroughly analyzing these aspects.

Methods: A deliberate survey of the review was conducted, coordinating on recent advancements in the diagnosis, clinical presentation, and management of SLE. Information was gathered from peer-looked journals, clinical rules, and contextual investigations. Accentuation was put on recognizing diagnostic criteria, figuring out the scope of clinical manifestations, what's more, assessing the elements impacting patient results.

Results: The review highlighted several key discoveries: 1. Diagnostic Challenges: Due to SLE heterogeneity and symptoms overlap with other diseases, SLE diagnosis is complex. The American College of Rheumatology (ACR) and Systemic Lupus International Collaborating Clinics (SLICC) standards, along with serological tests for autoantibodies (e.g., anti-dsDNA, anti-Sm), are vital however not conclusive, requiring a thorough approach. 2. Clinical Manifestations: SLE has a wide range of symptoms that affect multiple organ systems: Cutaneous: photosensitivity, discoid rash, Malar rash. Musculoskeletal: Myopathy and Arthritis. Renal: Hematuria, proteinuria, and lupus nephritis Neurological/Psychiatric: Mood disorders, cognitive dysfunction, seizures, and psychosis Cardiopulmonary: Pericarditis, myocarditis, pleuritis, pneumonic hypertension. The hematology: Thrombocytopenia, anemia, and leukopenia 3. Patient Outcomes: Advancements in immunosuppressive treatments like corticosteroids, biologics like rituximab and belimumab), and early intervention have led to a better prognosis. However, due to its chronic nature, organ damage, and comorbidities (such as cardiovascular disease, infections, and osteoporosis), SLE continues to be associated with significant morbidity and mortality.

Conclusions: The diagnosis and various clinical manifestations of systemic lupus erythematosus have a significant impact on patient outcomes. Advances in diagnostic techniques and designated treatments have improved disease management, however progressing research is vital to enhance early diagnosis, and overall patient quality of

life. Furthermore, generally understanding personal satisfaction. Integrating genetic, immunological, and clinical data will be crucial in achieving these objectives.

PV240 / #328

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

PERFORMANCE OF THE 2019 EULAR/ACR AND 2012 SLICC CLASSIFICATION CRITERIA FOR SLE AS DIAGNOSTIC CRITERIA

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Background/Purpose: 2019 EULAR/ACR SLE criteria were validated for classification from cases of established SLE compared to other diseases (sensitivity 0.96 (0.95 - 0.98); specificity 0.93 (0.91 - 0.95))[1], but have not been assessed as diagnostic criteria in an undiagnosed cohort of ANA positive patients clinically suspected to have SLE. The aim is to evaluate, in these patients, the performance of 2019 EULAR/ACR SLE criteria against consultants' diagnosis of SLE after 3 years follow-up and consultants' treatment decision.

Methods: We included all consecutive consenting patients with ANA positive ≥ 1:80, new symptoms of ≤ 1 year, and SLE treatment naïve who had been referred to a specialist lupus clinic from primary care. 2019 EULAR/ACR SLE criteria and 2012 SLICC criteria were evaluated by research fellows at the time of the enrollment (T0) and evaluated annually, or on additional visits, during a 3-years follow-up. Clinical charts (at T0, and at the visit in which patients met classification criteria or last follow up visit for those who did not meet them, T1) were anonymized and any documented diagnosis was redacted. Charts were reviewed by 4 consultants who had been independent of the patients' clinical care to assess the diagnosis as well as confidence in diagnosis and suggested treatment decision. Inter-rater agreement was analysed by Cohen's k.

Results: 141 patients were included. Table 1 reports baseline characteristics. At T1, SLE was diagnosed by consultants in 26 patients (18.4%); a moderate inter-rater agreement was observed (k=0.52; CI 0.31–0.72). The 2019 EULAR/ACR classification criteria were met in 36 patients (26%) and the 2012 SLICC criteria in 33 patients (23.4%). Other consultants' diagnoses were: Undifferentiated CTD (UCTD, 19.1%), Sjögren's Disease (SjD, 8%), inflammatory arthritis (IA, 3.5%). Table 2 reports sensitivity, specificity, PPV, NPV of the 2019 EULAR/ACR SLE and 2012 SLICC criteria. At T1, in 21 patients (14.8%) SLE diagnosis was agreed by the consultants and 2019 EULAR/ACR SLE criteria;

consultants' suggested treatments for these patients were: immunosuppressant (IS) +/- hydroxychloroquine (HCQ) in 11 cases (52.4%), HCQ alone in 9 (42.8%), and no treatment in 1 (4.8%). In 5 patients (3.5%) SLE was diagnosed by consultants but not classified by the EULAR/ACR SLE criteria; the suggested treatment from the consultants were: IS in 3 cases (60%), HCQ in 2 (40%). In 15 patients where 2019 EULAR/ACR criteria were met, consultants did not diagnose SLE (10.6%); consultants' diagnoses were: SjD (40%), UCTD (33.3%), IA (26.7%%); treatment were: 7 HCQ (46.7%; in 1 case with im steroid), 5 IS (33.3%), 1 im steroid (6.7%) and no treatment in 2 (13%). In addition to the analyses above, at T0, the consultants diagnosed 11 patients who did not meet EULAR/ACR criteria as SLE. But at T1, 6/11 (55%) of these were subsequently classified as SLE. Thus, SLE could be diagnosed earlier than using classification criteria in some patients.

Table 1: Features at baseline

Characteristics	
Age (median, IQR)	48 (IQR 36-57) years
Female	125/141 (88.7%)
Caucasians	102/141 (72.7%)
Family History of RMD	46/141 (32.6%)
Anti-dsDNA positive	54/141 (38.3%)
Low C3 and/or C4	7/141 (5.0%)

Table 2: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value

	EULAR/ACR 2019 SLE criteria	SLICC 2012 criteria
Sensitivity % (95% CI)	80.8% (60.7 – 93.5)	76.9% (56.4 – 91.0)
Specificity	87.0% (79.4 – 92.5)	88.7% (81.4 – 93.8)
Positive Predictive Value	58.3% (45.7 – 69.9)	60.6% (46.9 – 72.8)
Negative Predictive Value	95.2% (90.1 – 97.8)	94.4% (89.4 – 97.2)
Accuracy	85.8% (79.0 – 91.1)	86.5% (79.8 – 91.7)

Conclusions: When used in a diagnostic setting, the performance of 2019 EULAR/ACR SLE criteria was less good than for classification. Patients meeting classification criteria were usually clinically diagnosed as SLE as well, but some patients with a consultant diagnosis of SLE did not meet criteria and in these cases, treatment decisions were similar to those meeting criteria. Classification criteria should be used with caution for the diagnosis when evaluating patients with suspected SLE. Future work will analyse a second cohort. **References:** 1 Aringer M, et al.ARD 2019 Sep;78(9):1151-1159.

PV241 / #806

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***
Late-Breaking Abstract

THE IMPACT OF CUMULATIVE ANEMIA EXPOSURE ON THE RISK OF RENAL DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that can involve multiple organ systems, including the kidneys, blood, and skin. Lupus Nephritis (LN) is the most severe complication of SLE, with treatment objectives aimed at preventing chronic kidney disease (CKD) and End-Stage Renal Disease (ESRD), optimizing quality of life, and improving survival. Anemia is the most common hematologic complication in SLE and is closely associated with disease activity, multi-organ dysfunction, and particularly the progression of renal damage. However, mild to moderate anemia has long been neglected in the diagnosis and management of SLE, and there is limited research on the impact of cumulative anemia exposure on renal damage in SLE patients. This study aims to utilize 12 years of natural follow-up data from SLE patients at Xiangya Hospital to conduct a real-world retrospective cohort study investigating the impact of cumulative anemia exposure on the risk of renal damage in SLE patients.

Methods: A study cohort was established using data from SLE patients with confirmed diagnoses who were treated at Xiangya Hospital between January 2010 and June 2022. Longitudinal hemoglobin (Hb) concentration data were used to construct hemoglobin concentration-time curves, and variables such as average hemoglobin concentration, proportion of anemia duration, and cumulative anemia exposure were defined. New-onset CKD and ESRD were selected as outcome indicators for survival analysis. Multivariable Cox regression models were employed to explore the effects of these anemia-related variables on the development of CKD and ESRD in SLE patients, with adjustments made for known renal prognostic risk factors. Subgroup analyses were conducted for LN patients. Sensitivity analyses examined the relationship between the proportion of mild, moderate, and severe anemia duration and the risks of CKD and ESRD. Restricted cubic spline Cox regression models were used to investigate the dose-response relationships between cumulative anemia exposure variables and the risks of CKD and ESRD.

Results: A total of 2,361 SLE patients were included in the study, with 88.1% being female. The median age was 33 years, and the median follow-up time was 57.5 months. Among these patients, 52% had LN, and the baseline mean estimated glomerular filtration rate (eGFR) was 98.5 ± 27.8 mL/min/1.73 m^2. Cox analysis revealed that an average hemoglobin concentration below the anemia threshold increased the risk of CKD by 6.18-fold and ESRD by 14.14-fold in SLE patients. Cumulative anemia exposure greater than 0 was associated with a 2.24-fold increased risk of CKD and a 9.46-fold increased risk of ESRD. Among LN patients, the associations between average hemoglobin concentration, cumulative anemia exposure, and the risks of CKD and ESRD were more pronounced. Sensitivity analyses showed that a proportion of moderate anemia duration greater than 0 significantly increased the risks of CKD and ESRD in both SLE and LN patients. Restricted cubic spline analysis indicated that the risks of CKD and ESRD increased with longer anemia duration and greater cumulative anemia exposure.

Conclusions: Prolonged anemia exposure is strongly associated with renal damage. Reducing the duration of moderate anemia and cumulative anemia exposure may serve as effective targets for improving renal outcomes in SLE patients.

PV242 / #5

Poster Topic: ***AS23 - SLE-Diagnosis, Manifestations, & Outcomes***

COMPREHENSIVE IMMUNOPROFILING OF PERIPHERY BLOOD IDENTIFIES KEY IMMUNE FEATURES ASSOCIATED WITH DISEASE PROGRESSION AND PATIENT STRATIFICATION OF SLE

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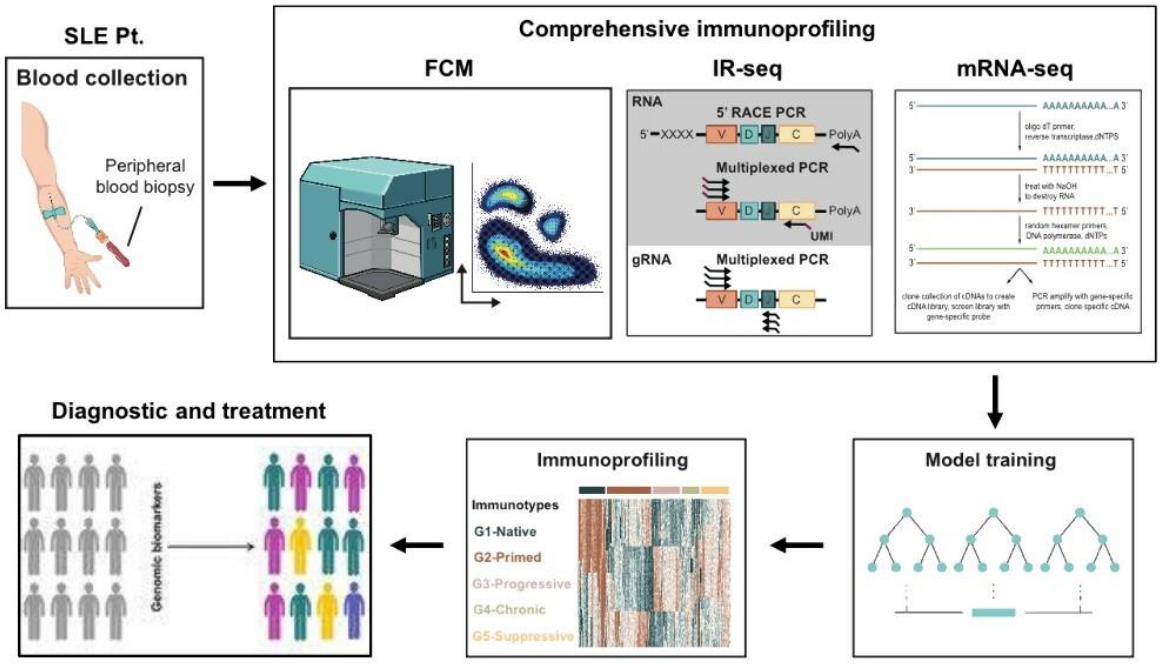
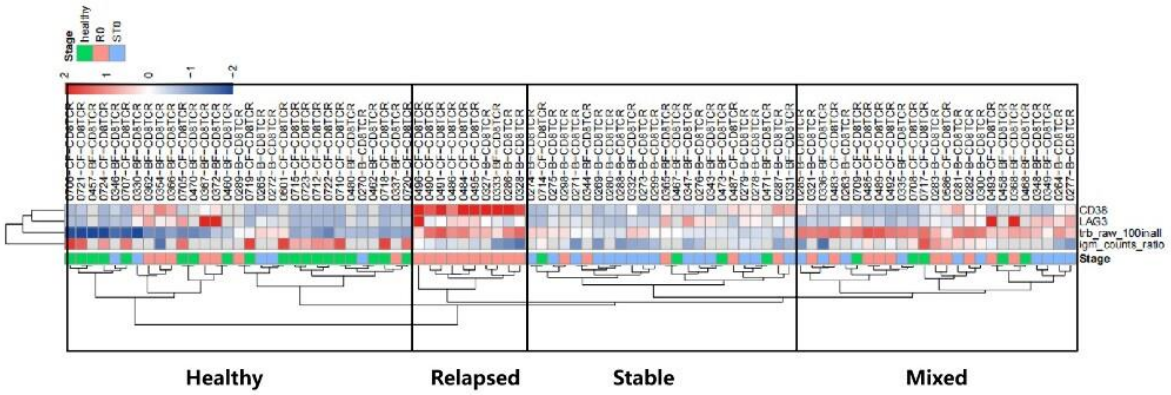
Background/Purpose: Background: To advance the development of immune biomarkers for diagnosing and treating Systemic Lupus Erythematosus (SLE), we have established a robust evaluation platform that integrates immune repertoire sequencing, T cell subtype profiling, and transcriptional sequencing.

Methods: Methods: This platform facilitates a systematic exploration of the peripheral immune status of SLE patients,such as TCR, BCR, bulk RNA-seq and flow cytometry. Then we compare these immune characteristics with status of SLE patients, which are associated with their clinical conditions. Fig 1 The flowchart of this study.



Results: Results: Notably, we observed significant clonal expansion, loss of naive T cells, and heightened activation and stress in both CD8+ and CD4+ T cells, suggesting a critical role of T cells in the pathogenesis of SLE. Furthermore, our analysis identified unique features in the immune repertoires of SLE patients compared to healthy donors, such as differential TRV-TRJ usage and the presence of public clones, which could serve as early diagnostic markers for SLE. For B cells, we identified a notable isotype switching and a prevalent usage of IgHV-IgHJ gene segments. This finding highlights the

dynamic adaptability of the B cell compartment in response to autoimmune challenges.By integrating several immune indices, we have developed a novel approach to categorize SLE patients into groups based on their adaptive immune activity, which shows a partial correlation with their disease status. Moving forward, we aim to amalgamate all gathered immune profiling data and apply cutting-edge analytical techniques, including machine learning, to discern various immunotypes. Fig 2. The model to categorize SLE patients into groups based on their adaptive immune activity



Conclusions: Conclusion: This stratification will enhance our ability to diagnose and tailor treatments for SLE patients to achieve favorable prognosis. Our study not only sheds light on the complexities of the immune system in SLE but also demonstrates the potential of comprehensive immunoprofiling in enhancing patient management in this challenging autoimmune disorder.

PV243 / #243

Poster Topic: ***AS24 - SLE-Treatment***

REAL WORLD OBSERVATIONAL STUDY OF ANIFROLUMAB IN ADULT SYSTEMIC LUPUS ERYTHEMATOSUS: SINGLE CENTER EXPERIENCE FROM THE UNITED ARAB EMIRATES

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multiorgan organ damage, drug-related toxicities related to prolonged treatment, and early mortality [1]. Anifrolumab, a human monoclonal antibody targeting the type I interferon receptor, was approved in 2021 for the treatment of moderate to severe SLE [2]. However, its efficacy and safety profile has not yet been described in our region. In this study, we assessed the efficacy and safety of anifrolumab in an Arab population at a tertiary care center in the United Arab Emirates.

Methods: Patients with SLE were identified from the hospital's electronic database between April 2015 and October 2024. Those aged 18 years or older who were receiving anifrolumab were included in the study. Data collected encompassed sociodemographic details, clinical features, SLE organ involvement, laboratory findings, previous and current medications along with their adverse effect profiles, and disease activity indices. Serial measurements of C3, C4, dsDNA, SLEDAI-2k, CLASI-A, and CLASI-D, as well as adverse effects related to anifrolumab, were tracked over a 12-month period. Descriptive statistics were used for data analysis.

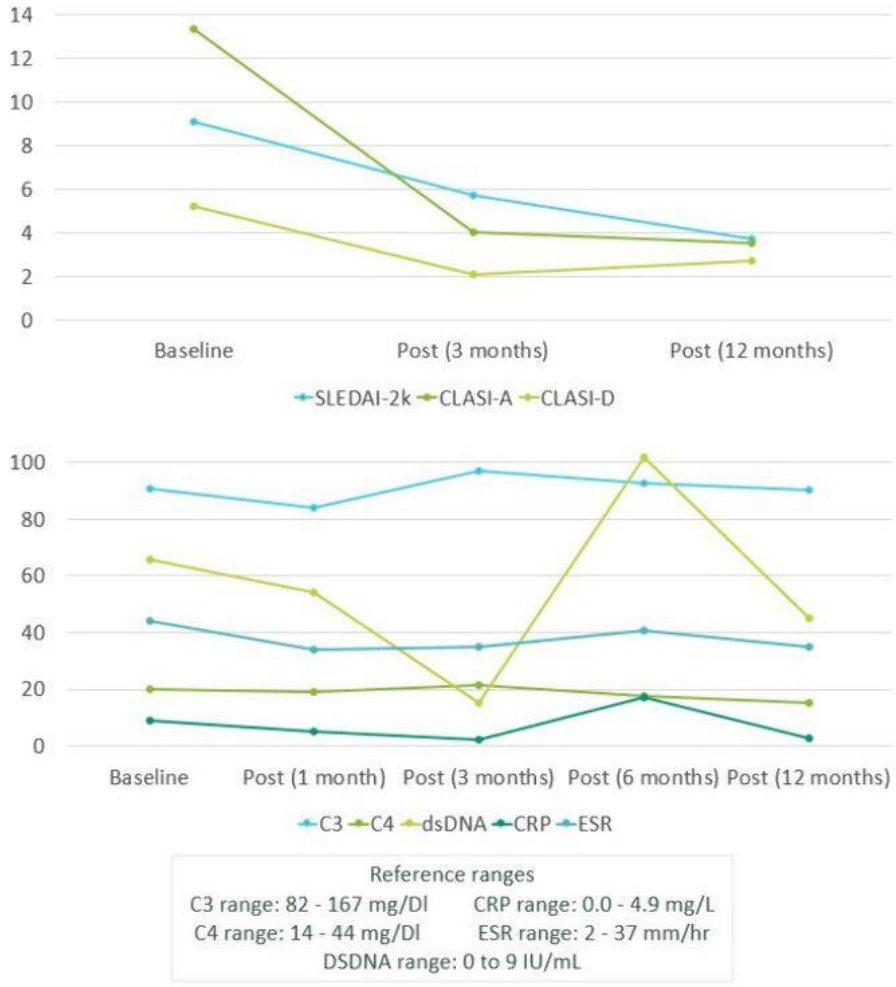
Results: We identified 21 patients with SLE who were treated with anifrolumab. The majority were Emirati nationals (76%) and predominantly female (86%). The mean age at SLE diagnosis was 29.4 ± 10.5 years, with a mean age of presentation to the clinic of 32.8 ± 10.5 years, and an average disease duration of 94 ± 75.2 months. Non-SLE dermatological conditions included cystic acne (3 patients), alopecia areata (2 patients), atopic dermatitis (1 patient), and seborrheic dermatitis (1 patient). The most commonly affected SLE domains were mucocutaneous (71%), musculoskeletal (67%), hematological (57%), renal (14%), and neurological (14%). Serological results showed positive ANA in 76%, anti-Smith in 43%, SSA in 62%, and SSB in 19%. Anifrolumab treatment was initiated at a mean age of 36.4 ± 11.6 years and continued for an average

of 9 ± 4.9 months. Concurrent therapies included hydroxychloroquine (67%), prednisolone (29%) with a mean dose of 7 ± 3.5 mg, azathioprine (24%), and mycophenolate mofetil (24%). Two patients reported minor adverse effects in the form of upper respiratory tract infections after starting anifrolumab, but did not require discontinuation of the medication (**Table 1**). Baseline laboratory values included mean C3 (91 ± 22.5 mg/dL), C4 (19 ± 10.3 mg/dL), dsDNA (65 ± 102.4 IU/mL), CRP (9 ± 16.9 mg/L), and ESR (46 ± 27.9 mm/hr). Baseline disease activity scores were SLEDAI-2k (8.9 ± 3.1), CLASI-A (11.8 ± 6.9), and CLASI-D (3.8 ± 6.5). At the 12-month follow-up, disease activity scores showed numerical improvement with SLEDAI-2k (3.7 ± 1.7), CLASI-A (3.5 ± 2.2), and CLASI-D (2.7 ± 3.3) (**Figure 1**).

Demographic and clinical characteristics of patients with SLE treated with anifrolumab (n = 21)	
Nationality (n, %)	
Emirati	*16, 76*
Non-Emirati	*5, 24*
Gender (n, %)	
Female	*18, 86*
Male	*3, 14*
BMI (kg/m^2, mean ± SD)	24.8 ± 4.9
Age at time of SLE diagnosis (years, mean ± SD)	29.4 ± 10.5
Age at presentation to clinic (years, mean ± SD)	32.8 ± 10.5
SLE disease duration (months, mean ± SD)	94 ± 75.2
Completed varicella zoster vaccination (n, %)	7, 33
Comorbidities (n, %)	
Tuberculosis	*2, 10*
Herpes zoster	*1, 5*
Diabetes mellitus	*1, 5*
Hyperparathyroidism	*3, 14*
Thyroid disease	*5, 19*
Osteoporosis	*2, 10*
Hypertension	*3, 14*
Hyperlipidemia	*5, 24*
Chronic kidney disease	*1, 5*
Asthma	*3, 14*
Depression	*4, 19*
Fibromyalgia	*3, 14*
Non-SLE dermatological conditions (n, %)	
Cystic acne	*3, 14*
Atopic dermatitis	*1, 5*
Seborrheic dermatitis	*1, 5*
Alopecia areata	*2, 10*
SLE organ domain involvement	
Ocular (n, %)	1, 5
Mucocutaneous (n, %)	15, 71
Acute cutaneous lupus	*3, 20*
Subacute cutaneous lupus	*4, 27*
Chronic cutaneous lupus	*8, 54*
Musculoskeletal (n, %)	14, 67
Arthritis	*7, 50*
Arthralgia	*14, 100*

Hematological (n, %)	12, 57
Anemia of chronic disease	*3, 25*
Leukopenia	*9, 75*
Idiopathic thrombocytopenia purpura	*1, 8.3*
Neurological (n, %)	3, 14
Headache	*2, 67*
Peripheral neuropathy	*2, 67*
Respiratory (n, %)	2, 10
Pulmonary embolism	*1, 50*
Pleural effusion	*2, 100*
Pleuritis	*2, 100*
Cardiac (n, %)	2, 10
Myocarditis	*1, 50*
Pericardial effusion	*1, 50*
Pericarditis	*1, 50*
Renal (n, %)	3, 14
Lupus nephritis III	*1, 5*
Lupus nephritis IV	*2, 10*
Lupus nephritis V	*1, 5*
Overlap syndromes (n, %)	
SLE and Sjogren's disease	*7, 33*
SLE and antiphospholipid syndrome	*4, 19*
Serologies (n, %)	
ANA	*16, 76*
Anti-Smith	*9, 43*
SSA	*13, 62*
SSB	*4, 19*
Topical treatment (n, %)	
Mometasone	*5, 24*
Clobetasol	*4, 19*
Triamcinolone	*2, 10*
Pimecrolimus	*3, 14*
Tacrolimus	*5, 24*
Previous therapy prior to anifrolumab (n, %)	
Prednisolone	*13, 62*
Hydroxychloroquine	*20, 95*
Methotrexate	*8, 38*
Cyclophosphamide	*1, 5*
Mycophenolate mofetil	*7, 33*
Belimumab	*7, 33*
Rituximab	*3, 14*
Adverse events due to non-anifrolumab therapy (n, %)	10, 48
Hair loss	*1, 10*
Ocular changes	*2, 20*
Elevated liver function tests	*2, 20*
Gastrointestinal upset	*3, 30*
Lower extremity pain	*1, 10*
Steroid-induced psychosis	*1, 10*
Steroid-induced avascular necrosis	*1, 10*
Age at time of anifrolumab initiation (years, mean ± SD)	36.4 ± 11.6

Adjunct therapy to anifrolumab (n, %) *Prednisolone* *Average prednisolone dose (mg, mean ± SD)* *Hydroxychloroquine* *Azathioprine* *Mycophenolate mofetil* *Belimumab*	 *6, 29* *7 ± 3.5* *14, 67* *5, 24* *5, 24* *1, 5*
Duration on anifrolumab (months, mean ± SD)	9 ± 4.9
Adverse events post-anifrolumab (n, %) *Upper respiratory tract infection*	2, 10 *2, 100*



Conclusions: Anifrolumab was well tolerated, showing consistent improvements in disease activity scores across multiple organ domains over a 12-month follow-up period.

PV244 / #178

Poster Topic: *AS24 - SLE-Treatment*

ANIFROLUMAB EFFECTS ON RESPONSE TO INFLUENZA VACCINE IN SLE

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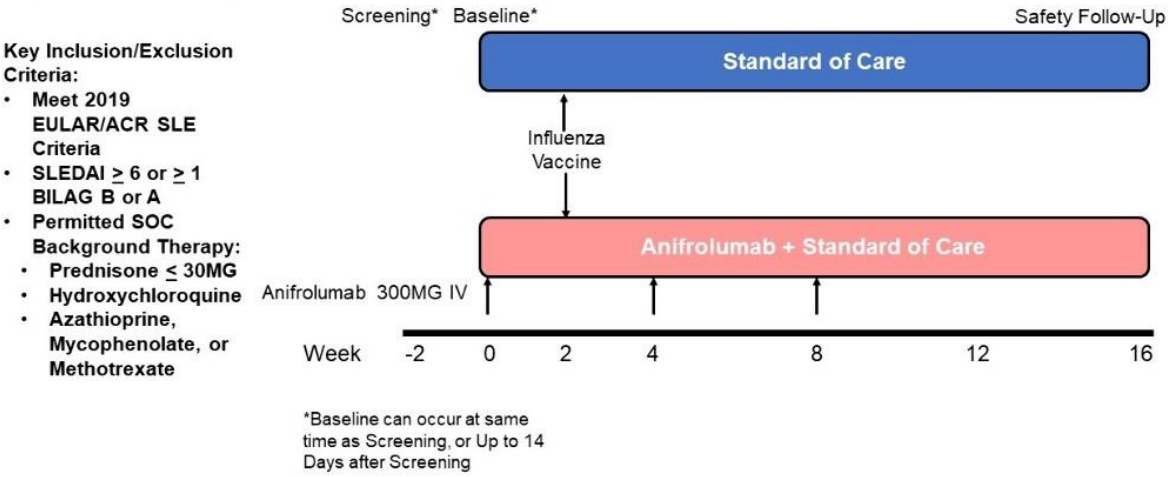
Background/Purpose: Risk for infections in systemic lupus may arise from immunosuppressant treatments or intrinsic immune defects. Disordered interferon signals are a hallmark of SLE. Anifrolumab, which targets the Type I Interferon Receptor (IFNAR), has been found to be safe and effective but, not surprisingly, inhibition of interferon signals is associated with some viral infections and herpes zoster reactivation. We previously reported a relationship between interferon activation and suppressed response to influenza vaccine [#]. The current study examined hemagglutinin inhibition and anti-influenza vaccine antibodies after the administration of flu vaccine in SLE patients on anifrolumab.

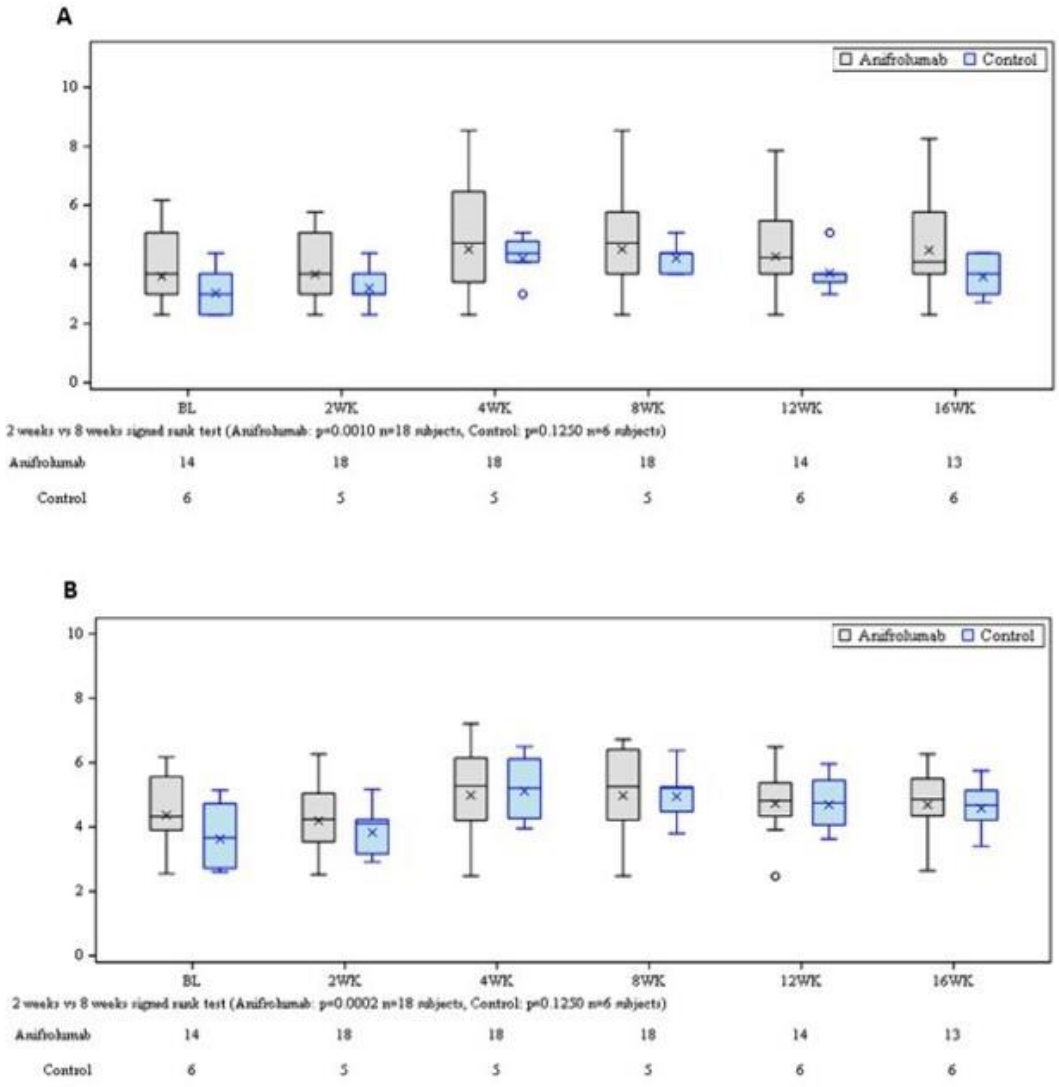
Methods: Between 2020 and 2023, 18 patients with active, moderate to severe SLE received 3 monthly doses of open label anifrolumab 300 mg IV. Two weeks after dose 1, an FDA-approved quadrivalent, season-specific influenza vaccination was given, In the third season (2022-23), 6 additional SLE patients participated in the protocol without receiving anifrolumab. All patients continued standard of care treatment (SOC) [1]. Vaccine response was quantified with a hemagglutinin inhibition assay (HAI) using predominate antigen of active strains each year, and results of an enzyme-linked immunosorbent assay (ELISA) measuring IgG to the relevant seasonal vaccine antigens. Comparison of responses before and after vaccination and in patients who did or did not receive anifrolumab was performed by non-parametric testing. The proportion in each group developing a twofold increase in values for each test at week 8 compared to baseline, utilized Fisher's Exact Test. Confidence intervals were derived with the Exact Clopper-Pearson Method.

Figure 1. Study Design



Results: In a combined analysis merging data from all three years, anifrolumab treated patients had no observable deficits in vaccine response by either HAI [2 A] or by antibody levels to the vaccine [2 B]. At week 8, geometric mean titers (GMTs) and geometric standard deviations (GSDs) for HAI were anifrolumab: 123.0 (5.39) and control: 69.6 (1.79). GMTs (GSDs) for anti-vaccine antibody concentrations were anifrolumab: 171.8 (3.59) µg/mL and control: 151.7 (2.62). Geometric mean fold rises (GMFRs) (GSDs) of HAI titers from baseline to week 8 were anifrolumab 1.6 (4.52), control: 3.0 (1.46) and GMFRs of anti-influenza IgG were anifrolumab: 1.5 (2.91) and control: 2.8 (3.61). No differences were noted when vaccine responses were evaluated separately for each influenza season. All 6 patients in the control group and 15 (78.9%) of patients in the anifrolumab group developed at least one adverse event (AE) during the study. All AEs were mild or moderate in intensity. There were no serious adverse events, deaths, adverse events of special interest, or adverse events leading to discontinuation of treatment. As an additional analysis, the SLEDAI Flare Index (SFI) was evaluated. There were 8 (42%) individual patients in the anifrolumab group and 6 (100%) of patients in the control group who were noted to have a flare, (p=0.0196). All flares were mild/moderate and either mucocutaneous or musculoskeletal. There were 8 total flares in the treatment group (n=19) and 11 (n=6) in the control group.

Figure 2. A) Anifrolumab Impact on Hemagglutination Inhibition (HAI) after Influenza Vaccine B) Anifrolumab Impact on Anti-Influenza Virus IgG Concentrations after Influenza Vaccine



Conclusions: Humoral antibody responses induced by seasonal influenza virus vaccination in adult SLE patients were comparable between patients receiving anifrolumab and those only receiving standard of care, with no evidence to suggest inhibition of vaccine response by anifrolumab. Anifrolumab was well tolerated with no unexpected safety findings in the context of influenza vaccination. # Crowe SR, Merrill JT, Vista ES, Dedeke AB, Thompson DM, et. al. Arthritis Rheum. 2011 Aug;63(8):2396-406.

PV245 / #126

Poster Topic: ***AS24 - SLE-Treatment***

RENAL OUTCOMES IN PATIENTS TREATED WITH ANIFROLUMAB FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN THE US: FINDINGS FROM A REAL-WORLD STUDY

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Background/Purpose: Renal disease is a common severe manifestation of systemic lupus erythematosus (SLE) [1] and renal function changes dynamically over time. [2] SLE treatment may stabilize renal function from a declining trajectory. Anifrolumab was approved for moderate to severe SLE; however, limited real-world (RW) data is available on renal outcomes after anifrolumab treatment. This analysis investigated the estimated glomerular filtration rate (eGFR) and urine protein-creatinine ratio (UPCR) results in adult patients with SLE before and during anifrolumab treatment.

Methods: This retrospective, observational cohort study included patients in the American Rheumatology Network (124 rheumatology practices across 27 states). Inclusion criteria: ≥ 18 years of age with SLE diagnosis at anifrolumab initiation (index date), ≥ 180 days of clinical history before index, ≥ 5 anifrolumab infusions in the 180 days post index and anifrolumab adherence during post-index measurements (average < 42 days between infusions), serum creatinine levels < 2.0 mg/dL, UPCR < 2.0 mg/mg, and no other biologic during anifrolumab treatment. Clinical outcomes were assessed for patients with scores at baseline (-180 to -1 days before index), and follow-up (181-360 days post index). Clinical scores (within 28 days after last treatment date) were only included if a patient was on active treatment during assessment. If multiple assessments were made during each period, the one closest to anifrolumab initiation was baseline and the measurement closest to 360 days post initiation was follow-up. Median (IQR) result was reported for each outcome measure.

Results: Of 169 eligible patients, 92.9% were female, 54.3% were white, and median age was 53.0 (IQR 44.0-63.0) years (**Table**). Of these patients, 98 had eGFR measures at both baseline and follow-up. Both eGFR measures (median [IQR]) were consistent with normal levels at baseline (93.9, [78.4-106.7] mL/Min/1.73M^2) and at follow-up (90.9, [79.5-103.1] mL/Min/1.73M^2) (**Figure A**). At baseline, 54/98 (55.1%), 36/98 (36.7%), and 8/98 (8.2%) patients had eGFR levels > 90 (normal or Stage 1 chronic kidney disease [CKD]), between 60-90 (Stage 2 CKD), and < 60 mL/Min/1.73M^2 (Stage 3-5 CKD), respectively. Similarly, at follow-up, 51/98 (52.0%), 36/98 (36.7%), and 11/98 (11.2%) patients had eGFR levels > 90, between 60-90, and < 60 mL/Min/1.73M^2, respectively.

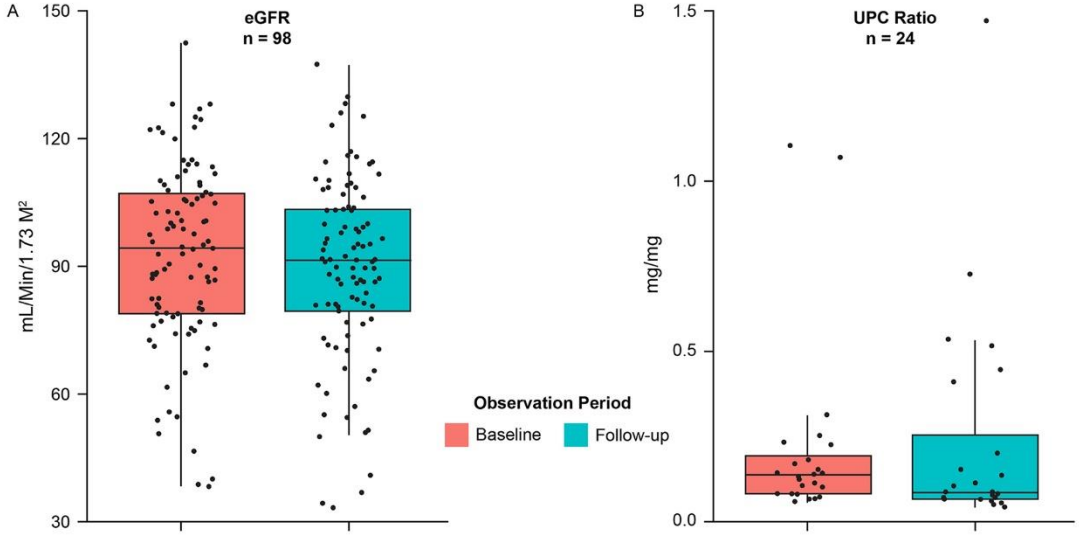
Median (IQR) UPCR results (n = 24) were 0.14 (0.08-0.19) mg/mg at baseline and 0.08 (0.06-0.25) mg/mg at follow-up (**Figure B**). Two of the 24 patients with baseline UPCR > 1 mg/mg remained stable (baseline: 1.11 and 1.07 mg/mg, follow-up: 0.44 and 0.72 mg/mg, respectively).

Table. Characteristics of Study Population and Subset at Baseline

Characteristic	Study Population (n = 169)	eGFR Subset (n = 98)	UPC Ratio Subset (n = 24)
AGE, n (%)			
19-34	18 (10.1)	11 (11.2)	2 (8.3)
35-44	27 (16.0)	17 (17.3)	5 (20.8)
45-54	46 (27.2)	26 (26.5)	8 (33.3)
55-64	38 (22.5)	20 (20.4)	7 (29.1)
65-74	28 (16.6)	16 (16.3)	1 (4.2)
75+	12 (7.1)	8 (8.2)	1 (4.2)
AGE, median (IQR)	53.0 (44.0-63.0)	52.0 (43.0-64.0)	49.5 (43.8-56.3)
GENDER, n (%)			
Female	157 (92.9)	90 (91.8)	23 (95.8)
Male	12 (7.1)	8 (8.2)	1 (4.2)
RACE, n (%)			
Black or African American	38 (22.5)	24 (24.5)	6 (25.0)
Other/Unknown	39 (23.0)	24 (24.5)	6 (25.0)
White	92 (54.3)	50 (51.0)	12 (50.0)
PRIOR THERAPIES (WITHIN −180 TO 0D OF INDEX), n (%)			
Only antimalarials	25 (14.8)	13 (13.3)	3 (12.5)
Only biologics	16 (9.5)	10 (10.2)	5 (20.8)
Only immunosuppressants	32 (18.9)	19 (19.4)	4 (16.7)
Antimalarials, biologics	15 (8.9)	8 (8.2)	2 (8.3)
Antimalarials, immunosuppressants	15 (8.9)	10 (10.2)	1 (4.2)
Biologics, immunosuppressants	10 (5.9)	7 (7.1)	1 (4.2)
Antimalarials, biologics, immunosuppressants	6 (3.6)	5 (5.1)	2 (8.3)
No known prior treatment	50 (29.6)	26 (26.5)	6 (25.0)

D, day; eGFR, estimated glomerular filtration rate; UPC, urine protein–creatinine.

Figure. Boxplots of eGFR (A) and UPC Ratio (B) measures (1 per patient per period) at Baseline and Follow-up (181-360 days). Boxplot represents median (middle line), lower and upper quartile (bottom and top horizontal line), IQR (colored area), and whiskers extend to 1.5 * IQR.



eGFR, estimated glomerular filtration rate; M, meter; min, minute; mL, millimeter; UPC, urine-protein creatinine.

Conclusions: In this RW study of patients with SLE on anifrolumab, baseline eGFR was within normal range and maintained up to 1 year after treatment initiation. Regardless of baseline proteinuria, UPCR remained stable up to 1 year after anifrolumab initiation.

This is consistent with anifrolumab effects on the kidney from the randomized clinical trial. [3] Further RW studies to determine long-term renal outcomes with anifrolumab are underway. **References:** [1] Kim Y. J Rheum Dis 2018;25:81-99. [2] Yip TCF. Lupus 2021;30:15-24. [3] Furie R. Arthritis Rheumatol 2023;75(suppl 9). **Acknowledgements:** This study was sponsored by AstraZeneca. Writing assistance was provided by Kelly Hunter, PhD, of JK Associates Inc., part of Avalere Health, and funded by AstraZeneca. Presented at EULAR 2024 and reused with permission of Kyttaris V, et al. POS1067 RENAL OUTCOMES IN PATIENTS TREATED WITH ANIFROLUMAB FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN THE US: FINDINGS FROM A REAL-WORLD STUDY. *Ann Rheum Dis.* 2024;83:979.

PV246 / #544

Poster Topic: *AS24 - SLE-Treatment*

DOWNREGULATION OF YTHDF2 IN THE SPINAL DORSAL HORN CONTRIBUTES TO THE GENESIS OF CHRONIC PAIN INDUCED BY SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Background: Chronic pain is a common and significant issue for patients with systemic lupus erythematosus (SLE) due to the limited effectiveness and safety of current analgesics. There is an urgent need to identify new and effective targets for managing SLE-associated chronic pain. Gaining insight into the cellular and molecular mechanisms driving SLE-induced chronic pain is essential to advance effective therapies. In studies using an SLE mouse model (MRL/lpr mice), we identified spinal neuroinflammation and abnormal neuronal activity as key contributors to chronic pain in SLE mice. Given the critical role of the YT521-B homology domain family 2 (YTHDF2) RNA-binding protein in epitranscriptomic regulation in neurological disorders, uncovering whether and how the YTHDF2 pathway regulates chronic pain in SLE mice could provide a promising new strategy for managing SLE-induced pain.

Methods: Methods: A spontaneous SLE mouse model, MRL/lpr mice, and their controls (MRL mice) were used. Behavioral tests were used to assess pain perception in the mice. Protein signaling molecules were analyzed using Western blotting and immunohistochemistry. Intrathecal injection of siRNA was used to manipulate gene expression in the spinal dorsal horn.

Results: Results: Female MRL/lpr mice had an increased hind paw volume (an indicator of arthritis) from 12 weeks of age, as measured using a water displacement plethysmometer. Meanwhile, lupus mice spontaneously developed hypersensitivity in their hind paws to radiant heat stimuli starting at 12 to 13 weeks of age, reaching a plateau between 14 and 16 weeks. Mechanical hypersensitivity (allodynia) emerged in the hind paws at 14 weeks and persisted through 16 weeks. Western blotting analysis showed that YTHDF2 protein levels in the spinal dorsal horn of MRL/lpr mice were significantly lower than those in control mice. Using immunohistochemistry techniques, we found that YTHDF2 protein is expressed in neurons, astrocytes and microglia in the spinal dorsal horn. Knockdown of YTHDF2 protein expression in the dorsal horn of normal control mice by intrathecal injection of YTHDF2 siRNA (1 μg/injection, b.i.d. for two days) induced thermal hyperalgesia and mechanical allodynia. This was accompanied by significantly increased neuronal activation, as evidenced by elevated c-fos protein and phosphorylated extracellular signal-regulated kinase (ERK) expression, as well as microglial activation indicated by increased ionized

calcium binding adaptor molecule 1 (Iba1) protein expression, and astrocyte activation evidenced by increased glial fibrillary acidic protein (GFAP) expression in the dorsal horn. These were concurrently accompanied by elevated phosphorylated-P38 activity, IL-1β, and IL-18 levels, along with reduced glial glutamate transporter-1 protein expression in the same area. The molecular and behavioral alterations induced by spinal YTHDF2 knockdown mimic those observed in lupus mice.

Conclusions: Conclusions: Our results suggest that downregulation of YTHDF2 in the spinal dorsal horn contributes to the genesis of lupus-induced chronic pain through regulating spinal neuroinflammation and neuronal activation.

PV247 / #135

Poster Topic: *AS24 - SLE-Treatment*

ADHERENCE TO RETINAL SCREENING GUIDELINES IN LUPUS PATIENTS TREATED WITH HYDROXYCHLOROQUINE - DATA FROM HIGHMARK CLAIMS

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Background/Purpose: In 2020, four major medical societies taking care of patients on hydroxychloroquine (HCQ) published a joint statement highlighting ophthalmologic screening guidlines to detect retinal toxicty. The risk of HCQ toxicity is less than 2% after 10 years, with upto 8.6% patients affected after 15 years of use. The joint statement recommends baseline retinal screening within few months of HCQ initiation primarily to rule out existing retinal disease that may interfere with future eye exams. After baseline eye exam, screening can be deferred for 5 years and thereafter should be performed annually. An optical testing with Optical Coherence T omography (OCT) and automated visual fields (VF) are the preferred modalities for evaluation. We studied the real world compliance to these recommendations in a cohort of lupus patients utilizing Highmark claims data.

Methods: We conducted a blended retrospective cohort - Highmark claims study of patients with Systemic lupus erythematosus (SLE) receiving treatment with HCQ. Patients with SLE from 1/2016 to 12/2023 were included. Patients over 18 years of age, with dignosis of lupus, Systemic lupus erythematosus (SLE), lupus nephritis (LN), cutaneous lupus based on ICD 10 codes who had subsequent refills of HCQ were included. These patients were seen atleast twice by rheumatology providers in the division of Rheumatology at Allegheny Health Network. Patients on Medicare and Highmark insurance and seeing either Ophthalmologist or Optometrist were included. A Highmark claims data was extracted on this cohort to investigate adherence to baseline eye exam (within 1 year) and yearly screening after 5 years.

Results: Among 227 patients with SLE, 204 (90%) were female, 179 (79%) were Caucasian, 124 (55%) were active smokers, 26 (11.4%) had Chronic kidney disease, 19 (8.3%) had diabetes, 3 (1.3%) had pre-existing retinal disease, 50 (22%) patients were on Medicare and 84 (37%) were seen by an Ophthalmologist. Among 227 patients, only 35% received baseline retinal testing upon HCQ initiation ($p<0.05$). Among those with 5 years of follow-up and 5 yearly visits, adherence was 11.8% ($p<0.05$). Insurance type and provider specialty significantly influenced adherence. Medicare Advantage members showed higher adherence compared to commercial insurance, and baseline

exams with an ophthalmologist were associated with better adherence. Adherence was not affected by comorbidities, prior retinal disease, or rurality.

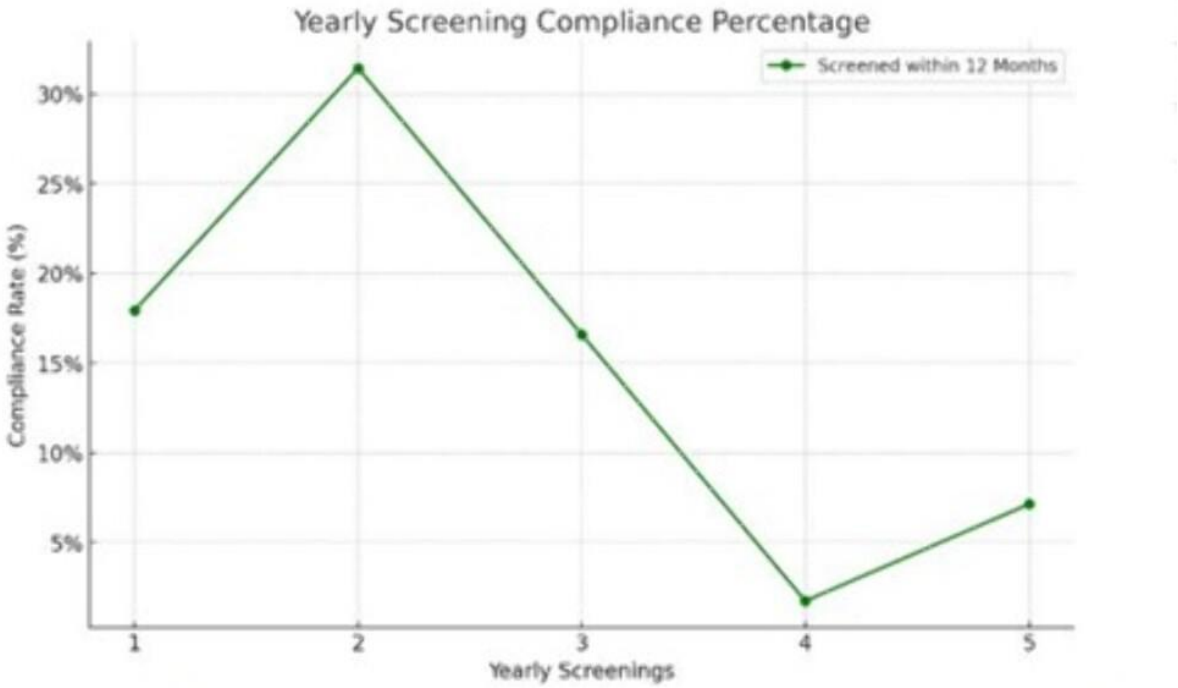

Figure 1: Compliance rate (%) for yearly screening from year 1 to 5

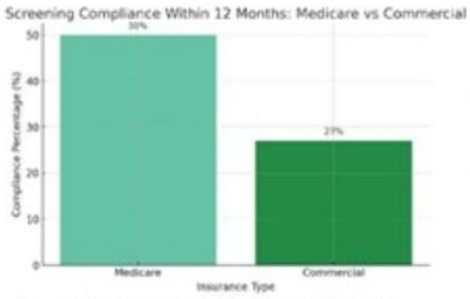

Figure 2: Higher compliance rate of Medicare members compared to Commercial Insurance

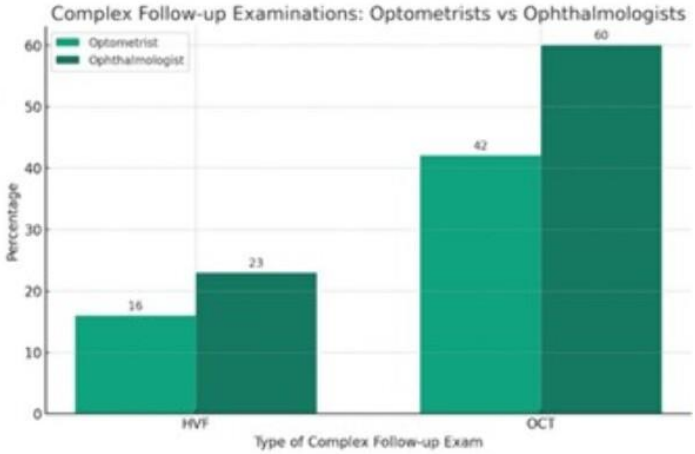

Figure 3: Humphrey visual-fields (HVF) and spectral-domain optical coherence tomography(OCT) performance rate by providers

Conclusions: Our study highlights poor compliance to screening guidelines for monitoring of retinal toxicity in patients with SLE taking HCQ. Improved education for both providers and patients on ophthalmology surveillance is crucial. Quality improvement initiatives will address this healthcare disparity in our system, aiming for safer HCQ prescribing practices.

PV248 / #665

Poster Topic: ***AS24 - SLE-Treatment***

REAL-WORLD OUTCOMES OF ANIFROLUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AT THE TORONTO LUPUS PROGRAM

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Background/Purpose: Anifrolumab (ANI), a human monoclonal antibody targeting the type I interferon receptor subunit 1 (IFNAR1), blocks the activity of this interferon and has shown efficacy in reducing disease activity in systemic lupus erythematosus (SLE). Real-world evidence is critical to understanding its utilization and outcomes. We aimed to describe the profiles of SLE patients treated with anifrolumab for at least three months at the Toronto Lupus Program and to evaluate treatment efficacy and safety.

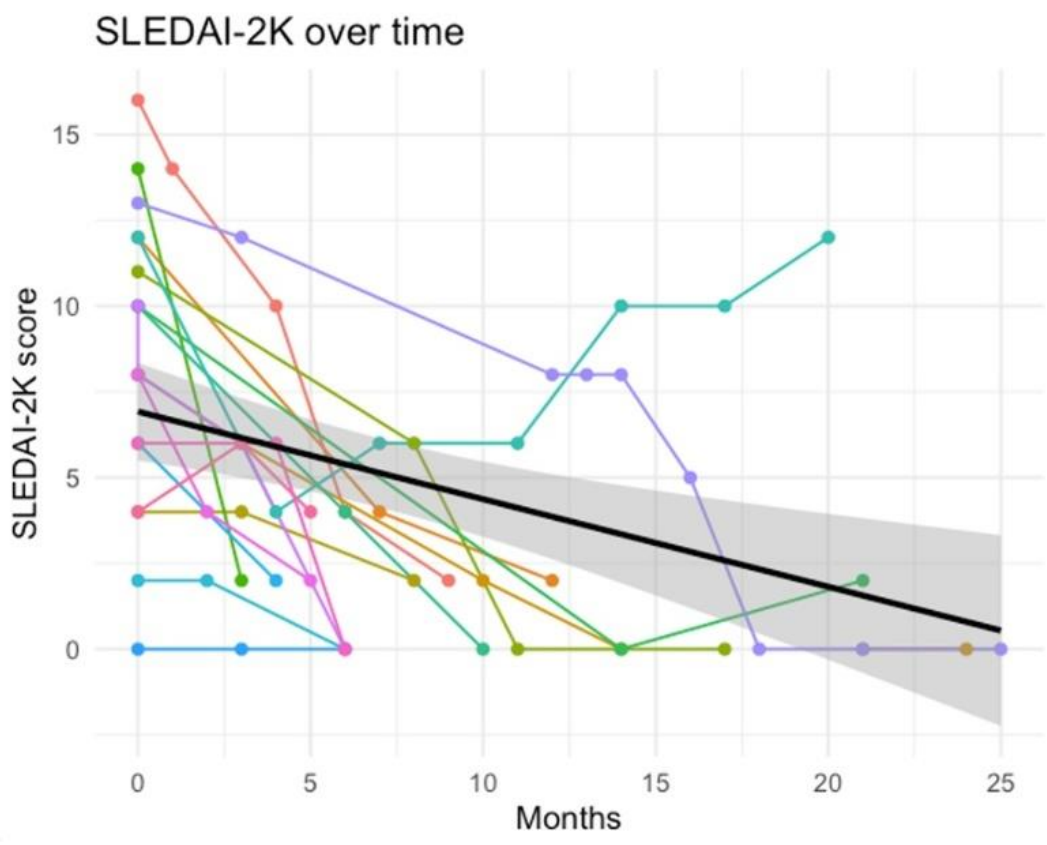
Methods: We identified patients from the University of Toronto Lupus Cohort who met the European Alliance of Associations for Rheumatology and American College of Rheumatology (EULAR/ACR) 2019 classification criteria and were treated with anifrolumab for at least three months. Demographic characteristics, clinical and laboratory variables, previous and concomitant therapy, and disease activity indices (by SLEDAI-2K, BILAG, CLASI and PGA) were evaluated at baseline and during follow-up, as well as time to symptoms response. Prednisone doses, safety outcomes, including infections and treatment discontinuations, were analyzed.

Results: Seventeen patients (76.5% female, 23.5% male) with a mean age of 40.8 years (SD 12.9) and a mean SLE duration of 14.3 years (SD 11.5) were included. Cumulative pre-existing organ involvement at anifrolumab start included mucocutaneous (100%), musculoskeletal (82.4%), serositis (41.2%), hematological (29.4%), renal (23.5%), neuropsychiatric (23.5%) and persistent fever (5.9%). Secondary antiphospholipid syndrome and Sjögren's syndrome were each observed in 11.8% of patients. The main reasons for initiating anifrolumab included skin rash (n = 14, 82.4%), musculoskeletal involvement (n = 7, 41.2%), alopecia (n = 5, 29.4%), along with the presence of other concomitant hematological involvement (leukopenia) and shrinking lung syndrome. Patients had a mean follow-up duration of 9.4 months (SD 7.4) on anifrolumab. At the initiation of anifrolumab, all patients were on prednisone and 13 patients (76.5%) were receiving hydroxychloroquine. Concomitant immunosuppressive treatments included mycophenolate mofetil in 8 patients (47.1%), methotrexate in 4 patients (23.5%), and a

combination of methotrexate and mycophenolate mofetil in 1 patient (5.6%). Prednisone use significantly decreased from a baseline mean dose of 9.4 mg/day (SD 9.25) to 2.5 mg/day (SD 7.5). During treatment, immunosuppressive concomitant therapies were reduced or discontinued in 7 patients (41.2%). SLEDAI-2K scores consistently decreased over time, reflecting significant improvements in disease activity (Figure 1). The median time to 50% improvement in clinical manifestations was 52 days (IQR 34-91), while the median time to total resolution of symptoms was 148 days (IQR 115-233). Anifrolumab was discontinued in 1 patient (5.9%) 20 months after starting treatment to initiate alternate therapy for the development of lupus nephritis during follow-up. Treatment was temporarily held in 1 patient (5.9%) due to refractory molluscum contagiosum occurring after 14 months of therapy; this patient was also on mycophenolate mofetil. No additional adverse events were reported. Overall, the treatment was well-tolerated.

Figure 1

SLEDAI-2K Scores Over Time.



Conclusions: Anifrolumab showed significant efficacy in reducing disease activity and prednisone use in SLE patients, with a good overall safety profile.

PV249 / #817

Poster Topic: *AS24 - SLE-Treatment*
Late-Breaking Abstract

ADVANCES IN TARGETED THERAPIES AND IMMUNOMODULATORY STRATEGIES IN LUPUS

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[1]LPCK therapeutics, Boston, United States of America, [2]Les Hôpitaux Universitaires de Strasbourg, Strasbourg, France

Background/Purpose: Lupus is a complex autoimmune disease characterized by a dysregulated immune response and multi-organ involvement. Despite advances in conventional therapies, refractory diseases and treatment toxicity remain a challenge. This manuscript reviews the evolving landscape of biomedicines and immunomodulatory therapies, focusing on targeted approaches to address SLE pathogenesis.

Methods: To provide an overview of therapeutic potential of new immunomodulatory agents targeting key pathogenic pathways in SLE, emerging treatment strategies, using cytokine inhibition, B/T-cell activation, co-stimulation blockade, kinase modulation, and cellular therapies, while addressing mechanistic insights from recent clinical trials. We have performed a comprehensive review and analysis of Systemic Lupus Erythematosus (SLE) clinical studies synopsis protocols, of randomized controlled trials (RCTs), and real-world data was conducted. Also, a review of published abstracts and publications of phase 1, 2 and 3 studies.

Results: Phase 3 Successes: Type I interferon receptor antagonists (e.g., anifrolumab) and BAFF/BLyS inhibitors (e.g., belimumab) have demonstrated robust efficacy in reducing disease activity and flares, for moderate-to-severe SLE. Voclosporin have demonstrated efficacy in lupus nephritis and JAK/STAT inhibitors such as upadacitinib show promise in lupus nephritis, with pivotal Phase 3 trials underway. **Phase 2 Innovations:** Anti-CD40L therapies (e.g., dapirolizumab pegol) exhibit potential in SLE by targeting B/T-cell interactions and glomerular inflammation. The depleting anti-BAFFR antibody ianalumab has also shown excellent preliminary efficacy in phase 2 trial. Anti-BDCA2 antibodies (e.g., litifilimab) and TYK2 inhibitors (e.g., deucravacitinib) improve cutaneous and systemic manifestations. **Phase 1 Explorations:** Novel strategies include epigenetic modulators (e.g., JNK inhibitors) to address DNA methylation, CAR-T cell therapies targeting B-cell markers (e.g., CD19) for refractory disease, and S1P receptor modulators to limit lymphocyte trafficking.

Conclusions: The SLE therapeutic landscape is undergoing rapid transformation, driven by precision targeting of cytokine signaling, co-stimulation pathways, and

intracellular kinase networks. While Phase 3 successes underscore the viability of immunomodulation, Phase 1/2 innovations in epigenetic and cellular therapies offer transformative potential for refractory cases. Collaborative efforts to standardize endpoints, validate predictive biomarkers, and ensure equitable access are essential to optimize outcomes and translate these advances into global patient care.

PV250 / #419

Poster Topic: ***AS24 - SLE-Treatment***

POTENT AND SPECIFIC KILLING OF SLE B CELLS WITH ALLONK® (AB-101), AN ALLOGENEIC CORD BLOOD-NK CELL THERAPY, IN COMBINATION WITH ANTI-CD19 OR ANTI-CD20 MONOCLONAL ANTIBODIES

Paul Rogers, Lisa Guerrettaz, Kun-Yu Teng, Claudia Palomino La Torre, Gina Chu, Sean Stromberg, Heather Raymon
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Background/Purpose: Systemic lupus erythematosus (SLE) is a systemic inflammatory disorder involving loss of tolerance and development of autoantibodies. B cells play a crucial role in the pathogenesis of SLE by producing autoantibodies that target self-antigens, leading to tissue damage and inflammation. In individuals with SLE, Natural Killer (NK) cells are often found to be fewer in number and functionally impaired, including defective antibody-dependent cellular cytotoxicity (ADCC), altered differentiation and abnormal cytokine production. Given the reported defects in NK cells from SLE patient samples, we hypothesize that administration of an NK cell therapy, in combination with B cell-depleting monoclonal antibodies (mAbs), will have the potential to induce deeper B cell depletion and improve efficacy, over the mAb alone. Here we demonstrate proof of concept for the use of an NK cell therapy to enhance the depletion of SLE donor B cells in the presence of anti-CD19 or anti-CD20 mAbs by an ADCC mechanism. AlloNK® is a non-genetically modified, allogeneic, off-the-shelf, cryopreserved NK cell product, currently being evaluated in a Phase 1 clinical trial in combination with rituximab or obinutuzumab in subjects with SLE or lupus nephritis (NCT06265220).

Methods: Comprehensive immunophenotypic analysis of B and NK cell subsets from SLE (n=9) and healthy donor (n=6) peripheral blood mononuclear cells (PBMC) was conducted by flow cytometry. In addition, PBMC were isolated from SLE donors (n=9) and co-cultured with AlloNK at various effector to target (E:T) ratios and mAbs concentrations to assess ADCC.

Results: To further investigate these findings, B and NK cell subsets from both SLE patients and healthy individuals were assessed. In SLE patient samples, there was an observed increase in transitional B and a decrease in activated memory B cells compared to healthy individuals. Additionally, SLE patient samples had a reduction in total NK, CD16 and NKG2D but an increase in $CD56^{bright}$ $CD16^{neg}$ NK cells compared to healthy donors. AlloNK, which has been optimized for ADCC through the pre-selection of cord blood units for the natural high-affinity variant of CD16 (158V/V), was tested in combination with anti-CD20 (rituximab, obinutuzumab) or anti-CD19 (tafasitamab) mAbs in a short-term ADCC assay to show specific killing of SLE donor B cells. After 4h,

the percentage of caspase 3/7^{+} B and T cells was determined by flow cytometry. At a 1:1 E:T ratio, AlloNK mediated killing of B cells in the presence of obinutuzumab (range 79-95%), rituximab (range 19-62%), and tafasitamab (range 24-77%) in a dose-dependent manner. Killing was specific as no off-target apoptosis of T cells was observed.

Conclusions: Taken together, these data suggest that AlloNK has the potential to be effective in combination with mAbs to induce deeper B cell depletion and improved efficacy, over the mAbs alone, in SLE and LN.

PV251 / #283

Poster Topic: ***AS24 - SLE-Treatment***

BE-EARLY: A PHASE 4, PROSPECTIVE, OPEN-LABEL STUDY TO EVALUATE THE IMPACT OF BELIMUMAB ON EARLY (≤ 2 YEARS) SYSTEMIC LUPUS ERYTHMETOSUS IN ADULTS

Karen Costenbader[1], Marta Mosca[2], Julia Harris[3], Roger Levy[4], Ciara O'Shea[5], Sofia Fernandes[6], Michelle Petri[7]
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Background/Purpose: Approximately 40% of patients with systemic lupus erythematosus (SLE) develop organ damage within the first 5 years of diagnosis due to uncontrolled disease activity and cumulative steroid exposure, impacting quality of life and increasing early mortality risk.[1] Intervention with a disease-modifying biologic such as belimumab (BEL) in the early disease stages might modify the disease course and prevent irreversible organ damage while minimizing the need for glucocorticoids (GCs) or exposure to immunosuppressants (IS). Evidence suggests that BEL induces better responses compared with standard therapy (ST) when used earlier in SLE, especially in patients with minimal or no organ damage or within 2 years of classification.[2,3] However, the use of BEL early in the disease course has been limited in clinical practice, mostly following the failure of ≥ 2 IS. Here, we present the BE-EARLY (BEL in Early SLE) study design, which will evaluate the efficacy and safety of BEL in adult SLE patients with early disease.

Methods: This Phase 4, prospective, open-label, single-arm, 3-year clinical study (GSK Study 219240; NCT06411249) will include approximately 350 participants from 11 countries with active, autoantibody-positive, early SLE (≤ 2 years since diagnosis) with no organ damage and inadequate response to initial ST (with/without a first conventional IS). Key eligibility criteria are shown in **Table 1**. Participants will receive BEL 200 mg/week subcutaneously as an add-on to initial ST for 52 weeks (Part A), with a long-term extension up to 104 weeks (end of study is the safety follow-up visit after Week 156; Part B). Key primary and secondary endpoints are shown in **Table 2**. Participants will be required to taper the average oral GC (oGC; prednisone equivalent) dose starting at Week 12 to ≤ 7.5 mg/day by Week 26, and to ≤ 5 mg/day by Week 48 (if the investigator considers the disease is stable and under control on ≤ 7.5 mg/day). No

changes in oGC dose are allowed between Weeks 48 and 52. An optional concomitant IS taper may be attempted after the Week 52 visit if the patient maintains Definition Of Remission in SLE (DORIS) criteria for ≥ 6 months. Descriptive summaries will be performed for all endpoints.

Table 1. Key eligibility criteria

Key inclusion criteria	Key exclusion criteria
• ≥ 18 years of age • ACR 2019 SLE classification ≤ 2 years • Autoantibody-positive (anti-nuclear antibodies or anti-dsDNA) • Incomplete response to first-line initial therapy (antimalarials, oGCs, IS alone or in any combination) • No organ damage (SDI = 0) • Active disease, defined as clinical SLEDAI-2K* > 4 or clinical SLEDAI-2K* ≤ 4 and GC dose ≥ 10 mg/day	• Second-line standard therapy • Doses of IS or oGC greater than the maximum allowed • Active lupus nephritis needing induction therapy or severe kidney failure • Active severe central nervous system lupus • Acute or chronic infection, requiring management • Serious depression/suicidality • Use of other biologics or investigational agents • Pregnancy/unwillingness to use necessary contraception

*Excluding anti-dsDNA and C3/C4.

ACR, American College of Rheumatology; dsDNA, double-stranded deoxyribonucleic acid; SDI, Systemic Lupus International Collaborating Clinics/ACR Damage Index; SLEDAI, SLE Disease Activity Index; SLEDAI-2K, SLEDAI 2000.

Table 2. Key primary and secondary endpoints

	Objectives	Endpoints
Primary	To describe the efficacy of BEL on disease activity in participants with early SLE	Achieving LLDAS* at Week 52
Key secondary	To describe the efficacy of BEL on:	
	• Achieving SRI-4 in participants with early SLE who have a SLEDAI-2K score ≥ 4 at baseline	Achieving SRI-4† at Week 52
	• Achieving and maintaining LLDAS in participants with early SLE	Maintaining LLDAS* for ≥ 25% of time from Day 1 to Week 52
	• oGC reduction in participants with early SLE who are taking an average oral prednisone equivalent dose > 5 mg/day at baseline	Achieving average oral prednisone equivalent dose ≤ 5 mg/day† at Week 52
	• Severe flare in participants with early SLE	Incidence of severe flare (modified SFI)‡ as assessed at Week 52
Other secondary	To describe the efficacy of BEL on:	
	• Skin improvement in participants with early SLE who have a CLASI activity score ≥ 10 at baseline	Achieving a ≥ 50% improvement in CLASI activity score at Week 52
	• Improvement in fatigue in participants with early SLE	Change from baseline in FACIT-Fatigue at Week 52
	• Remission in participants with early SLE	Attaining DORIS remission§ at Week 104
	• Organ damage progression in participants with early SLE who have no organ damage at baseline (SDI = 0)	Maintaining an SDI of 0 at Week 156
	To describe the safety and tolerability of BEL in participants with early SLE	Incidence of AEs, SAEs, AESIs up to Weeks 52, 104, and 156

*Defined as SLEDAI-2K ≤ 4, with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever) and no new features of lupus disease activity compared with the previous assessment, PGA ≤ 1, with 7-day average oral prednisone-equivalent dose ≤ 7.5 mg/day for SLE reasons and stable treatment (with or without conventional IS) and without discontinuing due to lack of efficacy, dying, or taking prohibited medications; †without discontinuing due to lack of efficacy, dying, taking prohibited medications, or treatment failure; ‡severe SFI flare analysis will be performed on the modified SLEDAI-2K SFI in which the modification excludes flares that were triggered only by an increase in SLEDAI-2K score > 12 but counts prohibited medication intake; §DORIS remission is defined as clinical SLEDAI-2K = 0 (excluding serology), PGA < 0.5, and prednisone-equivalent dose for SLE reasons ≤ 5 mg/day on stable maintenance therapy.

AE, adverse event; AESI, adverse event of special interest; CLASI, Cutaneous Lupus Disease Area and Severity Index; FACIT-Fatigue, Functional Assessment of Chronic Illness-Fatigue; LLDAS, Lupus Low Disease Activity State; PGA, Physician Global Assessment; SAE, serious adverse event; SFI, SELENA-SLEDAI Flare Index; SRI, SLE Responder Index.

Results: Currently, 22% of sites are active; the first patient was included in July 2024. The primary endpoint data are expected in 2027.

Conclusions: This clinical study will investigate the efficacy and safety of BEL in adults with early, active SLE, using relevant disease activity endpoints. The open-label design was selected as several other treatment options are available, and BEL is an approved biological therapy in the population of this study. It is expected that early BEL administration will benefit participants' short-term outcomes, such as improvements in disease activity, quality of life, and reduction in oGC use, as well as long-term

outcomes, including attainment of remission and prevention of organ damage. **References:** [1.] Urowitz MB. Arthritis Care Res 2012;64:132-7. [2.] Gatto M. Arthritis Rheumatol 2020;72(8):1314-24. [3.] Petri M. Ann Rheum Dis 2022;81:323 Funded by GSK. Accepted (abstract-only publication): EULAR European Congress of Rheumatology, 12–15 June 2024. Reused with permission. Petri M, et al. AB1033 UNDERSTANDING THE IMPACT OF BELIMUMAB ON EARLY (≤2 YEARS) SYSTEMIC LUPUS ERYTHEMATOSUS IN ADULTS: BeEARLY, A PHASE 4, PROSPECTIVE, OPEN-LABEL STUDY. Ann Rheum Dis 2024;83:1837. Presented: 26th Asia-Pacific League of Associations for Rheumatology Congress, 21–25 August 2024.

PV252 / #394

Poster Topic: ***AS24 - SLE-Treatment***

CHANGE IN GLUCOCORTICOID USE IN SYSTEMIC LUPUS ERYTHEMATOSUS IN A POPULATION-BASED INCEPTION COHORT OVER 4 DECADES: THE LUPUS MIDWEST NETWORK

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Background/Purpose: We aimed to examine glucocorticoid (GC) use over four decades in a population-based incident cohort of patients with SLE.

Methods: Residents of Olmsted County, MN, with incident SLE meeting the 2019 EULAR/ACR SLE classification criteria between 1976-2018 were included. Index date was defined as the date of criteria fulfillment. GC use (oral daily prednisone equivalents) was abstracted from the index date until death or last follow-up through 12/31/2023. Cumulative daily dose of GCs in the first year after SLE incidence was calculated. Logistic regression models of any GC use in the first year and linear regression models of log cumulative GC dose in the first year adjusted for age and sex were used to examine time trends.

Results: The study included 198 patients with SLE (mean age 44.4 [SD 17.8] years; 166 [84%] female) who were subdivided into 4 decades (1976-1988, 1989-1998, 1999-2008 and 2009-2018) for analysis (Table). Patients in the most recent decade were somewhat older at diagnosis, and the population became more diverse over time. DMARD use in the first year after SLE incidence became more common over time, and the proportion of patients initiating GC increased over time (age and sex adjusted p=0.045) while the proportion of patients using pulse GC in the first year remained stable over time. The starting dose of oral GCs decreased over the first 3 decades but increased again in the most recent decade (p=0.040). Cumulative GC use in the first year decreased over time (age and sex adjusted p=0.005). This association persisted after additional adjustment for DMARD use. Most of the decline in cumulative GC use occurred in the 2000s with very little improvement subsequently.

Table. Demographic and clinical characteristics of the incident cohort of patients with systemic lupus erythematosus in 1976-2018.

SLE incidence	1976-1988 (n=30)	1989-1998 (n=39)	1999-2008 (n=52)	2009-2018 (n=77)	Total (n=198)	p-value
Age at SLE incidence, years, mean (SD)	42.4 (19.3)	39.0 (16.9)	43.1 (17.0)	48.9 (17.4)	44.4 (17.8)	0.018
Female Sex	28 (93%)	36 (92%)	42 (81%)	60 (78%)	166 (84%)	0.093
Current smoker	7 (23%)	8 (22%)	6 (12%)	8 (10%)	29 (15%)	0.10
Oral GC use						
GC initiation within first year of SLE incidence	14 (47%)	27 (69%)	30(58%)	54 (70%)	125 (63%)	0.094
GC starting dose, mg/day, median (IQR)	40.0 (17.5-60.0)	20.0 (10.0-40.0)	11.2 (8.1-35.0)	30.0 (11.2-57.5)	20.0 (10.0-50.0)	0.040
Cumulative dose in first year among those using GC, gm, median (IQR)	3.2 (2.6-6.2)	4.6 (2.2-6.1)	2.8 (1.0-5.4)	2.6 (1.4-4.6)	3.1 (1.7-5.4)	0.13
Any GC pulses in first year	6 (20%)	11 (28%)	12 (23%)	25 (32%)	54 (27%)	0.51
DMARD use in first year	10 (33%)	29 (75%)	40 (77%)	64 (83%)	143 (72%)	<0.001

GC, glucocorticoid; SLE, systemic lupus erythematosus; DMARD, disease modifying anti-rheumatic drug *Non-Hispanic.

Conclusions: GC dosage at initiation had declined over time, but increased in the most recent decade, along with increases in the proportion of patients initiating GCs despite increased use of DMARDs. Cumulative GC use in the first year of SLE declined in the 2000s and has remained stable subsequently. These trends are mostly encouraging, but there is still room for more GC-sparing efforts in this population.

PV253 / #124

Poster Topic: ***AS24 - SLE-Treatment***

DORIS REMISSION IN PATIENTS WITH SLE TREATED WITH ANIFROLUMAB: POST HOC ANALYSIS FROM TULIP-1 AND TULIP-2 TRIALS IN PATIENTS WITH NO PRIOR IMMUNOSUPPRESSANT USE

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Background/Purpose: 2023 EULAR treatment recommendations for SLE present the option for early biologic use without prior failure of immunosuppressants/disease-modifying antirheumatic drugs (DMARDs), in patients with inadequate responses to antimalarials alone or in combination with glucocorticoids (GC). [1] There are limited data demonstrating clinical benefits with biologics in immunosuppressant-naïve patients with SLE treated with either antimalarials, oral GCs, or the combination. This post hoc analysis investigated DORIS (Definition of Remission in SLE) remission attainment in patients with moderate to severe SLE treated with intravenous anifrolumab 300 mg or placebo in the TULIP-1 (NCT02446912 [2]) or TULIP-2 (NCT02446899 [3]) phase 3 trials who had no reported history of prior immunosuppressant use.

Methods: This post hoc analysis included a subset of patients from the TULIP-1 and TULIP-2 trials who were 'immunosuppressant naïve', defined as patients with a treatment history of antimalarials or oral GCs at enrollment, or the combination of antimalarials and GCs, but without prior use of immunosuppressants or DMARDs. DORIS remission attainment was assessed for the period after randomization. DORIS remission was defined as total clinical SLEDAI-2K score (sum of all SLEDAI-2K items except increased DNA binding and low complement) = 0, Physician's Global Assessment < 0.5, and prednisone/equivalent dosage ≤ 5 mg/day. DORIS attainment was analyzed using a stratified Cochran–Mantel–Haenszel approach.

Results: A total of 257 patients (anifrolumab 300 mg, n = 127; placebo, n = 130) in the pooled TULIP-1 and TULIP-2 trial dataset were immunosuppressant naïve. Among this subgroup, 21 (16.2%) of immunosuppressant-naïve patients in the anifrolumab 300 mg group attained DORIS remission at Week 52 compared with 7 (6.0%) patients in the placebo group (treatment difference: 10.2% [95% CI: 1.3-19.1], nominal *P* = 0.0242).

DORIS attainment rates generally increased from baseline through to Week 52 (**Figure 1**).

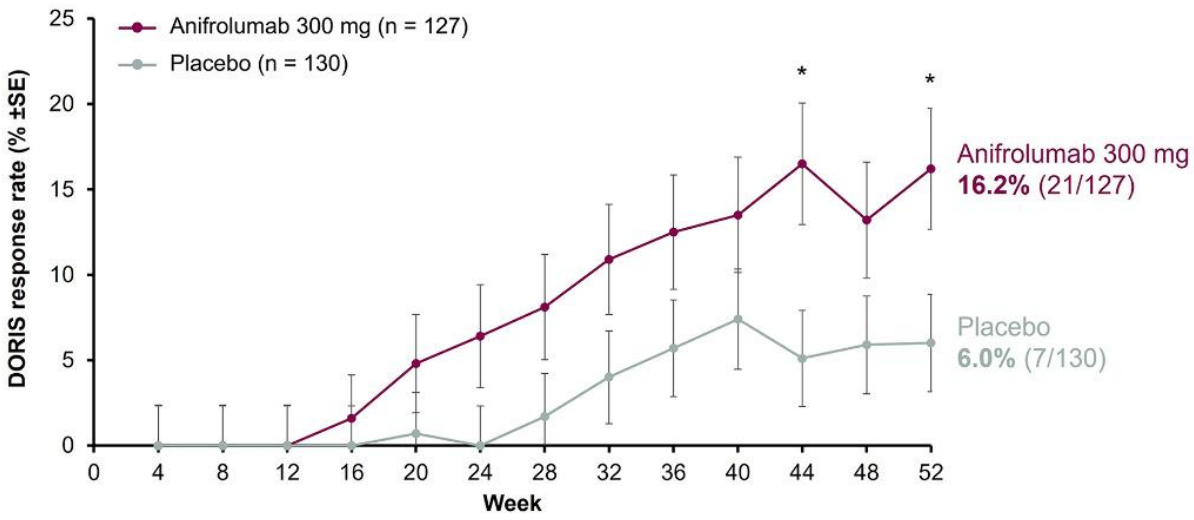

Figure 1. Attainment of DORIS remission across 52 weeks in patients with no reported history of prior immunosuppressant use.

*denotes nominal $P < 0.05$ calculated using using a stratified Cochran-Mantel-Haenszel approach, with stratification factors of SLEDAI-2K at screening, Day 1 glucocorticoid dosage, type I interferon gene signature at screening, and study (TULIP-1 vs TULIP-2).

Conclusions: In this post hoc analysis, a higher proportion of immunosuppressant-naïve patients with moderate to severe SLE treated with anifrolumab attained DORIS remission at Week 52 compared with those who received placebo. These results are consistent with EULAR recommendations to consider initiating treatment with biologics early, before immunosuppressants. **References:** [1.] Fanouriakis A. Ann Rheum Dis 2019;78:736-45.
[2.] Furie RA. Lancet Rheumatol 2019;1:e208-e19.
[3.] Morand EF. N Engl J Med 2020;382:211-21. **Acknowledgements:** This study was sponsored by AstraZeneca. Writing assistance was provided by Tamara Fink, PhD, of JK Associates Inc., part of Avalere Health, and funded by AstraZeneca. Presented at ACR 2024 and reused with permission of Andrea D, et al. DORIS Remission in Patients with SLE Treated with Anifrolumab: Post Hoc Analysis from TULIP-1 and TULIP-2 Trials in Patents with No Reported History of Prior Immunosuppressant Use [abstract]. *Arthritis Rheumatol.* 2024; 76 (suppl 9). https://acrabstracts.org/abstract/doris-remission-in-patients-with-sle-treated-with-anifrolumab-post-hoc-analysis-from-tulip-1-and-tulip-2-trials-in-patents-with-no-reported-history-of-prior-immunosuppressant-use/. Accessed October 31, 2024. Permissions were requested from the original abstract as cited above.

PV254 / #673

Poster Topic: ***AS24 - SLE-Treatment***

REAL-WORLD ASSESSMENT OF PATTERNS OF PAIN TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS: A PATHWAY VISUALIZATION STUDY USING EHR

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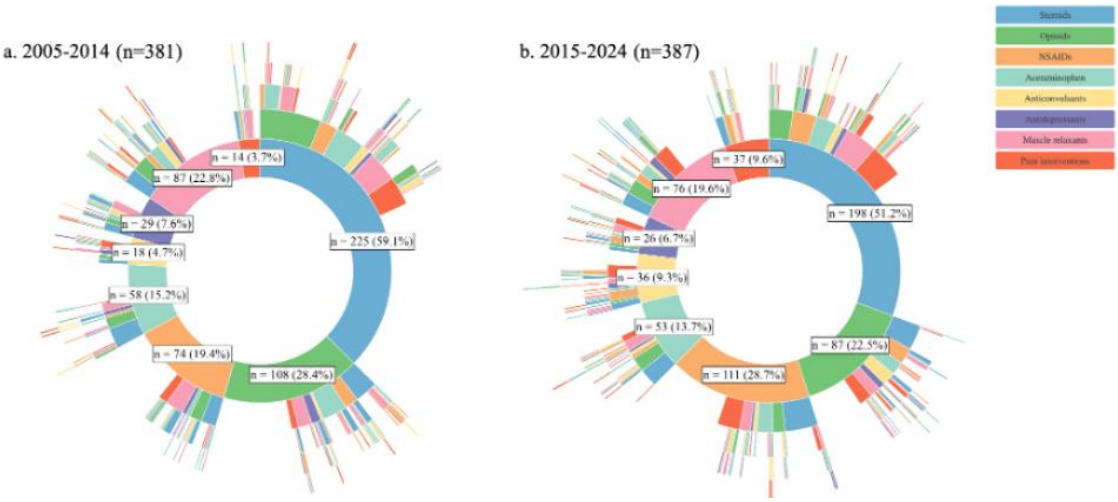
Background/Purpose: To characterize trends and demographic differences in pain management modalities among patients with SLE and assess the evolution of treatment strategies over the past two decades.

Methods: We retrospectively analyzed electronic health records from 2005-2024 at a single academic center. Using sequence analysis and Sankey diagrams, we mapped the progression of pain management modalities, including corticosteroids, opioids, NSAIDs, and non-pharmaceutical therapies, within two timeframes: 2005-2014 and 2015-2024. We evaluated transitions between therapies, demographic influences (age, sex, race/ethnicity), and shifts in treatment patterns over time.

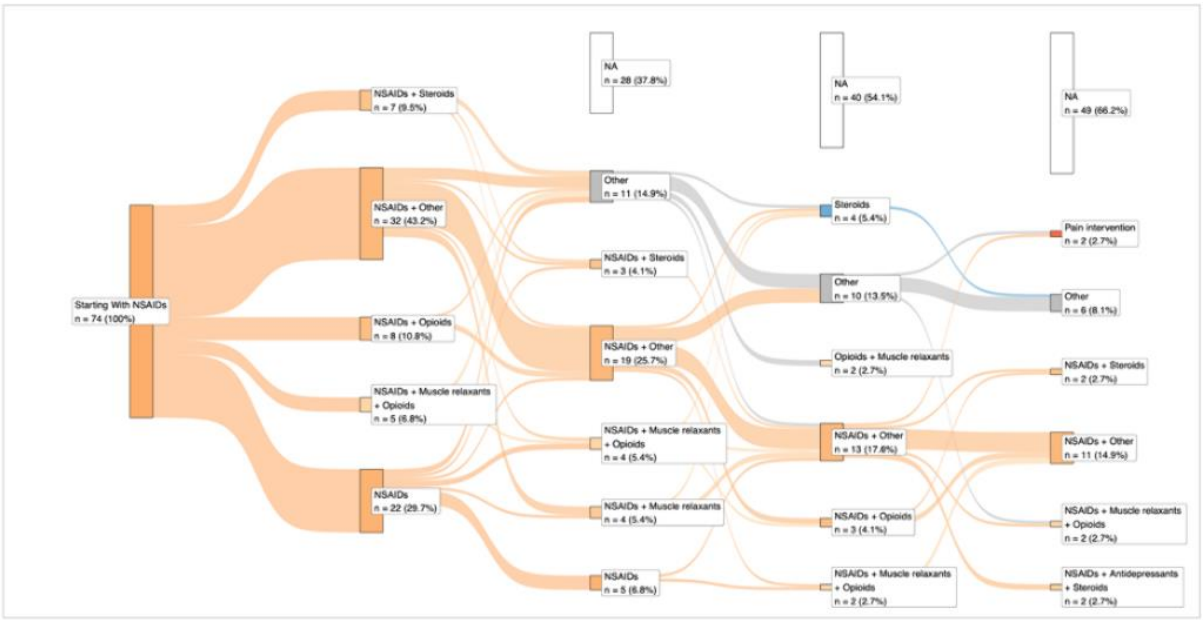
Results:

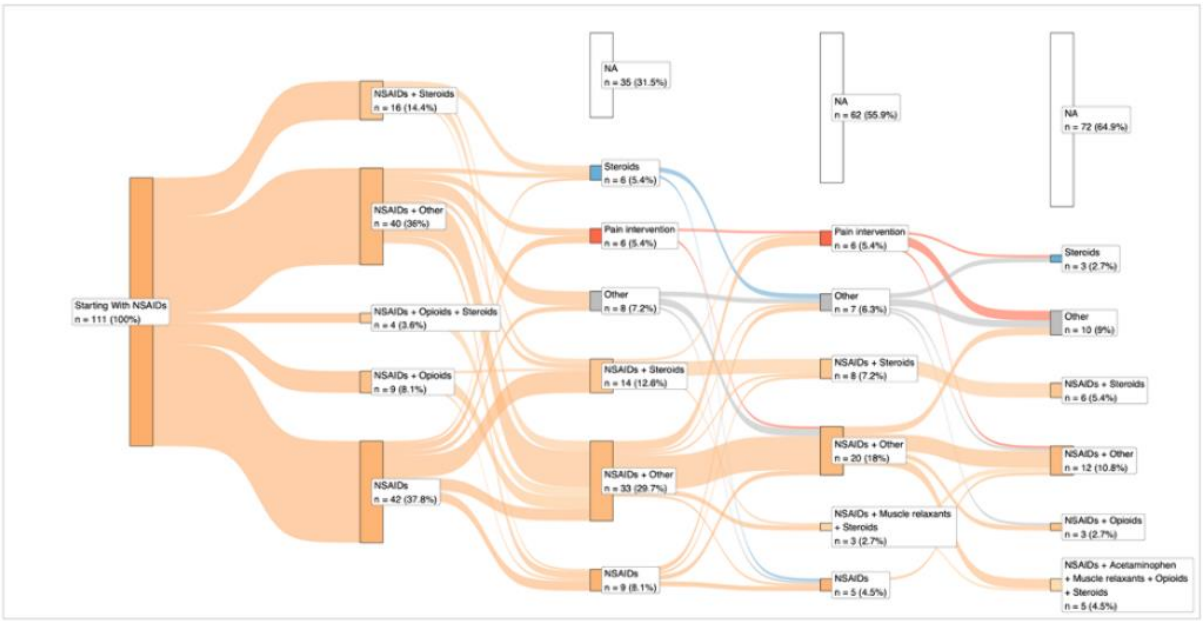


A total of 381 patients received at least one pain management modality during 2005-2014, while 387 patients received such modalities from 2015-2024. Steroid and opioid use as initial treatments decreased significantly from 59% to 51% and 28% to 23%, respectively, between the two periods. NSAIDs emerged as a primary choice, increasing from 19% to 29%. Additionally, younger patients and males in recent years received more diverse prescriptions, with observed racial differences indicating that Black and Hispanic patients were more likely to receive multiple pain management modalities. The overall number of pain prescriptions also declined, reflecting an adaptive, multimodal approach to pain management in SLE.

	2005-2014 (n=381)	2015-2024 (n=387)
	n (%)	n (%)
Sex		
Male	29 (7.6)	35 (9.0)
Female	352 (92.4)	352 (91.0)
Age (years)		
18-26	70 (18.4)	20 (5.2)
27-40	84 (22.0)	102 (26.4)
41-65	166 (43.6)	184 (47.5)
66+	61 (16.0)	81 (20.9)
Race		
Black	22 (5.8)	17 (4.4)
White	224 (58.8)	208 (53.7)
Asian	72 (18.9)	92 (23.8)
Other	54 (14.2)	53 (13.7)
Unknown	9 (2.4)	17 (4.4)
Ethnicity		
Hispanic	58 (15.2)	60 (15.5)
Non-Hispanic	309 (81.1)	297 (76.7)
Unknown	14 (3.7)	30 (7.8)
Insurance		
Private	192 (50.4)	226 (58.4)
Public	159 (41.7)	131 (33.9)
Unknown	30 (7.9)	30 (7.8)
Initial pain management modality		

Steroids	225 (59.1)	198 (51.2)
Opioids	108 (28.4)	87 (22.5)
NSAIDS	74 (19.4)	111 (28.7)
Anticonvulsants	18 (4.7)	36 (9.3)
Antidepressants	29 (7.6)	26 (6.7)
Muscle relaxants	87 (22.8)	76 (19.6)
Pain interventions	14 (3.7)	37 (9.6)
Acetaminophen	58 (15.2)	53 (13.7)





Conclusions: Our findings reveal an ongoing shift toward diversified, multimodal pain management in SLE with reduced reliance on steroids and opioids, particularly among younger patients. Demographic variations underscore the need for personalized and equitable pain management strategies in SLE, supporting future guidelines that incorporate both safety and patient-specific factors.

PV255 / #550

Poster Topic: ***AS24 - SLE-Treatment***

VARIATIONS IN TACROLIMUS WHOLE BLOOD CONCENTRATIONS DURING PREGNANCY AND ITS IMPLICATIONS FOR THERAPEUTIC DRUG MONITORING: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background/Purpose: Tacrolimus is a pregnancy-compatible immunosuppressive increasingly used in systemic lupus erythematosus (SLE) pregnancies. Physiological changes throughout pregnancy impact tacrolimus pharmacokinetics, altering the drug's whole blood concentrations during gestation. However, data is very limited to guide clinicians caring for pregnant women receiving tacrolimus in interpreting tacrolimus trough levels and adjusting the dosage. We completed a systematic review focusing on the variations of maternal tacrolimus trough levels and dosage during SLE and non-SLE pregnancies.

Methods: Using a combination of relevant search terms and keywords, we systematically searched Embase, Ovid, PubMed, Web of Science and Cochrane Library up to January 2024. All observational studies which measured whole blood tacrolimus trough levels during pregnancy were included without language or date restriction. Studies which were reviews, case reports, abstracts only, non-human, and had no tacrolimus levels during pregnancy were excluded from the review. We then used random-effects models to estimate standardized mean differences (SMD) or mean differences (MD), with 95% confidence intervals (CI) of tacrolimus trough levels and doses before and during pregnancy and in the postpartum.

Results: Of 404 publications identified, 124 duplicates were excluded and 282 were screened based on title and abstract, of which 53 full-text articles were assessed for eligibility. Eighteen articles were included in the systematic review and 13 in the meta-analysis. Only 2 studies assessed tacrolimus levels in SLE pregnancies, while the remainder were in pregnant organ transplant recipients (Figure 1). Tacrolimus levels

significantly decreased during pregnancy compared to pre-pregnancy (SMD -1.05; 95% CI -1.72, -0.37), and significantly increased in the postpartum compared to levels during gestation (SMD 0.87; 95% CI 0.37, 1.37) (Figure 2 A, B). Mean differences in tacrolimus trough levels were -1.56 ng/ml (95% CI -2.82, -0.31) between first trimester and before pregnancy, -0.49 ng/ml (95% CI -1.04, -0.07) between second and first trimesters, 0.63 ng/ml (95% CI 0.30, 0.96) between third and second trimesters, and 1.28 ng/ml (95% CI 0.60, 1.96) between the postpartum and third trimester. The variation in tacrolimus levels during pregnancy was usually addressed by increasing the dose during pregnancy vs pre-pregnancy (MD 1.35 mg/day, 95% CI 0.23, 2.48) and decreasing the dose in the postpartum vs pregnancy (MD -0.92 mg/day; 95% CI -1.8, -0.01) (Figure 2 C, D).

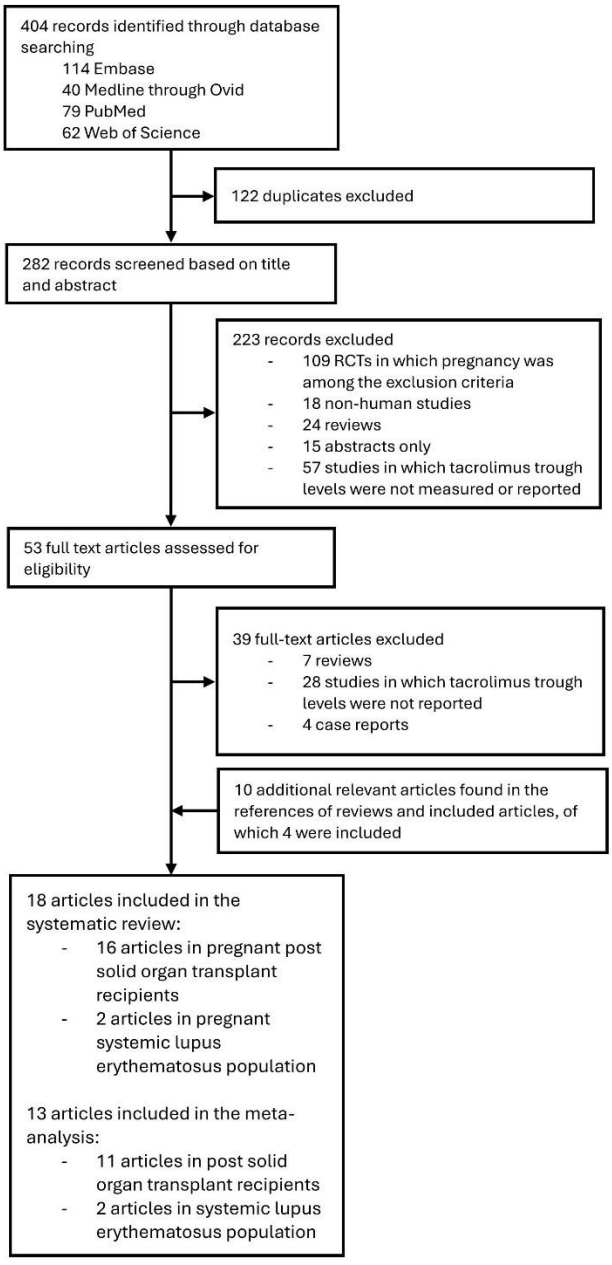
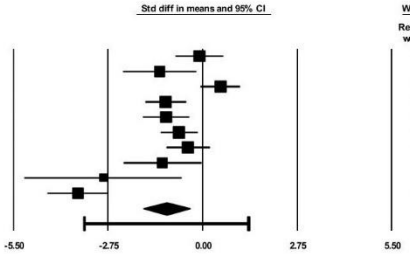


Figure 1. Flow-chart of study selection.

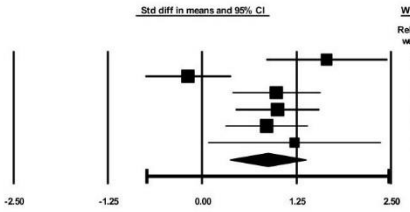
(A) Standardized mean difference of tacrolimus levels - During pregnancy and before pregnancy

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Sample Size	Relative weight	Std Residual
Akturk, Celebi et al. 2015	-0.095	0.354	0.125	-0.788	0.598	-0.269	0.788	16	10.82	0.97
Bhagra, Bhagra et al. 2015	-1.253	0.547	0.299	-2.325	-0.181	-2.291	0.022	8	9.32	-0.19
Golce, Herkloglu et al. 2021	0.520	0.294	0.086	-0.055	1.095	1.772	0.076	24	11.22	1.63
Hiramatsu, Yoshida et al. 2018	-1.076	0.303	0.092	-1.669	-0.483	-3.556	0.000	25	11.16	-0.03
Jain, Shapiro et al. 2004	-1.056	0.346	0.120	-1.735	-0.377	-3.049	0.002	19	10.87	-0.01
Kim, Jeong et al. 2015	-0.680	0.275	0.076	-1.219	-0.141	-2.473	0.013	28	11.34	0.38
Kitada, Nakai et al. 2023	-0.418	0.320	0.102	-1.044	0.209	-1.307	0.191	20	11.05	0.65
Sivaprasadan, Mathew et al. 2020	-1.168	0.578	0.334	-2.301	-0.034	-2.019	0.043	7	9.07	-0.11
Thakrar, Morley et al. 2014	-2.889	1.167	1.362	-5.177	-0.602	-2.475	0.013	3	5.05	-1.24
Yuksel, Yuksel et al. 2019	-3.627	0.451	0.203	-4.511	-2.743	-8.042	0.000	26	10.09	-2.53
Pooled	-1.045	0.342	0.117	-1.716	-0.374	-3.052	0.002	176		
Prediction Interval	-1.045			-3.436	1.347					



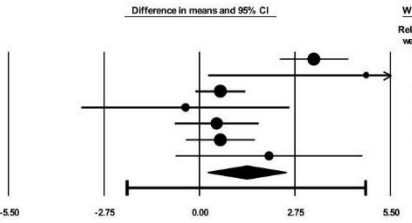
(B) Standardized mean difference of tacrolimus levels - Postpartum and during pregnancy

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Sample Size	Relative weight	Std Residual
Akturk, Celebi et al. 2015	1.649	0.409	0.167	0.847	2.451	4.030	0.000	16	14.96	1.28
Golce, Herkloglu et al. 2021	-0.188	0.289	0.084	-0.755	0.379	-0.651	0.515	24	18.53	-1.98
Hiramatsu, Yoshida et al. 2018	0.984	0.299	0.090	0.397	1.571	3.285	0.001	25	18.22	0.21
Kim, Jeong et al. 2015	0.995	0.283	0.080	0.440	1.550	3.512	0.000	28	18.71	0.24
Ozbilgin, Egeli et al. 2023	0.853	0.279	0.078	0.306	1.400	3.057	0.002	28	18.84	-0.03
Sivaprasadan, Mathew et al. 2020	1.222	0.582	0.339	0.080	2.363	2.098	0.036	7	10.73	0.48
Pooled	0.869	0.255	0.065	0.369	1.369	3.407	0.001	128		
Prediction Interval	0.869			-0.732	2.470					



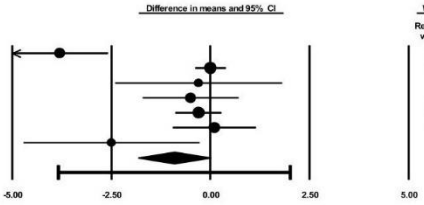
(C) Mean difference of tacrolimus doses - During pregnancy and before pregnancy

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Sample Size	Relative weight	Std Residual
Akturk, Celebi et al. 2015	3.300	0.503	0.253	2.314	4.286	6.559	0.000	16	19.17	1.65
Bhagra, Bhagra et al. 2015	4.800	2.317	5.366	0.260	9.340	2.072	0.038	8	4.81	1.35
Hiramatsu, Yoshida et al. 2018	0.600	0.368	0.135	-0.121	1.321	1.632	0.103	25	20.59	-0.67
Jain, Shapiro et al. 2004	-0.400	1.531	2.345	-3.402	2.602	-0.261	0.794	21	8.63	-0.94
Kim, Jeong et al. 2015	0.500	0.615	0.378	-0.705	1.705	0.813	0.416	28	17.87	-0.69
Sivaprasadan, Mathew et al 2020	0.600	0.508	0.259	-0.397	1.597	1.180	0.238	7	19.11	-0.64
Thakrar, Morley et al. 2014	2.000	1.372	1.883	-0.690	4.690	1.457	0.145	3	9.82	0.37
Pooled	1.353	0.573	0.328	0.230	2.476	2.361	0.018	108		
Prediction Interval	1.353			-2.085	4.791					



(D) Mean difference of tacrolimus doses - Postpartum and during pregnancy

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Sample Size	Relative weight	Std Residual
Akturk, Celebi et al. 2015	-3.800	0.617	0.381	-5.010	-2.590	-6.154	0.000	16	14.49	-2.58
Hiramatsu, Yoshida et al. 2018	0.000	0.198	0.039	-0.388	0.388	0.000	1.000	25	18.92	0.96
Jain, Venkataramanan et al. 1997	-0.300	1.075	1.156	-2.407	1.807	-0.279	0.780	27	9.48	0.43
Kim, Jeong et al. 2015	-0.500	0.617	0.381	-1.709	0.709	-0.810	0.418	28	14.50	0.37
Ozbilgin, Egeli et al. 2023	-0.300	0.295	0.087	-0.879	0.279	-1.016	0.310	28	18.14	0.63
Sivaprasadan, Mathew et al. 2020	0.100	0.535	0.286	-0.948	1.148	0.187	0.852	7	15.51	0.94
Zheng, Easterling et al. 2012	-2.500	1.134	1.285	-4.722	-0.278	-2.205	0.027	10	8.96	-1.08
Pooled	-0.915	0.460	0.212	-1.817	-0.012	-1.987	0.047	141		
Prediction Interval	-0.915			-3.838	2.008					



Random-effects models

Figure 1. **(A)** Forest plot of the standardized mean difference between tacrolimus whole blood concentrations during pregnancy (second or third trimester) and before pregnancy. **(B)** Forest plot of the standardized mean difference between tacrolimus whole blood concentrations in the post-partum and during pregnancy (second or third trimester). **(C)** Forest plot of the mean difference in mg/day between tacrolimus doses during pregnancy (second or third trimester) and before pregnancy. **(D)** Forest plot of the mean difference in mg/day between tacrolimus doses in the post-partum and during pregnancy (third trimester).

Conclusions: Tacrolimus whole-blood levels decrease in the first and second trimesters, then increase back to pre-pregnancy levels in the postpartum. Tacrolimus dosage in pregnancy is typically increased to maintain tacrolimus trough levels within usual therapeutic ranges. Increasing drug dosage could elevate the bio-effective fraction of tacrolimus (not measured by trough levels), raising concerns for safety and efficacy of dose augmentation during pregnancy. Further research is needed to guide clinicians in adjusting tacrolimus in SLE and non-SLE pregnancies to optimize therapeutic drug monitoring in high-risk populations.

PV256 / #543

Poster Topic: *AS24 - SLE-Treatment*

THERAPEUTIC DRUG MONITORING OF AZATHIOPRINE AND TACROLIMUS IN SLE PREGNANCIES: PRELIMINARY RESULTS FROM THE LEGACY COHORT

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Background/Purpose: Pregnant SLE women still face an unacceptably high risk of maternal and fetal morbidity, particularly when their disease is active. How to personalize SLE therapies to optimize pregnancy outcomes remains unknown. Though guidelines strongly recommend azathioprine (AZA) and tacrolimus (TAC) in specific SLE pregnancy scenarios, evidence to guide drug monitoring in this context is non-existent. Our aim is to evaluate the characteristics of SLE pregnancies according to the levels of AZA metabolites (6-TG) and TAC trough levels at the first pregnancy (baseline) visit.

Methods: LEGACY is a prospective cohort enrolling unselected SLE pregnancies ≤16 6/7 gestational weeks at 7 Systemic Lupus International Collaborating Clinics. We record demographics, disease activity, and drugs. In addition, whole blood samples are collected at baseline to determine AZA metabolites (e.g., erythrocyte-free 6-thioguanine, 6-TG) and trough TAC levels if applicable. The present study included Montreal LEGACY participants prescribed either AZA or TAC ≥3 months prior to their first pregnancy visit. We characterized AZA metabolite and TAC levels as continuous and categorical variables (i.e., non-adherent, sub-therapeutic, therapeutic, and supra-therapeutic, using established cut-offs in nonpregnant populations). We defined patients as non-adherent if they had undetectable or barely detectable levels despite appropriate dosing.

Results: Of 70 LEGACY pregnancies enrolled in Montreal, 23 (33%) and 6 (9%) were prescribed AZA and TAC, respectively. Among those prescribed AZA, only 9% had therapeutic levels, while 91% were subtherapeutic or non-adherent (Table 1). Compared to those with therapeutic levels, pregnancies with subtherapeutic or non-adherent AZA levels were more likely to occur in women of non-Caucasian ethnicity/race, on steroids, with longer SLE duration, and with prior lupus nephritis

(Table 2). Among those prescribed TAC, 50% (3/6) had therapeutic levels, while 33% (2/6) and 17% (1/6) were subtherapeutic and supra-therapeutic, respectively. No patients on TAC were identified as non-adherent. Less than half (43%) of pregnancies non-adherent to AZA were in Lupus Low Disease Activity State (LLDAS) at baseline. Of the pregnancies with sub-therapeutic TAC levels, 50% (1/2) were not in LLDAS, while all (4/4) pregnancies with therapeutic or supra-therapeutic TAC levels were in LLDAS at baseline.

Table 1. Number of pregnancies and mean drug dose at baseline visit according to AZA metabolite (6-TG) and TAC trough levels

		Non-adherent	Sub-therapeutic	Therapeutic	Supra- therapeutic
AZA (n=23)	**Pregnancies**, n (%)	7 (30)	14 (61)	2 (9)	-
	AZA dose in mg/kg, mean ± SD	2.5 ± 0.5	1.9 ± 0.5	2.0 ± 0.2	-
TAC (n=6)	**Pregnancies**, n (%)	-	2 (33)	3 (50)	1 (17)
	TAC dose in mg/kg, mean ± SD	-	0.04 ± 0.02	0.04 ± 0.02	0.03 ± 0

Table 2. Baseline maternal characteristics stratified according to AZA metabolite (6-TG) and TAC trough levels

		AZA (n=23)			TAC (n=6)		
		Non-adherent (n=7)	Sub-therapeutic (n=14)	Therapeutic (n=2)	Sub-therapeutic (n=2)	Therapeutic (n=3)	Supra-therapeutic (n=1)
Age in years, mean ± SD		34.0 ± 4.1	33.8 ± 3.9	29.0 ± 0.7	30.3 ± 3.3	31.3 ± 4.1	32.4 ± 0
Race/ Ethnicity, n (%)	Caucasian	1 (14)	4 (29)	2 (100)	2 (100)	2 (67)	1 (100)
	Hispanic	-	-	-	-	1 (33)	-
	Black	2 (29)	3 (21)	-	-	-	-
	Asian	2 (29)	5 (36)	-	-	-	-
	Arabic	1 (14)	-	-	-	-	-
Education in years, mean ± SD		15.7 ± 3.5	16.7 ± 3.1	17.0 ± 1.4	19.0 ± 1.4	14.3 ± 1.5	16.0 ± 0
Disease duration in years, mean ± SD		10.3 ± 6.5	10 ± 6.9	5.3 ± 0.7	9.3 ± 0	4.2 ± 1.1	3.8 ± 0
LLDAS*, n (%)		3 (43)	10 (71)	-	1 (50)	3 (100)	1 (100)
Prior or current lupus nephritis, n (%)		5 (71)	5 (36)	-	2 (100)	1 (33)	-
Steroid use, n (%)		2 (29)	1 (7)	-	-	-	-

*LLDAS: Lupus Low Disease Activity State

Conclusions: We observed that most SLE pregnancies prescribed AZA had sub-therapeutic levels, with nearly a third identified as non-adherent. Pregnancies with lower AZA and TAC levels may be less likely to achieve LLDAS. Despite low numbers, our preliminary results suggest the value of personalized drug monitoring as a novel approach to precision medicine in pregnant SLE women, that might improve efficacy, safety, and adherence in a high-risk population.

PV257 / #666

Poster Topic: ***AS24 - SLE-Treatment***

DOES ADDING CONCOMITANT IMMUNOSUPPRESSIVE THERAPY TO BELIMUMAB PROVIDE ADDITIONAL BENEFITS IN SLE? ANALYSIS FROM BEL-SPAIN: THE SPANISH BELIMUMAB MULTICENTRE REGISTRY

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Background/Purpose: Although belimumab has shown efficacy and safety as an adjunct to standard therapies such as immunosuppressive agents in treating systemic lupus erythematosus (SLE), its role as monotherapy is less well defined. Using data from a national belimumab registry, this study aims to assess whether the addition of immunosuppressive therapy (IS) to belimumab yields additional clinical benefits compared to belimumab monotherapy.

Methods: This retrospective longitudinal study analyzed data from the Spanish Belimumab Registry (BEL-Spain). Patients were included if they had completed at least 12 months of belimumab treatment and had documented data on the use of

concomitant IS at the 12-month follow-up. Patients were grouped based on IS use at 12 months, and data from baseline, 6-month, and 12-month visits were analyzed. Outcomes assessed included the Lupus Low Disease Activity State (LLDAS), DORIS-21 remission criteria, physician-assessed response, flare rates (SFI), and glucocorticoid (GC) usage. To address potential confounding, given that patients receiving combined therapy (belimumab+IS) are more likely to have more severe disease, overlap propensity score (PS) weighting was performed. The PS for receiving combined treatment was estimated using a multivariable logistic regression model, which included covariates such as age, disease duration, baseline disease activity (SLEDAI), GC dose, and the number of flares prior to starting belimumab. The primary outcome was the rate of DORIS-21 remission after 12 months of belimumab treatment

Results: Of the 377 patients in the registry as of November 2024, 258 met the inclusion criteria. Among these, 236 (91.5%) were female, and 218 (85.5%) were Caucasian. The mean age at belimumab initiation was 41.9 years (SD 12.6), with a mean disease duration of 11.4 years (SD 11). The baseline SLEDAI score was 11.8 (SD 10.5), and the mean SLICC Damage Index was 0.76 (SD 1.17). Of the 258 patients, 177 were receiving concomitant IS at 12 months, while 81 were not. **Table 1** compares the two groups in terms of disease activity indices and treatment response. At 6 and 12 months, there were no statistically significant differences between groups in the number of flares (including severe flares), physician-assessed response, or response in terms of achieving a DORIS-21 or LLDAS status. Although the concomitant IS group had a higher baseline SLEDAI, the change over time was similar between groups. Regarding GC use, more patients in the IS group were receiving GCs; however, the average dose was comparable between groups. **Figure 1** illustrates patient treatment trajectories based on the use of concomitant IS over 12 months. After applying overlap propensity score weighting, baseline covariates between the two groups were perfectly balanced. The percentage of patients achieving DORIS-21 remission after weighting was 25% versus 33% at 6 months, and 43% versus 46% at 12 months, in the IS and non-IS groups, respectively. Logistic regression analyses with overlap weighting yielded odds ratios (ORs) of 0.68 (95% CI 0.26–1.77, p 0.43) for DORIS-21 remission at 6 months, and 0.89 (95% CI 0.37–2.14, p 0.77) at 12 months.

Table 1: Baseline Characteristics and Treatment Response in Patients Receiving Belimumab With or Without Concomitant Immunosuppressive Therapy at 12 Months.

	IS therapy at 12 months (n=177)	No IS therapy at 12 months (n=81)	p-value
Characteristics			
Age at Belimumab Initiation (years), mean (SD)	39.68 (13.0)	46.8 (12.6)	NS
Disease Duration at Belimumab Initiation (months), mean (SD)	11 (11.9)	12.1 (10)	NS
Female, n (%)	160 (90.4)	76 (93.8)	NS
Ethnicity, n (%)			
- *Caucasian*	*150 (84.5)*	*68 (84)*	*NS*
- *Black*	*1 (0.6)*	*3 (3.7)*	*NS*
- *Hispanic*	*19 (10.7)*	*9 (11.1)*	*NS*
Meets ACR 97 Criteria, n (%)	173 (97.7)	71 (87.8)	**0.02**
Meets EULAR/ACR 2019 criteria, n (%)	*170 (96.0)*	*76 (93.9)*	NS
Previous Treatment (Before starting Belimumab)			
Hydroxychloroquine, n (%)	155 (87.6)	70 (86.6)	NS
Immunosuppressive Therapy, n (%)	168 (94.9)	62 (75.6)	**<0.001**
- *Methotrexate, n (%)*	*81 (46.0)*	*38 (46.9)*	NS
- *Leflunomide, n (%)*	*10 (5.7)*	*15 (18.8)*	***0.001***
- *Azathioprine, n (%)*	*53 (29.9)*	*28 (34.6)*	NS
- *Mycophenolate Mofetil, n (%)*	*79 (44.6)*	*13 (16.0)*	***<0.001***
- *Cyclosporine, n (%)*	*4 (2.3)*	*1 (1.3)*	NS
- *Tacrolimus, n (%)*	*8 (4.7)*	*0*	***0.05***
- *Cyclophasphamide, n (%)*	*22 (12.4)*	*8 (9.9)*	NS
Number of Previous IS, mean (SD)	1.83 (1.1)	1.59 (1.1)	NS
Previous Biologic, n (%)	39 (22.2)	21 (25.6)	NS
Use of GCs, n (%)	155 (88.1)	70 (86.4)	NS
GC Dose (prednisone equivalent mg/day), mean (SD)	12.04 (11.3)	11.24 (8.7)	NS
Previous Disease Activity (Before Starting Belimumab)			
SLEDAI, mean (SD)	10.30 (5.1)	9.05 (4.8)	NS
Flare Year Before Belimumab, n (%)	147 (84.0)	64 (79.0)	NS
Nº of Flares, mean (SD)	1.49 (0.4)	1.44 (0.9)	NS
Severe Flare, n (%)	50 (32.5)	17 (23.9)	NS
Nº of Severe Flares, mean (SD)	0.55 (0.6)	0.48 (0.6)	NS
SLICC/ACR-DI, mean (SD)	0.65 (1.1)	1.0 (1.4)	**0.026**
Indication of Belimumab			
Multi-Organ Activity, n (%)	110 (63.2)	41 (50.0)	NS
Cutaneous Activity, n (%)	5 (2.9)	4 (4.9)	NS
Articular Activity, n (%)	31 (17.8)	27 (32.1)	NS
Renal Activity, n (%)	12 (6.9)	1 (1.2)	NS
Hematologic Activity, n (%)	10 (5.8)	4 (4.9)	NS
Serositis Activity, n (%)	3 (1.7)	2 (2.4)	NS
Asthenia Activity, n (%)	2 (1.2)	2 (2.4)	NS
Disease Activity at 6 Months of Belimumab			
SLEDAI, mean (SD)	4.84 (3.9)	3.86 (3.4)	NS
Change in SLEDAI, mean (SD)	5.43 (5.6)	5.25 (4.6)	NS
Flare, n (%)	45 (26.6)	16 (20.3)	NS
Nº of Flares ,mean (SD)	0.49 (0.7)	0.55 (0.8)	NS
Severe Flare, n (%)	4 (2.9)	2 (3.2)	NS
Nº of Severe Flares, mean (SD)	0.09 (0.4)	0.08 (0.3)	NS
Medical Response, n (%)	125 (81.7)	61 (84.7)	NS
Remission DORIS 2021, n (%)	46 (28.6)	28 (37.8)	NS
LLDAS, n (%)	83 (51.2)	46 (62.2)	NS
Concomitant Treatment at 12 Months of Belimumab			
Hydroxychloroquine, n (%)	131 (81.4)	54 (74)	NS
Concomitant IS, n (%)	177 (100)	0	—
Use of GC, n (%)	133 (76.9)	48 (60.8)	**0.02**
GC Dose (prednisone equivalent mg/day) , mean (SD)	5.7 (5.3)	4.75 (3.7)	NS
Disease Activity at 12 Months of Belimumab			
SLEDA, mean (SD)	3.84 (3.9)	2.85 (2.8)	**0.05**
Change in SLEDAI, mean (SD)	6.47 (5.7)	6.14 (5.0)	NS
Flare, n (%)	49 (28.3)	17 (21.8)	NS
Nº of flares, mean (SD)	0.27 (0.6)	0.19 (0.5)	NS
Severe flare, n (%)	10 (5.8)	2 (2.6)	NS
Nº of severe flares, mean (SD)	0.06 (0.3)	0.03 (0.2)	NS
Medical response, n (%)	129 (78.2)	62 (83.8)	NS
Remission DORIS 2021, n (%)	77 (48.1)	36 (51.4)	NS
LLDAS, n (%)	104 (65)	52 (74)	NS

IS, immunosuppressive therapy; NS, not significant; GC, glucocorticoids; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC/ACR-DI, Systemic Lupus International Collaborating Clinics / American College of Rheumatology Damage Index; DORIS 2021, DORIS 2021 remission criteria; LLDAS, Lupus Low Disease Activity StateData are expressed as number of patients and percentage [n (%)], or as mean and standard deviation [mean (SD)].

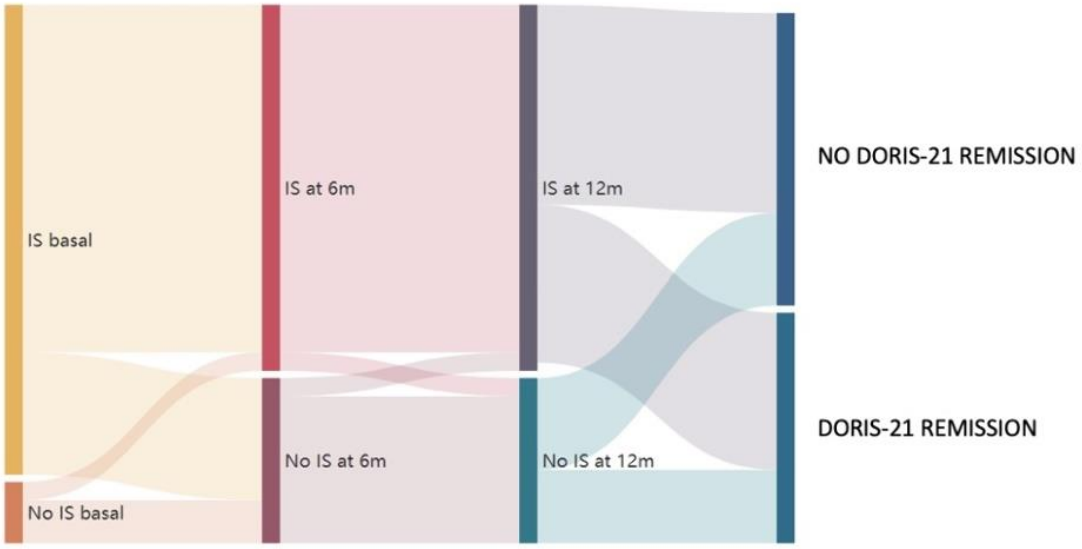

Figure 1: Patient treatment trajectories based on the use of concomitant IS over 12 months

Conclusions: According to BEL-Spain Registry data, the addition of concomitant IS to belimumab did not appears to confer major additional clinical benefits in terms of disease activity reduction, flare rate, or treatment response. These findings suggest that belimumab monotherapy may be a viable option for certain SLE patients. Prospective studies are needed to validate these observations and to identify patient subgroups who may benefit from combination therapy.

PV258 / #502

Poster Topic: ***AS24 - SLE-Treatment***

COMPARATIVE ANALYSIS OF BELIMUMAB, ANIFROLUMAB, AND RITUXIMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE STUDY OF CLINICAL AND ANALYTICAL OUTCOMES

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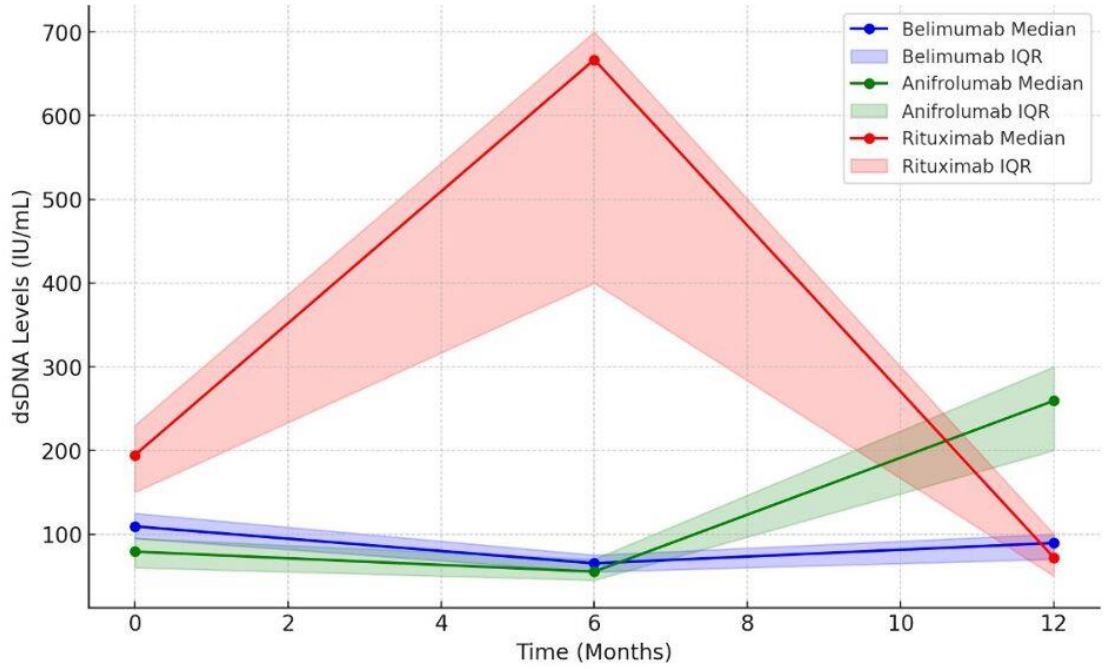
Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disorder with multisystem involvement, often presenting with high disease activity and diverse clinical manifestations. The advent of biological therapies has marked a significant advance in disease control for SLE patients. The latest ACR/EULAR 2023 guidelines recommend Belimumab and Anifrolumab as first-line options for moderate to high disease activity, with Rituximab reserved for refractory cases. Despite these guidelines, clinical responses vary considerably, necessitating close monitoring of laboratory parameters to assess and optimize disease management. **Objectives**: This study aimed to evaluate the clinical and analytical outcomes in SLE patients treated with Belimumab, Anifrolumab, and Rituximab over a one-year period. Specifically, we sought to determine which treatment best controls disease activity through analysis of hemoglobin (Hb), leukocyte, lymphocyte, and platelet counts, complement levels (C3 and C4), and double-stranded DNA (dsDNA) antibody levels.

Methods: We conducted a retrospective study at a tertiary hospital, examining the use of Belimumab, Anifrolumab, and Rituximab in patients diagnosed with systemic lupus erythematosus (SLE) between 2010 and 2024. Diagnosis of SLE was established using the 2019 ACR/EULAR criteria. Data were collected on demographic variables, clinical manifestations of SLE, and laboratory parameters (hemoglobin, leukocytes, lymphocytes, platelets, C3, C4, and dsDNA) over one year of treatment for each biological therapy.

Results: A total of 45 patients were included in the study, with 25 receiving Belimumab, 14 receiving Anifrolumab, and 6 receiving Rituximab. The median age at diagnosis of 34.33 years (IQR: 16–60) and 93.33% being female. Of these, 95.56% received concomitant hydroxychloroquine therapy (mean dose: 355.81 mg/day). Clinical manifestations observed included articular involvement (95.56%), cutaneous involvement (71.11%), hematologic symptoms (84.44%), neurological symptoms (46.67%), and renal involvement (33.33%). The median treatment duration varied by therapy, with 18 months for Belimumab, 6 months for Anifrolumab, and 14 months for Rituximab. Discontinuation rates were higher in patients treated with Belimumab (10

patients) and Anifrolumab (5 patients) compared to Rituximab (3 patients), with causes including infections, lack of efficacy, and adverse events. Concomitant corticosteroids were used by 88% of Belimumab patients (median prednisone dose: 7.5 mg/day), 78% of Anifrolumab patients (5 mg/day), and 83.33% of Rituximab patients (10 mg/day). Anifrolumab provided the most consistent control over Hb levels, rare leukocyte drops below 4,000/µL, and stable lymphocyte and platelet counts, staying above 1,500/µL and 150,000/µL, respectively, with complement levels (C3 and C4) remaining mostly stable; however, dsDNA levels significantly increased by the end of the treatment period, suggesting ongoing disease activity. Belimumab showed moderate efficacy with generally stable Hb and leukocyte counts above threshold, along with lymphocyte and platelet counts; nevertheless, periodic drops in complement levels indicated some consumption, and dsDNA fluctuations pointed to intermittent disease activity. Rituximab, showed less consistent control, with Hb levels varying and occasional anemia, frequent drops in leukocyte and lymphocyte counts below thresholds and fluctuating platelet and complement levels, with notable complement consumption and persistently elevated dsDNA levels reflecting ongoing disease activity. Image 1. Progression of dsDNA levels over 12 months



Conclusions: Anifrolumab demonstrated strong control over hematologic parameters and complement levels but did not achieve lower dsDNA levels, leaving the clinical significance of this finding unclear. In contrast, Belimumab and Rituximab, despite greater variability in hematologic control, maintained better stability in dsDNA and complement levels.

PV258a / #409

Poster Topic: ***AS24 - SLE-Treatment***

BARICITINIB FOR THE TREATMENT OF RHUPUS SYNDROME

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Background/Purpose: The "Rhupus syndrome" is a rarely described and underdiagnosed disease that exhibits characteristics of both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) in the same patient, often presenting more frequently in a sequential manner. Since there is no validated therapeutic strategy, treatment is based on clinicians' experience with approved treatments for either of the two entities, generally based on the predominant clinical manifestations.

Methods: We conducted a retrospective observational review of medical records from the Rheumatology Department at our hospital between 2019 and 2023, identifying patients diagnosed with Rhupus, who received baricitinib. The diagnosis of Rhupus was assigned to patients who met the diagnostic criteria for both Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE). The study involves a comprehensive analysis of clinical outcomes and medication safety profiles for these patients.

Results: A total of 8 patients diagnosed with Rhupus undergoing baricitinib treatment were included. 87.5% were female (median age of 60.5 years, and median follow-up of 12 years). The predominant clinical presentation was RA in 75% of the patients and SLE symptoms in 25%. All patients were ANA positive, while 75% had anti-citrullinated protein antibodies (ACPA) and 87.5% were rheumatoid factor (RF) positive. At the initiation of baricitinib treatment, 62.5% were also taking methotrexate, 37.5% were on hydroxychloroquine, and the median dose of prednisone was 8.75 mg/day. The median duration of baricitinib treatment was 2.5 years. Data on the evolution of activity parameters during the treatment are presented in Table 1. **Table 1. Evolution of activity parameters during treatment.**

Parameter	0m
Tender Joint Count (TJC), median (IQR)	7.5 (2
Swollen Joint Count (SJC), median (IQR)	3.5 (2
DAS 28, median (IQR)	4.47
CRP, median (IQR), mg/dL	0.25

Parameter	0m
ESR, median (IQR), mm/h	14 (2
VASp, median (IQR), mm	65 (5
VASm, median (IQR), mm	60 (6

There were 3 reports of serious infections, 2 due to Herpes zoster infections, one of which required suspension of treatment.

Conclusions: Baricitinib, possibly in combination with other DMARDs, appears to be a promising option for the management of Rhupus, offering benefits in terms of reducing disease activity and improving patient quality of life. These preliminary findings warrant further investigation with larger sample sizes to confirm the efficacy and safety of baricitinib in Rhupus.

PV258b / #492

Poster Topic: *AS24 - SLE-Treatment*

BELIMUMAB FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS IN REAL WORLD: A SINGLE CENTER STUDY

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Background/Purpose: Objectives To analyze the effectiveness and safety of Belimumab in SLE patients with data from a Real- World cohort.

Methods: A single center observational study was performed including SLE patients who had initiated treatment with Belimumab from September 2017 to January 2023. Demographic, clinical, laboratory, effectiveness and safety variables were collected. Effectiveness was evaluated according to changes from the baseline in SLEDAI-2K and disease activity markers (proteinuria, complement consumption and/or Anti DNAds). Safety data was collected including any adverse event (AE) due to any cause. AE was considered serious (SAE) if it was life-threatening or result in hospitalization, disability or in death.

Results: 15 patients were included in the study. Nine patients were still receiving the drug with a mean drug survival of 15.6 months. Belimumab allowed steroid tapering in all cases, but treatment was discontinued just in 1 patient. Treatment also improved disease activity markers in all patients. Belimumab was well tolerated, and the AE reported were infection (14 events) and malaise in 1 patient. In 11 cases, infection was mild (9 upper respiratory tract infection, 1 urinary tract infection and 1 gastroenteritis). 3 severe infections were registered (1 pneumonia, 1 pyelonephritis and 1 meningitis). Regarding LN patients, treatment exposure achieved was 10.85 patients/year. Renal Biopsy demonstrated class III in a patient (20%) and class IV in 4 patients (80%). Mean proteinuria at baseline was 6.66g/24h. In 3 cases, Belimumab was started in the first 6 months after LN diagnosis was established. In 4 cases (80%), Belimumab addition allowed significant reduction of proteinuria and corticosteroids. In 2 out 5 (40%) treatment was discontinued, one case due to an insufficient response and in the other, to a SAE (Cryptococcus neoformans meningitis).

Table 1. Baseline characteristics

Characteristic	All SLE patients n=15 (100%)	No Lupus Nephritis N=10 (37%)	Lupus Nephritis n=5 (51%)
Age – years (ds)	36.4 (11.4)	30.5 (6.9)	48.2 (9.2)
Female sex – number (%)	14 (93.3%)	10 (100%)	4 (80%)
Formulation use at baseline – number (%)			
Intravenous	5 (33.3%)	3 (30%)	2 (40%)
Subcutaneous	10 (66.7%)	7 (70%)	3 (60%)
Disease features – number (%)			
Neuropsychiatric involvement	3 (20%)	2 (20%)	1 (20%)
History of Lupus Nephritis	5 (33.3%)	0 (0%)	5 (100%)
Arthritis	10 (66.7%)	7 (70%)	3 (60%)
Cutaneous	7 (46.7%)	4 (40%)	3 (60%)
Mucosal Ulcers	4 (26.7%)	2 (20%)	2 (40%)
Hematological	13 (86.7%)	8 (80%)	5 (100%)
Serositis	2 (13.3%)	1 (10%)	1 (20%)
Steroid treatment - Number	15 (100%)	10 (100%)	5 (100%)
Mean glucocorticoid dosage – mg of prednisone or equivalent	24.4 (18.03)	15.2 (7.6)	35.4 (20.62)
Concomitant medication – number (%)			
Antimalarial	14 (93.3%)	9 (90%)	5 (100%)
Methotrexate	5 (33.3%)	5 (50%)	0 (0%)
Azathioprine	4 (26.7%)	4 (40%)	0 (0%)
Mycophenolate	5 (33.3%)	0 (0%)	5 (100%)
Cyclophosphamide	1 (6.67%)	0 (0%)	1 (20%)
SLEDAI – mean total score	15.7 (5.4)	14.6 (6.01)	18 (4.2)

Characteristic	All SLE patients n=15 (100%)	No Lupus Nephritis N=10 (37%)	Lupus Nephritis n=5 (51%)
SLE immunological tests			
ANA positivity	**15 (100%)**	**10 (100%)**	**5 (100%)**
Complement component 3	**15 (100%)**	**10 (100%)**	**5 (100%)**
Complement component 4	**15 (100%)**	**10 (100%)**	**5 (100%)**
Anti-double stranded DNA positivity	**15 (100%)**	**10 (100%)**	**5 (100%)**
Anti-double stranded DNA titers	**204.08 (220.6)**	**59.2 (29.6)**	**431.2 (206.75)**

Conclusions: Belimumab maintained an acceptable safety profile and an adequate effectiveness. Intravenous and subcutaneous formulations showed similar performance. Belimumab addition resulted in reduction in proteinuria and corticosteroid use.

PV259 / #49

Poster Topic: ***AS24 - SLE-Treatment***

A SELECTIVE SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION 3 INHIBITOR ALLEVIATES THE MURINE LUPUS

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Background/Purpose: The Signal Transducer and Activator of Transcription 3 (STAT3) is a transcription factor crucial for regulating gene expression. It can be activated by various cytokines, which are implicated in the development of systemic lupus erythematosus (SLE). Studies have demonstrated the efficacy of inhibiting the Janus-activated kinase (JAK)/STAT3 pathway in both lupus animal models and patients. However, many existing STAT3 inhibitors lack specificity, complicating efforts to attribute the observed effects exclusively to STAT3 inhibition. In this study, we examined a novel small molecule selectively inhibits STAT3 (HCB-5018), could ameliorate disease severity by downregulation of STAT3 in MRL/lpr lupus-prone mice.

Methods: MRL/lpr mice were orally administered HCB-5018 from 14 to 18 weeks of age, five days a week for four weeks, followed by the collection of serum, urine, and tissue samples for analysis. The major organs associated with SLE, including the spleen, lymph nodes, and kidneys, were analyzed. Serum ELISA analysis was conducted to measure key indicators of SLE and inflammatory cytokines. Enzyme-linked immunosorbent assays, histological analysis, immunohistochemical staining, and western blotting were performed to evaluate key markers of SLE and protein expression.

Results: Mice treated with HCB-5018 exhibited improvements in the manifestations of the SLE, with decreased levels of anti-dsDNA antibodies and inflammatory cytokines such as IL-17 and increased levels of C3 complement than vehicle-treated mice. HCB-5018-treated mice exhibited significantly lower urine albumin levels. In addition, histopathological analysis of kidney tissue confirmed that HCB-5018 decrease in the number of mesangial cells, proliferation of endothelial cells, and infiltration of inflammatory cells around the glomeruli in MRL/lpr mice. Furthermore, a significant reduction in the expression of phosphorylated STAT3 was observed in the lymph nodes, spleen and kidney of mice treated with HCB-5018.

Conclusions: These results suggest that the STAT3 pathway is implicated in lupus progression in mice and that selective targeting of STAT3 is effective in alleviating the

development of murine lupus. Therefore, HCB-5018 represent a potential candidate for novel therapeutic strategies for SLE management through selective STAT3 inhibition.

PV260 / #333

Poster Topic: ***AS24 - SLE-Treatment***

THE TAIWAN COLLEGE OF RHEUMATOLOGY CONSENSUS FOR THE MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Systemic lupus erythematosus (SLE) exhibits diverse clinical presentations and requires regionally-specific management strategies. Building upon established international guidelines, The Taiwan College of Rheumatology developed the first set of recommendations for SLE management to focus on the unmet needs in clinical practice in Taiwan. This consensus aims to empower healthcare professionals and optimize patient outcomes in Taiwan.

Methods: Rheumatologists from various practicing institutions formed a 15-member panel, through a modified Delphi process, developed consensus statements, which encompasses various aspects of SLE care in Taiwan, including screening and diagnosis; disease monitoring; treatment strategies; and pregnancy. The expert panel reviewed and refined statements through two meetings with anonymous voting based on a 5-point Likert scale. Consensus is defined as ≥75% agreement to the proposed statements.

Results: In total, 32 statements achieved consensus. These statements incorporate the latest scientific evidence with insights from Taiwanese experts to address the unique disease characteristics and challenges faced by patients in the region.

Conclusions: These could serve as a guide to specialists, family physicians, speciality nurses, and other healthcare professionals in Taiwan in the management of SLE.

PV261 / #833

Poster Topic: *AS24 - SLE-Treatment*
Late-Breaking Abstract

DEVELOPMENT OF A QUANTITATIVE SYSTEMS PHARMACOLOGY (QSP) MODEL FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) FOR THERAPEUTIC EVALUATION IN A VIRTUAL POPULATION

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Background/Purpose: Despite numerous recent clinical trials, systemic lupus erythematosus (SLE) has an unmet need with only two approved biologics, while other autoimmune conditions have seen an explosion in approvals of targeted therapies. As such, the complex pathogenesis of SLE warrants ongoing efforts for novel therapeutic investigation and mechanistic insights. Quantitative systems pharmacology (QSP) modeling is becoming an integral tool of drug development through combining physiologic, mechanistic disease models with therapeutic exposure-response relationships. By generating a mathematical representation of molecular and cellular mechanisms in a disease, QSP can evaluate therapeutic effects and provide insight into linking clinical endpoints to optimal biological network targets, clinical trial design, and dosing strategies. A QSP model was developed to characterize clinical endpoint data, assess dosing strategies, and compare mechanism of action contribution to disease pathophysiology for a suite of therapies in moderate to severe SLE, including B-cell Activating Factor (BAFF) inhibitors, type I interferon (IFN) inhibitors, tyrosine kinase 2 (TYK2) inhibitors, and standards of care. In this study, two IFN biologics: anifrolumab, acting upon the IFN receptor, and sifalimumab, acting upon IFN-α, are compared to assess model performance.

Methods: An ordinary differential equation (ODE)-based QSP model for SLE was constructed to describe the interplay of cells and biomolecules, tissue-level phenomena, and clinical endpoints. These interactions were modeled using literature-reported and internal information from in vitro/ex vivo assay. SLE Responder Index-4 (SRI4), Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), and swollen joint count (SJC) clinical endpoints are included to support clinical evaluation. Thales, a QSP modeling platform designed to streamline optimization of virtual patient populations (SimPops), was utilized to calibrate the model to 45 clinical trials and 29 treatment arms simultaneously, thereby capturing the variability of patients

representing a broader SLE population. Anifrolumab trials were included in the model calibration data, while sifalimumab trials were withheld to be used only for model validation. Model assessment was evaluated by quantifying percentage of datapoints that fell within model confidence intervals.

Results: The model's calibrated SimPops captures SRI4, CLASI, and SJC profiles within 95% CIs across the various dosing levels of anifrolumab in the training dataset and successfully predicted sifalimumab drug effects in the validation dataset. Notably, the model reproduces clinical endpoint profiles for the trial placebo groups despite differing baseline patient characteristics and tapering protocols across the anifrolumab and sifalimumab trials. Furthermore, the model exhibits a greater SRI4 response at week 52 for anifrolumab when compared to sifalimumab, in agreement with the anifrolumab (NCT01438489) and sifalimumab (NCT01283139) trials. The difference in patient improvement may be attributable to the broader, systemic effects of targeting the IFN receptor as opposed to the IFN-α cytokine alone.

Conclusions: An SLE QSP model was successfully developed and optimized a SimPops that accurately captures clinical endpoint data for two IFN biologics. The Thales platform and QSP model framework allows for efficient addition of clinical trials, biological mechanisms, and therapeutics as new data becomes available, allowing for more robust predictions of novel therapeutics and combinations. Further, key determinants of individual patient response can be explored to identify patient subgroups that are best suited for specific therapies. Overall, the continuously evolving QSP model can serve as a foundation for SLE therapeutic development by providing a mechanistic understanding of SLE.

PV262 / #104

Poster Topic: ***AS24 - SLE-Treatment***

IANALUMAB'S DUAL MODE OF ACTION: TARGETING B CELLS THROUGH ENHANCED B CELL DEPLETION AND BLOCKADE OF B CELL-ACTIVATING FACTOR RECEPTOR SIGNALING

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Background/Purpose: B cells are key players in the pathogenesis of systemic lupus erythematosus (SLE), Lupus Nephritis (LN) and other systemic auto-immune diseases, supporting B cell depletion as an attractive therapeutic strategy in these patients. However, survival signals mediated by high level of B cell-activating factor (BAFF) may interfere with B cell depletion, as well as drive disease flares. Ianalumab, an investigational afucosylated monoclonal antibody targeting BAFF-receptor (BAFF-R), has been shown to deplete B cells through enhanced antibody-dependent cellular cytotoxicity (ADCC) with concurrent blockade of BAFF:BAFF-R mediated signals. [1] Here, we extensively characterize the properties of ianalumab on B cells *in vitro*, as well as its ability to deplete circulating and tissue B cells in B6 mice and in the spontaneous non-obese diabetic (NOD) mouse model of Sjögren's disease (SjD).

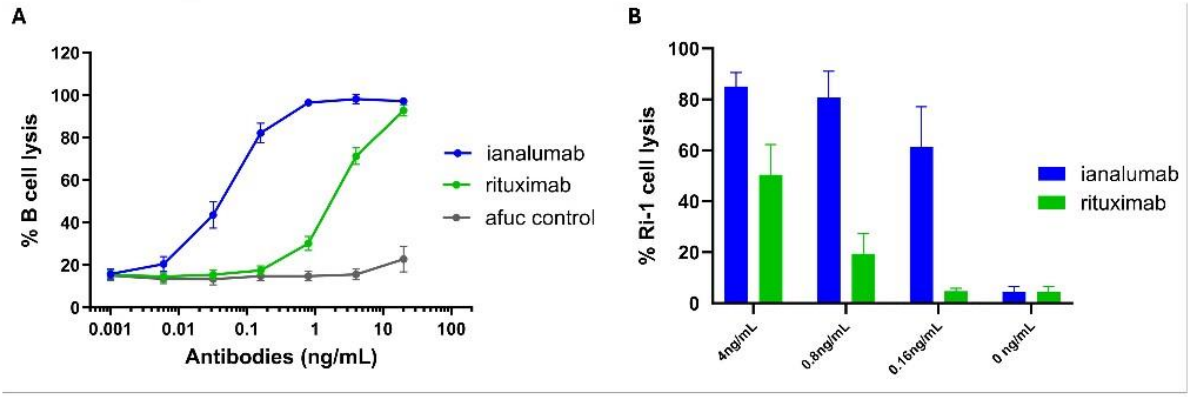
Methods: The binding affinity and specificity of ianalumab were evaluated using Biacore and flow cytometry. *In vitro* B cell killing was assessed using peripheral blood mononuclear cells or isolated NK cells and B cells from healthy volunteers (HVs) and patients with SLE or SjD. *In vitro* blockade of BAFF stimulation was evaluated through competition assays with labeled BAFF, Western blots of Nuclear Factor Kappa B Subunit 2 (NF-*k*B2) intact and cleaved forms, B cell proliferation measured by thymidine incorporation, and quantification of IgG secretion. The efficacy of B cell depletion following administration of ianalumab in B6 and NOD mice was investigated using flow cytometry and/or histology in blood and relevant organs.

Results: Ianalumab demonstrated high affinity and selectivity for BAFF-R. In an ADCC assay co-culturing purified NK cells with B cells from HVs, ianalumab showed a 44-fold increased potency compared to rituximab (**Fig. 1A**). This increased potency was also observed when NK cells from patients with SjD and SLE were tested (**Fig. 1B**). Additionally, ianalumab effectively prevented BAFF from binding to BAFF-R expressing cells. This blockade of BAFF-R on human B cells correlated with effective inhibition of BAFF-induced cleavage of NF-κB2 (p100), proliferation and IgG production. Notably, ianalumab was able to inhibit B cell proliferation with the same potency, when induced by a BAFF trimer or 60-mer (**Fig. 2**). *In vivo*, ianalumab induced a significant reduction of

B cell subpopulations in blood and lymphoid organs of B6 mice. In addition, ianalumab was able to reduce B cells in the salivary glands of NOD mice, showing its ability to reduce B cells in the target organs of mice suffering from systemic autoimmunity.

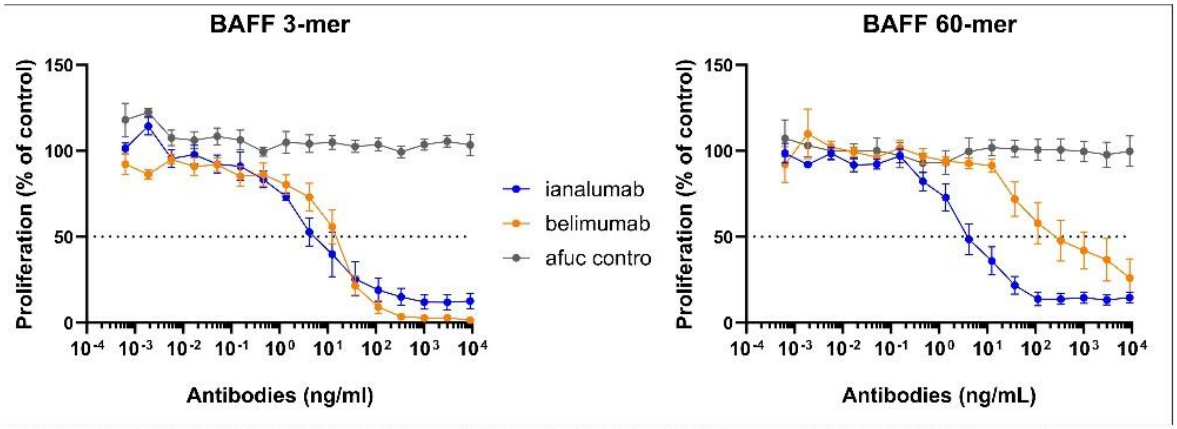
Conclusions: Ianalumab, through its dual mechanism of action, addresses limitations of first-generation B cell targeting therapies for auto-immune diseases by providing more potent B cell depletion and additional BAFF-R blockade on remaining B cells. Accordingly, patients with SLE (NCT03656562) or SjD (NCT02962895) treated with ianalumab for up to 52 weeks showed sustained reduction in disease activity in phase 2 trials. [2,3] Ongoing phase 3 studies in SjD, SLE and LN will provide further evidence on the efficacy and safety of ianalumab in larger patient populations. **Reference:** 1. McWilliams EM, et al. Blood Adv. 2019;3:447-60. 2. Shen N, et al. [abstract]. Arthritis Rheumatol. 2023;75 (suppl 9). 3. Bowman SJ, et al. Lancet. 2022;399:161-71.

Figure 1. Ianalumab shows superior potency to rituximab in ADCC. A. B cells and NK cells from HVs (N=7 donors) where cocultured in the presence of ianalumab, rituximab or an irrelevant afucosylated antibody, and B cell lysis was evaluated after 60 min. **B.** NK cells from patients with SjD (N=3 donors) were cocultured with RI-1 cells in the presence of ianalumab or rituximab and Ri-1 cell lysis was evaluated after 60 min.



ADCC, antibody-dependent cellular cytotoxicity; HVs, healthy volunteers, NK, natural killer; SjD, Sjögren's disease

Figure 2. Ianalumab inhibits proliferation of human B cells from HVs (N=7 donors) stimulated by BAFF in combination with anti-IgM. Purified B cells were stimulated with BAFF 3-mer or BAFF 60-mer, in the presence of anti-IgM. Cell proliferation was measured by 3H-thymidine incorporation.



ADCC, antibody-dependent cellular cytotoxicity; HVs, healthy volunteers, NK, natural killer; SjD, Sjögren's disease

PV263 / #331

Poster Topic: ***AS24 - SLE-Treatment***

PATIENT PREFERENCES FOR TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS—A QUALITATIVE STUDY

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Background/Purpose: Systemic lupus erythematosus (SLE) requires long-term treatment with medications that carry risks of side effects and toxicities, including the risks of ocular toxicity from hydroxychloroquine, infection from oral and biologic immunosuppressants, and glucocorticoid toxicity from prednisone use. The objective of this study was to evaluate how patients approach lupus treatment decisions, including harms/benefits trade-offs with ongoing use of hydroxychloroquine and other medications for SLE.

Methods: We conducted a qualitative study of patients with SLE using focus groups. We identified potential study participants with a diagnosis of SLE at Massachusetts General Hospital and affiliate hospitals. We randomly selected patients for invitation to participate in virtual focus groups, with intentional oversampling of racial minority groups, males, and patients with lupus nephritis. Virtual focus groups were conducted by a physician moderator using a standardized focus group guide. Topics included key factors in patients' decision-making process for lupus treatment decisions in general, specific factors involved in the use of hydroxychloroquine, involvement in treatment decisions, and sources of information used to make treatment decisions. Focus groups were audio recorded and transcribed. Two researchers conducted an inductive thematic analysis of the focus group transcripts through an iterative process using Dedoose. Selected themes and subthemes were independently verified by a third assessor.

Results: Twenty-eight individuals with SLE participated in one of four focus groups. The mean age was 47 years, and they were 89% female, 14% Black or African American, 11% Hispanic, and 21% Asian (**Table 1**). These participants had a range of lupus manifestations, including 39% with lupus nephritis and 32% with neurologic lupus, and the median disease duration was 9 years (IQR 6-16 years). All study participants were prior or current users of hydroxychloroquine, and the majority had used oral glucocorticoids and one or more oral immunosuppressants. There were nine major themes and 18 sub-themes identified along with illustrative quotes (**Table 2**). Patients with lupus emphasized both short-term and long-term considerations, including the

priorities of avoiding short-term side effects of medications, controlling lupus disease activity, and also avoiding long-term damage from both medication toxicity and lupus itself. Preferences to avoid glucocorticoid toxicity and to maintain quality of life and physical function were also common drivers of lupus treatment decisions. The concern for future organ damage was a key factor for the decision to continue long-term hydroxychloroquine use, illustrated by a participant's quote, "The hydroxychloroquine is like an insurance so you don't get more damage to something else, sometimes out of a flare." The risk of hydroxychloroquine retinopathy was the primary shared concern related to hydroxychloroquine use, but patients consistently reported that routine screening for hydroxychloroquine retinopathy provided reassurance about the safety of continuing the medication. Trust in their medical team was a key factor that supported confidence in treatment decisions.

Table 1. Characteristics of Study Participants

Characteristics	N (%) or Mean (SD)
Age, years	47.0 ± 11.9
Sex	
Female	25 (89.3)
Male	3 (10.7)
Race and Ethnicity	
White, non-Hispanic	15 (53.6)
Asian	6 (21.4)
Black of African American	4 (14.3)
Hispanic	3 (10.7)
Duration of SLE	
> 5 years	22 (78.6)
≤ 5 years	6 (21.4)
Lupus Manifestations	
Lupus nephritis	11 (39.3)
Inflammatory arthritis	22 (78.6)
Cutaneous lupus	20 (71.4)
Serositis	12 (42.9)
Neurologic lupus	9 (32.1)
SLE Medication Use, Current or Prior	
Hydroxychloroquine	28 (100)
Oral glucocorticoids	24 (85.7)
Mycophenolate	17 (60.7)
Methotrexate	10 (35.7)
Azathioprine	8 (28.6)
Rituximab	7 (25)
Cyclophosphamide	6 (21.4)
Belimumab	6 (21.4)
Anifrolumab	1 (3.6)
Serologic Markers	
dsDNA antibody	23 (82.1)
Smith antibody	13 (46.4)
Antiphospholipid antibodies	16 (57.1)
SSA (Ro) and/or SSB (La) antibodies	9 (32.1)
Insurance Type	
Private Insurance	15 (53.6)
Medicaid	10 (35.7)
Medicare	3 (10.7)

Table 2. Themes Highlighting Important Factors for Patients in Making Lupus Treatment Decisions

Themes	Theme Subcategories	Illustrative Quotes
Avoiding side effects	Fear of medication side effects	"I was terrified with it because when I read about the side effects and what it could do, it took me some time to [decide], should I take this medicine or not?"
	Avoid fatigue and brain fog	"One of my biggest concerning factor is, is this going to make me tired, because I am already-- the fatigue with lupus is so crushing. So, if it's going to cause me to be tired, I have to really-- I have to really keep that in mind."
	Minimize infection risk	"Adding more immunosuppressive drugs when I already have really low blood count is really worrying about keeping the lupus under control but opening myself up for more and more infection."
Avoiding organ damage	Avoid long-term organ damage	"The hydroxychloroquine is like an insurance so you don't get more damage to something else, sometimes out of a flare." "One of the major things that's always in the back of my head, it's organs. Is everything working fine right now? I know we do our blood work when we check up every now and then, and everything is fine, and we keep moving forward, but in 10, 15, 20 years, is everything going to be fine?"
	Avoid liver and kidney toxicity	"I do worry about my liver functions going up and down with the different agents I've been on. At least, we track them. We follow them. And so when the liver functions are elevated, we stop the drug and try something different."
	Avoid hydroxychloroquine eye toxicity	"Is this damaging my eyes very rapidly or not? Fortunately, it's not. It's very slow going, slow depositing. So, it is definitely a risk versus the benefit." "It does weigh in the back of your head because without your eyesight-- lupus can be isolating as it is…So now you're adding in that you've lost your eyesight. And then that adds that added layer of isolation."
	Avoid glucocorticoid toxicity	"Prednisone, it's good for one thing, but it's bad for the other because-- what I don't like about the prednisone, you take it long term, and it could mess with your bones. And what I don't like about it, too, it raises your blood sugar level."
Controlling lupus activity		"Sometimes if a flare is really, really bad, you've got to do what you have to do to get out of it at that moment."
Trade-offs between medications	Minimize glucocorticoid use	"I hate prednisone. So, I will do everything under the sun not to go on prednisone…so, it's finding that balance between all the different [medications]."
	Balancing treatment effects	"I think the biggest thing for me is the quality of life, where you have to outweigh the side effects versus what are the negative aspects of me coming off medication"
	Minimize medications	"My goal is to be off of everything I can be off of because I do worry about all those effects down the line."
Quality of Life and Convenience	Maintain functional status	"Overall, I think for me, it really is all about quality of life and for me, being able to continue to work and just not be in pain so much and less fatigue." "My main focus was to just stay working, just maintain less pain and more joint dexterity."
	Minimize burdens from pills	"I am 100% guilty of just forgetting pills or only taking half of my pills because it takes me 20 minutes to choke them down. I think I take 16 pills a day or something like that. But the pill fatigue from managing all the pills is my biggest nemesis"
	Minimize burdens from lab monitoring	"Doing blood tests every two weeks, for some once a month, some, three months. And all of those trips and lost time from work really add up especially because I don't live close to my lab. And so I have to take multiple hours off to go and do it. So again, not a deal breaker, but definitely part of the consideration."
Cost		"I think price is a big one. Most of the stuff I'm on is not that expensive…but when you start getting into three, four different medications, the price can run up sometimes.
Sources of medication-related information	Trust in medical team/doctor	"My doctors kept telling me that this is the safest compared to everything else, so I stay on it." "One other factor for me was having your specialists that are involved in your treatment plan agree on the medication…having them both agree on the same treatment plan was really helpful and helped me be more confident in the treatment that I was receiving too."
	Outside sources of information (internet, social media)	"I sometimes go to online support groups just to hear how people's experience is in it. And I know it's anecdotal, but it's really, the collective knowledge that people who've been taking meds for a long time is important for me to listen to as well." "I do my own Google research and verify with my doctors, but I think that helps guide me into asking better questions about medications, about different treatment options."
Involvement in treatment decision	Urgent treatment decisions	"So at that point, after the biopsy, everything was so swollen, and I could barely move out of bed. So, I was open to whatever kind of thing that they [recommended]."
	Long-term treatment decisions	"I've done my own research on the medication. So, I take it in hopes to prevent any sort of flares or things like that"
	Lack of autonomy	"I don't think that it's ever been really explained or discussed. I guess that was just the dose that was chosen when I was first diagnosed at 17."
Reassurance of retinopathy screening		"I've been on hydroxychloroquine long term. And the fact that it's kept me under control for so long. So, it's definitely worth the sort of just going to the eye doctor every six months. It's worth that for the long-term benefits of everything that's been under control for so long."

Conclusions: Patients with SLE face ongoing treatment decisions for this chronic condition, and they incorporate multiple factors to balance both the short- and long-term harms and benefits of medications.

PV264 / #825

Poster Topic: *AS24 - SLE-Treatment*
Late-Breaking Abstract

DESIGN OF A PHASE 2A, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF MK-6194, AN INTERLEUKIN-2 MUTEIN, IN ADULT PARTICIPANTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Regulatory T cell (Treg) dysfunction is a key feature of systemic lupus erythematosus (SLE). Preliminary studies expanding Tregs in patients with SLE using low-dose interleukin 2 (IL-2) have demonstrated promising results. However, use of IL-2 is limited due to its short half-life requiring frequent injections and the narrow therapeutic window for Treg selectivity poses the risk of activating other immune responses (e.g. pathogenic T effector, natural killer [NK] cells). Compounding these challenges, SLE is immunologically and clinically heterogenous with a high variability in disease activity and organ system involvement. Interpretation of SLE trial results is further complicated by various background treatments, imperfect outcome measures, and need for experienced investigators. Therefore, there are challenges to the development of treatments for Treg expansion in SLE.
MK-6194 is an IL-2 mutein with enhanced Treg selectivity, increased affinity for the alpha chain of the IL-2 receptor (CD25) and decreased affinity for the beta chain (CD122), which is Fc-conjugated for increased half-life. In a phase 1 trial, subcutaneous (SC) MK-6194 was generally well tolerated (up to a single dose of 10 mg; up to doses of 5 mg every 2 or 4 weeks) by healthy participants with no serious adverse events (AEs) or dose-limiting toxicities. Injection site erythema was the most common AE. A dose-dependent increase in Treg number was observed, peaking between Days 8–11 with no attenuation after repeated injections and minimal impact on non-Treg or NK cell numbers. These data support further evaluation of MK-6194 as a potential treatment for SLE. To test this hypothesis in a phase 2a SLE trial, analysis of past trials highlights the importance of accurate assessment of eligible patients with clinically significant disease activity and limited background therapy.

Methods: This multicenter, randomized, double-blind, placebo-controlled phase 2a trial is currently enrolling eligible adults (**Table**) with moderate-to-severe SLE (**Figure**)

randomized (1:1:1) to receive SC placebo or MK-6194 in one of two dosing regimens for 52 weeks (main trial period) followed by a double-blind long-term extension (NCT06161116). The primary efficacy endpoint is the proportion of participants with Systemic Lupus Erythematosus Responder Index-4 (SRI-4) response at Week 28. The primary safety endpoint is the number of AEs and AEs leading to trial discontinuation. Secondary endpoints include SRI-4 response at Week 52, British Isles Lupus Assessment Group-Based Composite Lupus Assessment (BICLA) and Cutaneous Lupus Erythematosus Disease Area and Severity Index-50 (CLASI-50) responses at Weeks 28 and 52, and change from baseline in tender/swollen joint counts. Exploratory endpoints include immunologic parameters, pharmacokinetics/pharmacodynamics, anti-drug antibodies, and biomarker parameters. Patient eligibility and accuracy of disease activity scoring throughout the trial will be adjudicated by an experienced, blinded clinical team.

Table. Inclusion/exclusion criteria

Key inclusion criteria	Key exclusion criteria

• Diagnosis of SLE ≥ 6 months prior to screening
• Positive ANA (titer ≥ 1:80) or positive anti-dsDNA antibody or positive anti-Sm antibody, or positive anti-SSA/Ro antibody at screening
• Presence of ≥ 1 of the following SLE manifestations at screening and randomization:
  ○ Active lupus rash with CLASI-A erythema and scale/hypertrophy combined score of ≥ 2
  ○ > 2 tender/swollen joints in wrists, MCPs, or PIPs
• Hybrid SLEDAI total score of ≥ 6 at screening and clinical hybrid SLEDAI score of ≥ 4 at screening and randomization
• Receiving ≥ 1 permitted background therapy* for SLE
	• History of (or current) inflammatory condition other than SLE that may interfere with disease activity assessments or corticosteroid taper, confound the study results, or pose an additional risk to the participant
	• Active or clinically significant infection‡, or any infection requiring chronic systemic anti-infective therapy
	• Symptomatic heart failure (NYHA class III or IV), or myocardial infarction or unstable angina pectoris ≤ 6 months prior to screening
	• Severe chronic pulmonary disease requiring oxygen therapy
	• Organ transplantation requiring continued immunosuppression, or major surgery ≤ 3 months prior to screening or planned during the study
	• Known systemic hypersensitivity to IL-2, modified IL-2 including MK-6194, or its inactive ingredients
	• Known history of lymphoproliferative disease including lymphoma, or signs and symptoms suggestive of possible lymphoproliferative disease§
	• Drug-induced CLE, drug-induced SLE, active severe lupus nephritis, or active/unstable neuropsychiatric lupus
	• APS diagnosis with history of vascular thrombosis, catastrophic APS, or pregnancy morbidity ≥ 6 months prior to screening
	• History of any malignancy, except for successfully treated non-melanoma skin cancer or localized carcinoma *in situ* of the cervix
	• Receiving > 1 immunosuppressant or > 1 oral NSAID¶, or daily oral NSAID at greater than maximum recommended dosage
	• Received prohibited medications**

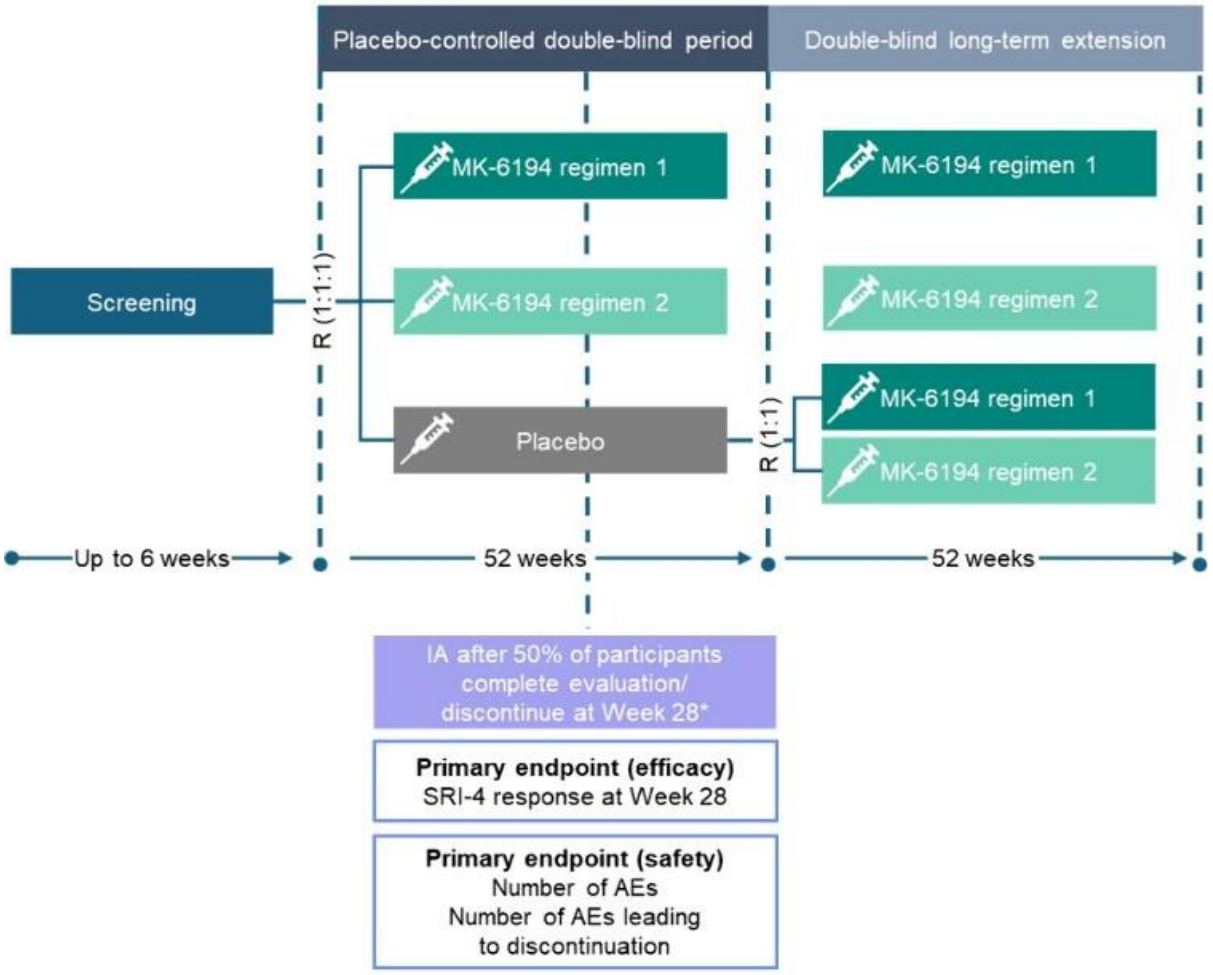
For full details on the inclusion and exclusion criteria please refer to NCT06161116.

*One immunosuppressant or dapsone and/or one antimalarial and/or oral corticosteroids; †In the opinion of the investigator; ‡Including HBV, HCV, HIV, COVID-19, or TB; §Such as lymphadenopathy and/or splenomegaly; ¶Excluding low-dose aspirin (< 350 mg/day); **Within specified timeframes prior to randomization (and prohibited during the study).

ANA, antinuclear antibody; APS, antiphospholipid syndrome; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-A; CLE, cutaneous lupus erythematosus; dsDNA, double-strand deoxyribonucleic acid; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IL, interleukin; MCP, metacarpophalangeal joint; NSAID, non-steroidal anti-inflammatory drug; NYHA, New York Heart Association; PIP, proximal interphalangeal joint; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; Sm, Smith; SSA/Ro, Sjögren's-syndrome-related antigen A autoantibody; TB, tuberculosis.

Table: Figure:

Figure. Trial design and key endpoints



*An interim futility analysis will be performed after the first 50% of randomized participants complete the Week 28 evaluation or prematurely discontinue the study.
AE, adverse event; IA, interim analysis; R, randomization; SRI-4, Systemic Lupus Erythematosus Responder Index-4.

Results: The trial is actively recruiting approximately 270 participants in 17 countries across North America, Latin America, Europe, the Middle East and Asia-Pacific regions. Estimated primary trial completion will be April 2027.

Conclusions: This currently recruiting phase 2a trial was designed to address challenges in the development of Treg expansion therapy for SLE. MK-6194, a novel IL-2 mutein, was developed for Treg selectivity with longer half-life. The trial protocol utilized knowledge gained from past SLE publications to increase the likelihood of interpretable data.

PV265 / #821

Poster Topic: *AS24 - SLE-Treatment*
Late-Breaking Abstract

SUPERDIMERIC ANTIBODY-LIKE MOLECULE WITH DUAL FC DOMAINS PROVIDES POTENT B CELL DEPLETION WITH MINIMAL CYTOKINE INDUCTION VIA TARGETING OF CD19, CD20 AND FC GAMMA RECEPTORS

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Background/Purpose: Potent tissue B cell depletion using CD19-targeting CAR-T cells or T cell engagers in patients with autoimmune diseases such as Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) has led to durable clinical responses in early clinical studies and the results suggest the potential to reset the autoreactive immune system for long-term disease remission. However, there are limits to the safety and accessibility of CD19-targeting CAR-T cells or T cell engagers across large patient populations. While antibodies targeting CD20 have provided significant responses in several autoimmune diseases, they do not deplete $CD19^{+}/CD20^{-}$ autoantibody-secreting plasmablasts or pro-B cells in bone marrow. Antibodies targeting CD19 have shown efficacy in Neuromyelitis optica spectrum disorder (NMOSD) and IgG4-related disease in clinical trials. Deep and broad depletion of B cells by targeting both CD19 plus CD20 with an antibody-based approach may provide additional clinical benefits by restoring immune homeostasis in autoimmune diseases with low risk of cytokine-mediated adverse events.

Methods: Here we describe HB2198 generated using the GEM-DIMER™ platform. HB2198 was designed for bivalent target binding to both CD20 (Fab domains derived from rituximab) and CD19 (Fab domains derived from humanized version of FMC63, the parental antibody used to generate approved CD19-targeting CAR-T cell therapies) and importantly, contains two Fc domains both with amino acid variants S239D and I332E, further increasing Fc-gamma receptor binding and immune effector functions. We assessed the B cell depletion, T and NK cell activation, and inflammatory cytokine release in response to HB2198 by flow cytometry, ELISA, and functional assays *in vitro* using cell lines and primary immune cells from healthy individuals and patients. Pharmacodynamic effects *in vivo* were evaluated in non-human primates.

Results: HB2198 exhibited enhanced Antibody Dependent Cellular Cytotoxicity (ADCC) and Antibody Dependent Cellular Phagocytosis (ADCP) immune effector functions over conventional antibodies targeting CD19 or CD20. HB2198 potently depleted B cells from healthy human whole blood after overnight culture. Further, HB2198 depleted memory B cells from healthy and SLE patient PBMCs *ex vivo*. Importantly, little or no

induction of inflammatory cytokines IFN-γ, IL-6, TNF-α, or IL-2 was detected *in vitro* and *in vivo*. These findings contrasted with dose-dependent, potent *in vitro* cytokine induction observed in the presence of a CD20-CD3 T cell engager. Infusion of HB2198 into cynomolgus monkeys led to >99% depletion of circulating B cells within 1-3 days and durable depletion of memory B cells with minimal inflammatory cytokine response *in vivo*.

Conclusions: HB2198 demonstrated potent B cell depletion *in vitro* and long-term reduction in memory B cell depletion *in vivo*, suggesting the potential for broad and deep depletion of autoantibody producing cells. Importantly, minimal induction of proinflammatory cytokines was observed *in vitro* and *in vivo*. These data support the advancement of HB2198 in autoimmune indications where depletion of $CD19^+$ and/or $CD20^+$ cells would provide clinical benefit.

PV266 / #632

Poster Topic: ***AS24 - SLE-Treatment***

RITUXIMAB SUPER-RESPONDERS: CHARACTERISTICS OF PATIENTS WITH MORE THAN 3 YEARS RESPONSE TO A SINGLE CYCLE OF TREATMENT

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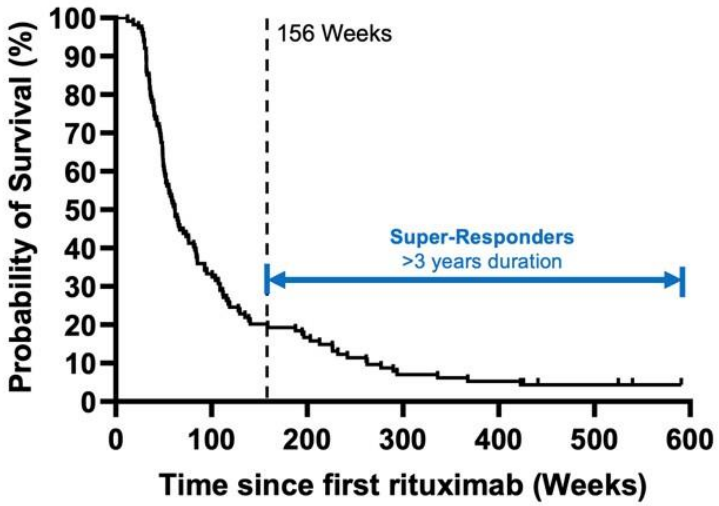
Background/Purpose: Rituximab has been used to treat SLE for 20 years but efficacy is limited by inadequate B-cell depletion. Emerging therapies such as CD19 CAR-T-cells have been reported to induce deeper B-cell depletion and thereby drug-free remission up to 18 months. However, with rituximab, we showed that depth of depletion and rate of repopulation were highly variable, and related to patient factors e.g. complement levels and FCGR genotype. Using highly sensitive flow cytometry protocol, plasmablast repopulation below 0.0008 x 10^9/L predicted longer response[1]. Anecdotally, we have observed "rituximab super-responders" with sustained remission after one cycle of rituximab. The objectives of the study were to assess a) incidence of rituximab-super-response, with or without concomitant immunosuppressant; and b) factors associated with super-response after the first rituximab cycle, with a view to personalise anti-CD20 antibodies in SLE.

Methods: We conducted an observational study of consecutive rituximab-treated SLE patients in a single centre over 20 years who had followed an on-demand retreatment strategy. Usual practice was to continue concomitant immunosuppressants but taper glucocorticoids. Univariable and multivariable logistic regression analyses were performed to identify factors associated with rituximab super-response, with $p<0.1$ associated with the deviance used for inclusion into the model.

Results: Of 149 first-cycle-rituximab-treated patients, 114 were included in the study [excluded due to non-response in Cycle 1=17; received fixed retreatment at 6-9 months=15; deaths within the first 3 years=2; and discontinued rituximab due to psoriasis=1]. Based on survival curve, we defined super-responders as >3 years (Figure 1). This occurred in 23/114 patients (20%) with median (IQR) duration of response 263 (212,423) weeks. At baseline, rituximab-super-responders had: mean (SD) age 35 (14) years, 20/23 (87%) female, ancestry European=9/23 (39%); South Asian=6/23 (26%), Chinese/SE Asian=2/23 (9%); African=5/23 (22%); and Mixed=1/23 (4%)], concurrent APS 6/23 (26%), disease duration 2.8 (1,5) years, median (IQR) SLEDAI-2K 11 (7,15), and median (IQR) numeric BILAG score 21 (13,25). Sustained suppression of plasmablasts was observed at 3 years: median (IQR) 0.0008 (0.0002,0.0045). 8/23 Rituximab-super-responders (34.8%) were not prescribed immunosuppressants or withdrew them during

follow up (drug free remission). In multivariable analysis of 114 patients, factors associated with duration of response >3 years were non-European ancestry (OR 4.6, 95% CI 1.6-12.7)) and concurrent APS, (3.2, 0.99-10.35), while longer disease duration (0.89,0.80-0.99 per year) was associated with lower odds of rituximab-super-response. No other factors (age, sex, anti-dsDNA+, low C3/C4, number of antibodies, concomitant immunosuppressant, disease activity score, and active BILAG A/B in 5 most frequent domains) were predictive.

Figure 1: Kaplan-Meier plot of relapse-free survival after a first cycle of rituximab



Conclusions: Sustained drug-free remission is not confined to patients who have received CAR-T CD19 but may be observed following rituximab. 1 in 5 rituximab-treated patients had >3 years response to their first cycle, and 1 in 12 had sustained, immunosuppressant-free remission. Rituximab-super-response is associated with patient characteristics typically denoting disease severity (early disease, non-European ancestry and APS), as well as marked suppression of plasmablast repopulation. This suggests that sustained drug-free remission is a feature of the overall immune environment rather than the modality of B-cell killing. Given their safety and low cost, anti-CD20 monoclonal antibodies in early poor-prognosis SLE may be preferable to intensive therapy in refractory disease. Future work will include more detailed biomarker evaluation of this cohort. **Reference:** 1. Md Yusof MY et al, Ann Rheum Dis. 2017 Nov;76(11):1829-1836

PV267 / #708

Poster Topic: ***AS24 - SLE-Treatment***

REAL-WORLD EXPERIENCE OF EFFECTIVENESS OF NON-MEDICAL SWITCH FROM ORIGINATOR TO BIOSIMILAR RITUXIMAB AND BETWEEN BIOSIMILARS IN CONNECTIVE TISSUE DISEASES AND VASCULITIS

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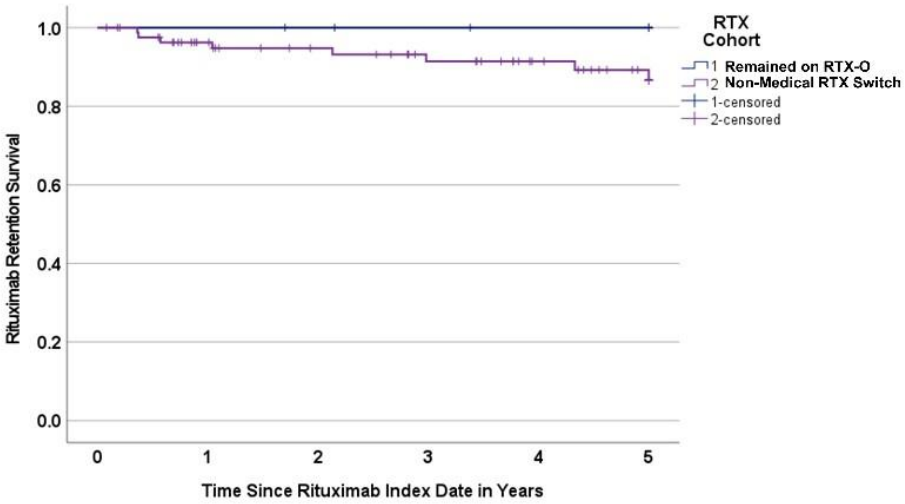
Background/Purpose: In rheumatoid arthritis (RA), we previously showed that non-medical switch from rituximab originator (RTX-O) to rituximab biosimilar (RTX-B) was largely effective with comparable 18-month retention rates between those who switched vs remained on RTX-O, 76% and 82% respectively[1]. However, the uptake of non-medical switch in SLE and other connective tissue diseases and vasculitis (CTD-VAS) has been slow due to a concern with cross-reactivity of antibodies. Our study objectives were to evaluate the effectiveness of non-medical switch from RTX-O to RTX-B or between RTX-Bs in CTD-VAS.

Methods: We conducted a retrospective observational cohort study of rheumatic and musculoskeletal diseases (RMD) patients in a single centre between October 2017 (Index date) and November 2024. During this period, all patients were encouraged to switch to RTX-B (Truxima®) unless declined by the patient or specified by the treating clinician. Furthermore, between 2021-2023, patients on Truxima® were switched to Rixathon® and then reverted to Truxima® in 2024 due to contractual agreement. Due to differences in disease activity tools, clinical responses were graded into full response; partial; and non-response. Other measures of effectiveness include the depth of CD20+ cells depletion by highly sensitive flow cytometry and 5-year rituximab retention rate between those who underwent non-medical switch (Group 1) vs remained on RTX-O (Group 2).

Results: At Index date, of 829 RMD patients treated with rituximab, 306 (37%) were given for CTD-VAS, while the remaining for RA. Of these, 84/306 (27%) underwent non-medical switch, Group 1 [RTX-O to RTX-B=58 (69%); between RTX-Bs=26 (31%)]. They had mean (SD) age 51 (15) years, 61 (72%) were female, 61 (72%) had European ancestry, and diagnoses were SLE (54%), AAV (31%), Sjogren (5%), Myopathies (2%) and other CTD (8%). 16/306 (5%) patients remained on RTX-O (Group 2), while 206/306 (67%) initiated treatment with RTX-B. At the last follow-up, of 84 patients in Group 1, 72 (86%) remained on RTX-B [64/72 (89%) switched from RTX-O to RTX-B; 6/72 (8%)

switched between RTX-Bs; and 2/72 (3%) reverted to previous RTX-B brand]. 5/84 (6%) of patients on RTX-B reverted to RTX-O and regained response. Reasons were infusion reaction=1, serum sickness=1; neutropenic sepsis 5 days post-rituximab switch=1; skin lesion=1; incomplete depletion and inferior response=1. Of 82/84 and 74/84 patients in Group 1 with paired clinical response and B-cells data respectively, there was no difference in response rate (partial or full) and CD20+ cell complete depletion in the rituximab cycle before and after switch, p=0.289 and p=0.815 respectively (McNemara's test). Patients in Group 2 had more comorbidities, number of rituximab cycles, and number of previous immunosuppressants than those in Group 1. At 5 years, 8/84 (9.5%) patients discontinued rituximab in Group 1 (inefficacy=7 including 2 who reverted to RTX-O); death due to pneumonia=1), while all 16 patients in Group 2 continued therapy. Unadjusted Kaplan-Meier analysis showed no difference in 5-year rituximab retention between Group 1 and Group 2; p=0.152 (Figure 1).

Figure 1: Kaplan-Meier plot of rituximab retention survival from Index date



Conclusions: Conclusion: Our findings support the non-medical switch either from RTX-O to RTX-B or between RTX-Bs in CTD-VAS with no difference in clinical response and depth of B-cell depletion before and after switch. 5-year rituximab retention rate was very good regardless of non-medical switch and appeared higher than in RA. Analysis of outcomes of patients who initiated RTX-B is in progress and will help estimate number needed to harm with non-medical rituximab switch. **Reference:** Melville A et al. Rheumatology. 2021 Aug 2;60(8):3679-3688.

PV268 / #674

Poster Topic: ***AS24 - SLE-Treatment***

CLINICAL EFFICACY, SAFETY, AND IMPACT ON PERIPHERAL BLOOD IMMUNOPHENOTYPES OF ANIFROLUMAB IN SLE PATIENTS WITH MINOR FLARES FOLLOWING LLDAS ACHIEVEMENT : LOOPS REGISTRY AND FLOW STUDY

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Background/Purpose: Anifrolumab (AFM) has demonstrated efficacy and safety in patients with systemic lupus erythematosus (SLE), but the effect of type I interferon modulation on the immune abnormalities in these patients is unclear. This study aimed to investigate the relationship between changes in immune phenotype and the efficacy of AFM in patients with SLE who experienced minor flares after lupus low disease activity state (LLDAS).

Methods: Patients with SLE who achieved LLDAS but experienced minor flares due to mild or moderate organ damage according to the clinical items of the revised SELENA flare index were divided into two groups: Those who received standard of care (SoC, n = 18) with increased glucocorticoid (GC) doses or additional immunosuppressants and those who received only additional AFM treatment (n = 50). Effectiveness and safety were compared 26 weeks after intensification using propensity score-based inverse probability of treatment weighting (PS-IPTW). Peripheral blood immunophenotypes at baseline were analyzed and compared with age- and sex-matched healthy controls (HC, n=70) about the standardized NIH/FOCIS Human Immunophenotyping Consortium protocol. Immunophenotype changes and their impact on re-achieving LLDAS at Week 26 were also analyzed in SLE patients who experienced minor flares after LLDAS.

Results: After PS-IPTW adjustment, there were no differences in baseline characteristics between the groups. The 26-week persistence rate of the AFM group was 90.0% (45/50). The LLDAS achievement rate was significantly higher in the AFM group (SoC group: AFM group = 33%:87%, $p < 0.001$). The SELENA-SLEDAI scores significantly decreased in both groups, and no significant difference was observed between the groups at 26 weeks (SoC group: AFM group = 2.1±2.0:1.8±1.7, $p = 0.453$). The mean dose of GC was markedly reduced in the AFM group (3.6±3.1→2.1±2.7, $p < 0.001$), and the GC mean dose at Week 26 was significantly lower in the AFM group (SoC group: AFM group = 5.7±1.8:2.1±2.7, $p < 0.001$), leading to GC discontinuation in three patients. The incidence of adverse events was significantly lower in the AFM group (SoC group: AFM

group = 47%:12%, p < 0.001), particularly for infections (SoC group: AFM group = 38%:12%, p < 0.001). In peripheral blood immunophenotype analysis, in comparison with HC, SLE patients had a higher proportion of activated Tfh cells (p=0.003), activated Th17 cells (p=0.0025), and plasmocytes (p=0.015), and a lower proportion of naïve B cells (p=0.010). There were no significant differences in baseline immunophenotypes between the AFM and SoC groups. At 26 weeks, both groups exhibited decreased plasmocyte proportions. In the AFM group, the proportions of activated Th17 cells (p = 0.014), Tfh cells (p < 0.001), and activated Tfh cells (p = 0.018) significantly decreased at 26 weeks compared to baseline. In both the SoC group and the AFM group, no baseline clinical features were associated with achieving LLDAS or DORIS remission. However, in the AFM group, patients with a higher baseline proportion of plasmocytes were more likely to achieve DORIS remission. In the SoC group, there were no peripheral blood immune phenotype characteristics associated with LLDAS or DORIS remission.

Conclusions: In SLE patients who experience a minor flare after achieving LLDAS, disease activity may be effectively controlled by adding AFM alone, without the need to increase immunosuppressants or glucocorticoids. Among these patients, AFM appears to be particularly effective in those with a high baseline proportion of plasmocytes prior to its initiation.

PV269 / #125

Poster Topic: ***AS24 - SLE-Treatment***

LUPUS LOW DISEASE ACTIVITY STATE ATTAINMENT AND REDUCED GLUCOCORTICOID USE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE TULIP LONG-TERM EXTENSION TRIAL OF ANIFROLUMAB

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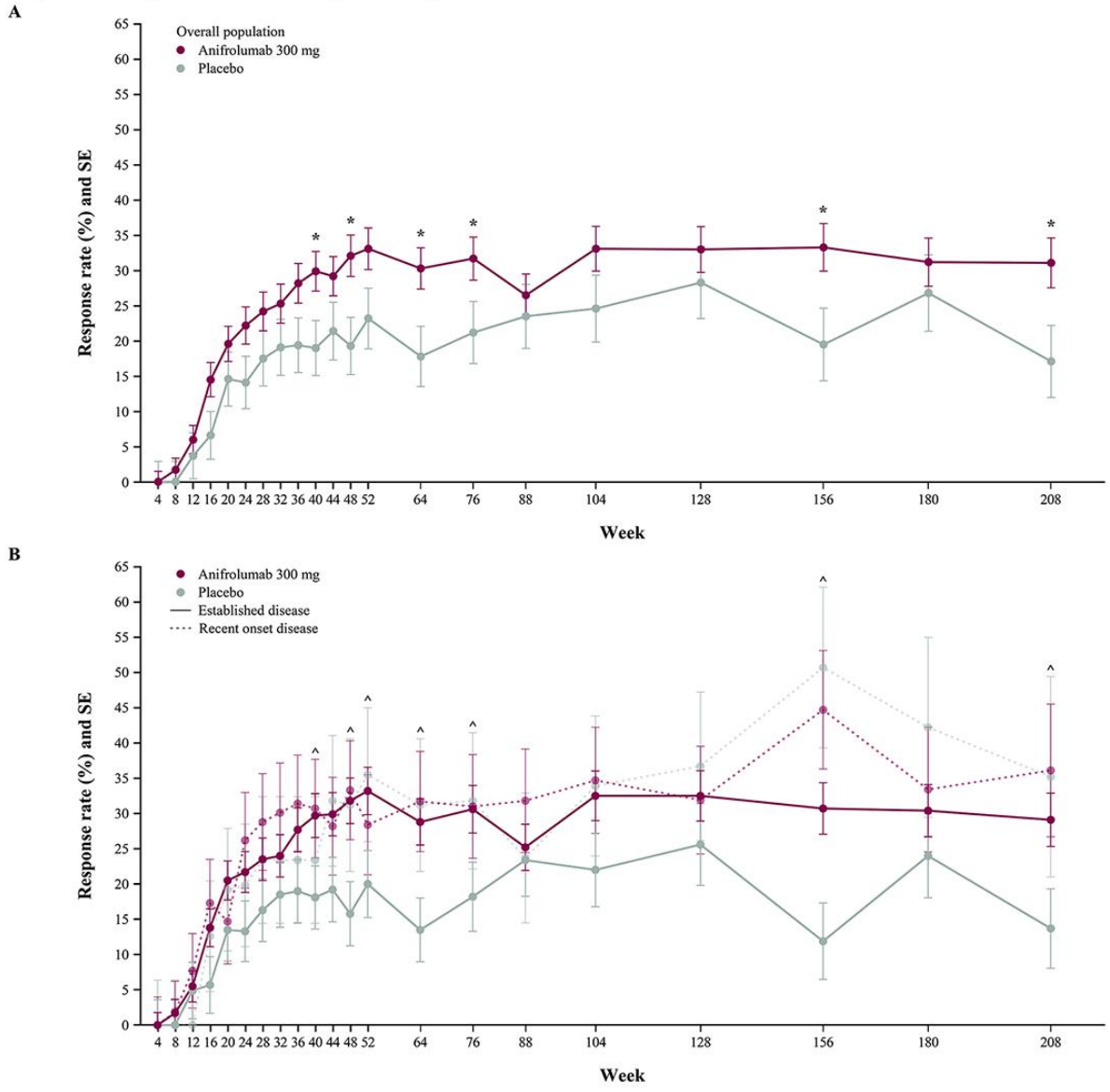
Background/Purpose: Attainment of Lupus Low Disease Activity State (LLDAS) is associated with reductions in disease flares, damage accrual, oral glucocorticoid (GC) use, and mortality in patients with systemic lupus erythematosus (SLE). In a post hoc analysis of pooled data from the 52-week phase 3 TULIP-1/-2 trials, patients with SLE treated with anifrolumab were more likely to attain LLDAS compared with placebo. [1] Although criteria for attainment of LLDAS requires a GC dosage of ≤ 7.5 mg/day, the European Alliance of Associations for Rheumatology 2023 guidelines recommend ≤ 5 mg/day GC for patients with SLE. [2] In the present analysis, the long-term impact of anifrolumab treatment on LLDAS attainment together with GC reduction to ≤ 5 mg/day during the 3-year TULIP long-term extension (LTE) study was evaluated.

Methods: In the TULIP-LTE study (NCT02794285), patients with moderate to severe SLE despite standard therapy received anifrolumab 300 mg or placebo as an extension of their assigned treatment in the 52-week TULIP-1/-2 trials. [3] Patients were followed from baseline (of TULIP-1/-2) through the LTE (Week 208). Response was defined as LLDAS attainment together with GC dose reduction to ≤ 5 mg/day (LLDAS+GC ≤ 5) at the same visit; response rates were analyzed using a stratified Cochran–Mantel–Haenszel method. Responses were also analyzed by disease onset (established [SLE diagnosis > 2 years pre-randomization] vs recent onset [SLE diagnosis ≤ 2 years pre-randomization]). LLDAS attainment was defined as (all): SLE Disease Activity Index 2000 ≤ 4 without major organ activity, no new disease activity, Physician's Global Assessment (0-3) ≤ 1, prednisone/equivalent ≤ 7.5 mg/day, standard immunosuppressant dosing, no restricted medications (TULIP-1/-2 period only), and no investigational product discontinuation.

Results: LLDAS+GC ≤ 5 response rates were higher with anifrolumab treatment vs placebo overall throughout TULIP-LTE (**Figure 1A**; anifrolumab vs placebo, Week 52: 33.1% [81/254] vs 23.2% [25/108]; Week 208: 31.1% [58/194] vs 17.1% [11/65]). LLDAS+GC ≤ 5 response rates were higher through Week 208 with anifrolumab vs placebo in patients with established disease (**Figure 1B**; 29.1% [46/162] vs 13.7% [7/53]); treatment differences between groups were not consistent through Week 208 among patients with recent onset disease, given the small sample size.

Figure 1. LLDAS+GC ≤ 5 in patients in the overall population (A) and by disease onset (B) treated with anifrolumab compared with placebo over the 3-year LTE period



Time from diagnosis subgroup	Treatment group	Total patients at each Week, n								
		52	64	76	88	104	128	156	180	208
Overall	Anifrolumab 300 mg (n = 257)	254	251	249	245	238	227	214	205	194
	Placebo (n = 112)	108	104	102	99	93	83	76	73	65
Established disease	Anifrolumab 300 mg (n = 212)	210	207	206	202	196	187	177	171	162
	Placebo (n = 86)	82	78	77	74	69	62	59	58	53
Recent onset disease	Anifrolumab 300 mg (n = 45)	44	44	43	43	42	40	37	34	32
	Placebo (n = 26)	26	26	25	25	24	21	17	15	12

GC, oral glucocorticoid; LLDAS, Lupus Low Disease Activity State; LTE, long-term extension; SE, standard error; SLE, systemic lupus erythematosus.
Response rates and differences in response rates between treatment groups were calculated using a stratified CMH approach. Last observation carried forward was used to impute missing data for TULIP-1/-2, but not for data captured in the LTE. Nominal P-values < 0.05 are designated with an * for overall patients and ^ for patients with established disease.

Conclusions: Anifrolumab treatment was associated with higher rates of LLDAS attainment together with GC reduction to ≤ 5 mg/day vs placebo, overall and in patients with established disease. Thus, LLDAS attainment and GC reduction are treatment goals that can be achieved with anifrolumab. **References:** [1.] Morand EF. Ann Rheum Dis 2023;82:639-645.
[2.] Fanouriakis A. Ann Rheum Dis 2024;83:15-29.
[3.] Kalunian KC. Arthritis Rheumatol 2023;75:253-265. **Acknowledgements:** This study was sponsored by AstraZeneca. Writing assistance was provided by Tamara Fink, PhD, of JK Associates Inc., part of Avalere Health, and funded by AstraZeneca. Presented at EULAR 2024 and reused with permission of Morand E, et al. POS0528 LUPUS LOW DISEASE ACTIVITY STATE ATTAINMENT AND REDUCED GLUCOCORTICOID USE IN PATIENTS WITH SLE IN THE TULIP LONG-TERM EXTENSION TRIAL OF ANIFROLUMAB. *Ann Rheum Dis.* 2024;83:958.

PV270 / #457

Poster Topic: ***AS24 - SLE-Treatment***

DRUG LEVELS AND ANTI-DRUG ANTIBODIES OVER TWO YEARS OF BELIMUMAB THERAPY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Although methods to measure belimumab concentrations and anti-drug antibodies (ADA) are available, the clinical significance of drug monitoring and how immunogenic belimumab is in patients with systemic lupus erythematosus (SLE) remain unclear. This study aimed to assess ADA incidence in patients with SLE and to investigate associations between belimumab concentrations and clinical response, serological outcomes, and adverse events.

Methods: We included 100 patients treated with intravenous belimumab. Clinical data and biological samples were collected at baseline and months 3, 6, 12, and 24. Belimumab levels were determined by quantitative sandwich ELISA, and ADA by an acid-dissociation radioimmunoassay. Clinical activity was evaluated with the SLE disease activity index 2000 (SLEDAI-2K), revised SLE activity measure (SLAM-R), and physician's global assessment (PhGA). Serological markers included complement C3, C4, and anti-dsDNA antibodies. Adverse events were retrieved from case-report forms and medical charts. We performed cross-sectional analyses using Spearman's correlation coefficients, and longitudinal analyses using generalised estimating equations.

Results: Belimumab concentrations varied widely (median: 25.8; IQR: 20.9–43.5 μg/mL), but were stable over time at the group level. Pre-existing ADA were detected in 2 patients, but no patient developed ADA during follow-up. Belimumab levels moderately correlated with SLEDAI-2K (ρ: -0.37; p=0.003) and PhGA (ρ: -0.41; p=0.005) at month 6, while longitudinal analyses revealed associations with SLEDAI-2K (β: -0.10; SE: 0.05; p=0.031) and SLAM-R (β: -0.32; SE: 0.13; p=0.014). Despite moderate correlations between belimumab levels and serological markers at month 6, there were no

associations in longitudinal analyses. There was no relationship between belimumab levels and adverse events.

Conclusions: Belimumab yielded no immunogenicity. Belimumab levels were associated with clinical activity but not with serological activity or adverse events.

PV271 / #799

Poster Topic: *AS24 - SLE-Treatment*
Late-Breaking Abstract

TREATMENT PATTERNS AND OUTCOMES OF ACTHAR GEL IN SYSTEMIC LUPUS ERYTHEMATOSUS: A PHYSICIAN-REPORTED CHART REVIEW

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Background/Purpose: Acthar Gel is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides. Acthar Gel is approved by the U.S. Food and Drug Administration (FDA) for the treatment of several autoimmune disorders and medical conditions known to cause inflammation, including systemic lupus erythematosus (SLE). This study aims to describe the characteristics of patients with SLE treated with Acthar Gel, utilization patterns of the medication, and physicians' assessments of its effects on patients' health status.

Methods: This study was prospectively designed with a predefined protocol and statistical analysis plan. The study employed a chart review methodology, where 41 U.S. rheumatologists reviewed 56 patient charts for individuals treated with Acthar Gel for SLE within the past 24 months. Patients with known contraindications to Acthar Gel were excluded from the study. In November 2024, physicians searched patient records starting from April 1, 2022. Data included demographics, comorbidities, symptoms, prior treatments and health outcomes following Acthar Gel treatment.

Results: The study included 56 SLE patients with an average age of 42 years and mean BMI of 27.5 kg/m^2. Most were female (84%) and African-American (50%). Common comorbidities included chronic joint disease (34%), hyperlipidemia (34%), hypertension (34%) and arthritis/osteoarthritis (30%). Prior to Acthar Gel treatment, 63% of patients reported fair-to-poor health status, with a mean rating of 3.6 out of 5 (where 1 = excellent and 5 = poor). Frequent symptoms included joint pain (84%), rashes (68%) and fatigue (68%). Most were previously treated with antimalarial drugs (64%), corticosteroids (64%), immunosuppressive drugs (57%) and biologic disease-modifying antirheumatic drugs (DMARDs) (55%). The average time since diagnosis was 4.8 years and the average duration of Acthar Gel treatment was 8 months. Most patients (91%) were dosed at 40-80 units twice per week. Physicians reported that 89% of patients experienced improved health status after Acthar Gel treatment. Improvements among these patients included overall symptoms (82%), pain (54%), fatigue (44%), reduced corticosteroid use (44%), physical function (38%) and strength (28%).

Conclusions: This study demonstrates that Acthar Gel is an effective treatment option for SLE. Patients experienced improvements in multiple areas such as symptoms, pain relief, fatigue, reduced corticosteroid use, physical function and strength. These findings underscore the utility of Acthar Gel in enhancing outcomes for patients with SLE.

PV272 / #675

Poster Topic: ***AS24 - SLE-Treatment***

IMMUNOSUPPRESSANTS AND LUPUS-RELATED DAMAGE: A PROPENSITY SCORE ANALYSIS OF THE BIRMINGHAM LUPUS COHORT

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Background/Purpose: Non-corticosteroid immunosuppressants as azathioprine (AZA), mycophenolate mofetil (MMF), cyclophosphamide (CYC), calcineurin inhibitors (CNIs) and methotrexate (MTX) are widely used in the treatment of SLE. However, their effectiveness in preventing organ damage remains unclear as observational studies are subject to confounding by indication (where patients with more severe disease are more likely to receive these medications). This study aimed to identify the relationship between the use of immunosuppressive medications and the development of organ damage in SLE patients.

Methods: The Birmingham Lupus Cohort is a longitudinal observational cohort of patients with SLE. All patients fulfilled the 1997 ACR Updated Classification Criteria for SLE. At each medical consultation, the disease activity was assessed using the classic BILAG index (or BILAG-2004), and damage was evaluated using the SLICC/ACR damage index (SDI). In addition, serological test results, and treatment plans, including any change in the management plan, were recorded. Propensity scores were estimated for the likelihood of receiving each immunosuppressive medication based on covariates including age, gender, ethnicity, year of diagnosis, year of enrollment, disease duration, smoking, antimalarial use, immunosuppressive use, and baseline SDI. For the treatment group, the baseline was the first exposure to the index medication, while for the control group, baseline was the first date with a disease activity score of A or B in any domain of the BILAG index. Multivariable Cox Proportional Hazard models were developed to study the effect of each immunosuppressive medication on organ damage in SLE patients over 10 years of follow-up, adjusted for propensity score, disease activity, and corticosteroid use.

Results: We included 361 SLE patients of whom 334 (92.5%) were female. There were 214 (59.2%) White, 66 (18.2%) African or Caribbean, 69 (19.1%) South Asian, 8 (2.2%) East Asian patients, and 16 (4.4%) from other ethnic backgrounds. The median (IQR) age at enrolment was 34 (26 - 45) years. The frequencies of patients who were ever treated with non-corticosteroids-immunosuppressive drugs were as follows: AZA (49.8%), MMF (30.7%), CNI (16.3%), MTX (22.9%), and CYC (25%). After 10 years of

follow-up, a total of 166 (45.9%) had 1 or more items of organ damage. In separate multivariable Cox Proportional Hazard models with the development of a new item of damage as the dependent variable, after adjusting for propensity scores, use of corticosteroids, and disease activity. There was an inverse association between the development of organ damage and the use of AZA (hazard ratio [HR] 0.59 [95% CI: 0.44, 0.79]), MMF (HR 0.41 [95% CI: 0.27, 0.62]), CNI (HR 0.34 [95% CI: 0.19, 0.60]), and MTX (HR 0.49 [95% CI: 0.30, 0.78]), suggesting a protective effect. However, the use of CYC (HR 1.12 [95% CI: 0.62, 2.04]) was not found to be protective against further organ damage (Table 1). The multivariable Cox models prior to propensity adjustment are summarized in Table 1.

Table 1: Multivariate analysis of immunosuppressive medications and the presence of organ damage, pre and post propensity adjustment

Variables	Multivariable cox regression HR (95% CI) *	Multivariable cox regression HR (95% CI) (Propensity adjusted) ^
AZA	0.91 (0.69, 1.20)	0.59 (0.44, 0.79)
MMF	0.97 (0.70, 1.34)	0.41 (0.27, 0.62)
CNI	0.79 (0.46, 1.34)	0.34 (0.19, 0.60)
MTX	0.90 (0.59, 1.37)	0.49 (0.30, 0.78)
CYC	2.84 (1.59, 5.06)	1.12 (0.62, 2.04)

*Adjusted for disease activity and use of corticosteroid

^Adjusted for disease activity, use of corticosteroid and propensity score (age, gender, ethnicity, year of diagnosis, year of enrollment, disease duration, smoking, antimalarial use, immunosuppressive use, and baseline SDI)

Conclusions: AZA, MMF, CNI, and MTX may have protective effect against the development of organ damage. Treatment with CYC was not associated with new organ damage although further residual confounding cannot be excluded.

PV273 / #773

Poster Topic: *AS24 - SLE-Treatment*
Late-Breaking Abstract

HYPERPIGMENTATION AS AN ADVERSE EFFECT OF ANTIMALARIAL USE AND THE ASSOCIATION WITH RETINOPATHY AND PREDISPOSING FACTORS: A SYSTEMATIC REVIEW.

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Background/Purpose: Antimalarials are essential in treating various dermatological and rheumatological conditions like systemic lupus erythematosus. Hyperpigmentation is a known side effect, most often seen with chloroquine than hydroxychloroquine, affecting over 25% of users after prolonged use. These drugs alter antigen processing and increase lysosomal pH, affecting the skin by modifying UV absorption and inflammatory mediators. Antimalarial drugs can bind to iron and melanin, which stimulates melanocytes and may cause increased pigmentation in the skin. While the exact link between hyperpigmentation and retinopathy is not fully established, reports have suggested a possible association. Retinal toxicity is more likely to occur with chloroquine and higher doses of hydroxychloroquine. Studies suggest that factors like ecchymosis and the use of anticoagulants or antiplatelet agents may influence hyperpigmentation. This study explores the relationship between antimalarial use and mucocutaneous hyperpigmentation, considering factors such as retinopathy, trauma/ecchymosis, and concurrent anticoagulant use.

Methods: We have conducted a systematic review to examine the association between antimalarial use and hyperpigmentation and the possible link to retinopathy and predisposing factors. A comprehensive search strategy was developed using a combination of database-specific subject headings and text words for the main concepts of hyperpigmentation and the drugs chloroquine or hydroxychloroquine. Results were limited to humans. Studies from 1960 to May 2024, including cohort, cross-sectional, case reports, and case series, were identified on September 5, 2024 through Ovid MEDLINE and Embase. A total of 1760 studies were screened, and 71 studies were extracted and included in the review. The reference lists of included publications were also searched and considered for inclusion. A supplementary search was conducted on Google Scholar on December 26, 2024, using the following search terms: hyperpigmentation, antimalarial, drug adverse effect, chloroquine,

hydroxychloroquine, skin pigmentation, antimalarial side effects. The first 100 results from that search were screened.

Results: The analysis involved 71 studies with a total sample size of 318 patients. Of these, 89.6% were female and 7.2% were male. The most common diagnosis was systemic lupus erythematosus (SLE), accounting for 74.6% of patients, followed by rheumatoid arthritis (RA) at 8.8%. Other diagnoses included Sjögren's syndrome (6%), discoid lupus erythematosus (DLE) (4.1%), undifferentiated connective tissue disease (0.9%), and subacute cutaneous lupus erythematosus (SCLE) (0.3%). There were 4.7% of patients with other conditions, and 0.3% had no report on the diagnosis. In terms of treatment, 70.4% of patients were treated with hydroxychloroquine (HCQ), 17.6% with chloroquine, and 6.3% with other combinations of antimalarials. Hyperpigmentation was mostly blue-gray (9.9%), with the face and neck (40.5%), legs (34.6%), and hands (21.6%) being the most affected areas. Preceding ecchymosis was reported in 23.5%, and 18.5% were using anticoagulants/antiplatelets. Biopsies were performed in 27.5% of cases. Retinopathy was noted in 3.1%, with no strong correlation to hyperpigmentation. Of those who discontinued antimalarials (52.2%), 35.5% experienced fading pigmentation, with partial (24.2%) or complete (10.6%) resolution.

Conclusions: Hyperpigmentation is a common side effect of antimalarials. No correlation was found with the presence of hyperpigmentation and retinopathy with use of hydroxychloroquine. The role of anticoagulants and ecchymosis remains uncertain. Discontinuation of antimalarials does not always lead to the resolution of pigmentation. Further research is needed to better understand the mechanisms of hyperpigmentation and improve its treatment.

PV274 / #146

Poster Topic: ***AS24 - SLE-Treatment***

ANIFROLUMAB IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS – SINGLE TERTIARY CENTRE EXPERIENCE

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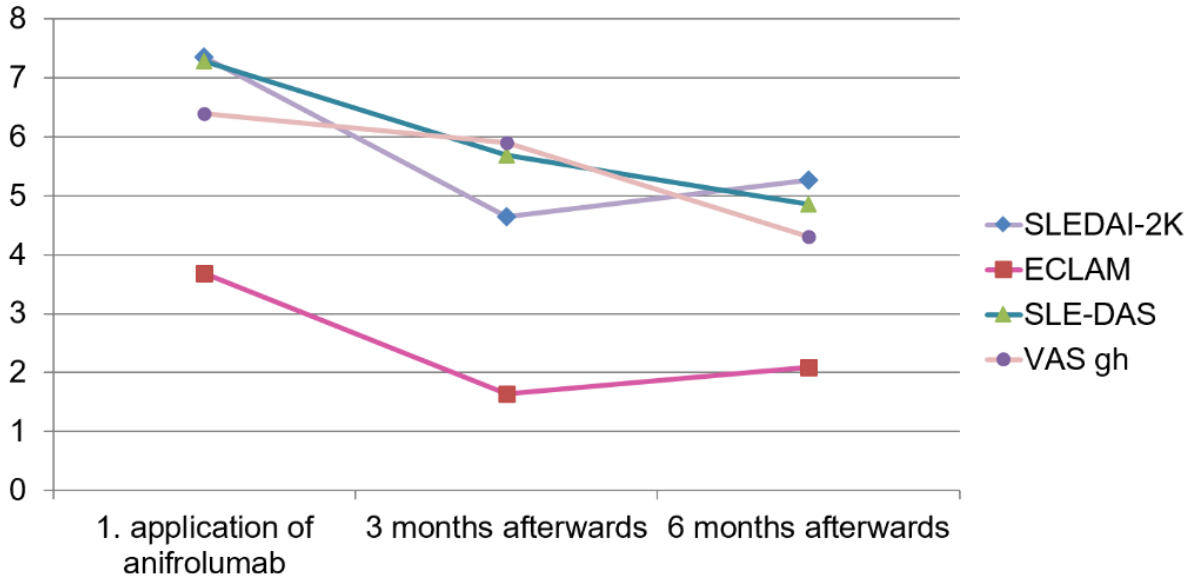
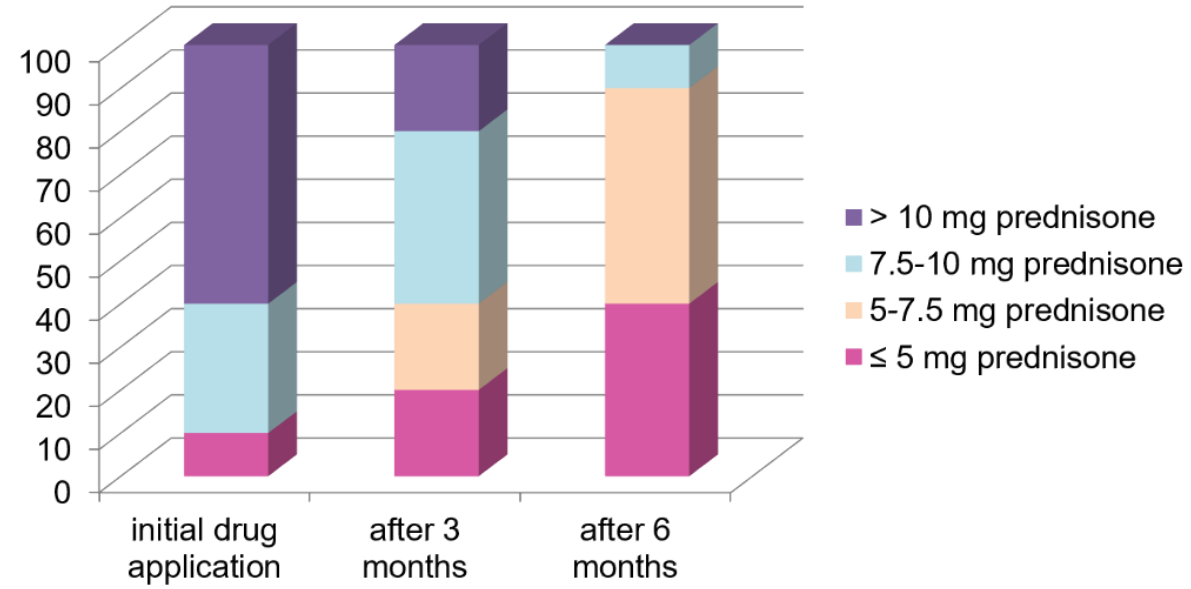
Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystemic, chronic, autoimmune disease that can affect any organ or organ system, most commonly the skin and mucous membranes, kidneys, serous membranes, hematopoietic system, musculoskeletal system, and central nervous system. The fundamental importance of interferon type I (IFN I) is in the defense against viral infections, while in patients suffering from SLE, IFN I pathways are emphasized both in the genetic predisposition of the disease, as well as in epigenetic modifications, therefore in the early stages of the disease, but also in supporting the active disease. Numerous disease symptoms as well as laboratory features of SLE are associated with the overexpression of genes that regulate IFN I, which opens the new perspectives and therapeutic opportunities for anifrolumab - a monoclonal antibody that inhibits type 1 interferon receptors.

Methods: The aim of the paper is to present the experience with the treatment of patients with SLE using anifrolumab in the Department of Clinical Immunology and Rheumatology, University Hospital Centre Zagreb, Croatia in the period from 31.7.2023. until 15.9.2024. with reference to demographic data, laboratory parameters, clinical manifestations, impact on disease activity, glucocorticoid cotherapy, but also side effects. In Croatia, anifrolumab is available from 2023. as an add on therapy in SLE adult patients who despite standard imunossupresive therapy have moderately to high clinically and serologically active disease. Standard methods of descriptive statistics, as well as trend analysis were used in data processing.

Results: In the mentioned period, 17 SLE patients were treated with the drug anifrolumab. Of these, 15 patients (88.23%) were female. The median age of the patients was 42.47 ± 2.97 years. The age at the time of diagnosis was 31.43 ± 13.74. On average, 9.07 ± 7.36 years passed from the diagnosis of SLE to the start of therapy. The leading clinical manifestations were skin-mucous, then articular and hematological, and constitutional symptoms, followed by serositis, Raynaud's phenomenon, sicca symptoms, and among the rarer manifestations were kidney affection and relapsing polychondritis, and antiphospholipid syndrome. All patients were treated with glucocorticoids and antimalarials, followed by azathioprine, mycophenolate mofetil,

methotrexate and cyclophosphamide. Two patients were previously treated with thalidomide, and in individual cases the therapy included rituximab, leflunomide and intravenous immunoglobulins. We noticed high drug persistence rate (88.23%). There were 10 adverse events, namely bilateral pneumonia, bronchitis in two cases, sinusitis, COVID-19, bartonellosis, purpura on the fingers, insufficient efficacy in two cases and infusion reaction. We analyzed impact of the drug on serologic and laboratory features (lymphocyte count, dsDNA, C3, C4), disease activity measured by SLEDAI-2K, SLE-DAS, ECLAM, VAS gh after three and six months of therapy respectively. A trend in disease activity indices is depicted in a graph 1 below. Data related to the trend analysis regarding complement components, lymphocytes and dsDNA are shown in separate graphs, as well as data concerning glucocorticoid reduction after three and six months on therapy, which one is enclosed here (graph 2).





Conclusions: Our results demonstrated that anifrolumab can be considered as an effective ,,add-on'' therapy of moderate to severe SLE. By monitoring disease activity indices (SLEDAI-2K, SLE-DAS, ECLAM, VAS), an advantageous trend in disease activity status was verified with an acceptable safety profile of the drug and a high persistence rate of a drug. Lower disease activity allowed us to perform substantial glucocorticoid dose reduction accounting for a positive impact on cumulative organ damage reduction.

PV275 / #231

Poster Topic: *AS24 - SLE-Treatment*

RITUXIMAB IN REFRACTORY SLE: 10 YEARS AFTER

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Background/Purpose: Purpose: The aim of this cross-sectional study of patients with refractory SLE treated with RTX was to explore for any potential long-term effect(s) of this B cell depletion approach.

Methods: Methods: We included patients with SLE having had i) received at least 1 cycle of RTX and ii) at least 10yr of follow-up after their first RTX infusion. Response was assessed at 1 year and at their latest evaluation that was ^{3} 10yr after RTX treatment initiation. In cases where the cSLEDAI-2k was employed, a response was defined as a cSLEDAI-2k of less than 4 in cases were the cSLEDAI-2k was ^{3} 4. In cases where the cSLEDAI-2k was 2-4 at baseline, a response was defined as a cSLEDAI-2k of 0. For cases of lupus nephritis, a complete response was defined as a proteinuria of < 500mg/24h and an eGFR 60 ml/min; a partial response was defined as a reduction of the proteinuria of > 50% of baseline values and an eGFR 60 ml/min. In cases of lung involvement, a response was defined as an FVC decline £ 5% predicted values.

Results: Results: RTX was administered in 62 patients with SLE treated at the 2 Rheumatology tertiary care centres of southwestern Greece. For this cross-sectional study we enrolled 23 patients (25 cases) with SLE (all Caucasian female, age range: 14 – 72yr, mean: 31yr) with active or relapsing disease, fulfilling inclusion criteria. The median disease duration was 6yr (range: 2mo-27yr) at the time of the first RTX treatment infusion. Clinical manifestations at the time of RTX introduction included lupus nephritis in 8 patients, arthritis in 6, neuropsychiatric involvement in 4, vasculitis in 2, lung involvement in 3 and hematological abnormalities in 3. RTX was also administered in 1 patient with lupus hepatitis and in 1 plasmapheresis-plus-steroid resistant case of thrombotic thrombopenic purpura. RTX treatment was associated with a clinical benefit in 82.14% of our patients after 1yr and in 74.48% after ^{3}10yr. The median cSLEDAI-2K score decreased from 5.83 ± 3.70 at baseline to 1.95 ± 2.40 ($p < 0.001$) at 1yr and to 2.37 ± 3.00 ($p < 0.001$) at the ^{3}10yr time-point of follow-up. Ten out of our 23 patients relapsed. The earliest relapse was seen at 6mo and the latest at 13yr after RTX treatment introduction. Eight relapsed patients were re-treated with RTX and 3/8 re-responded. The mean daily dose of corticosteroids was reduced both at the 1yr and at the ^{3} 10yr time-points; dose reductions were not statistically significant. Regarding

safety we report 1 COVID19-related death, viral infections in 2, allergic reactions in 4 and one patient with late-onset neutropenia.

Conclusions: Conclusion: Our data suggest that RTX may indeed represent an alternative therapeutic option in patients with SLE refractory to standard treatment with an acceptable safety profile and a potential long-term beneficial effect.

PV276 / #481

Poster Topic: *AS24 - SLE-Treatment*

LUPUS AND NUTRITION -THE FIRST STEP TO CONTROL YOUR FLARES?

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Background/Purpose: Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease, characterized by the presence of autoantibodies and diverse clinical manifestations, including one or even more organs. Still, the exact cause of Lupus is unknown, and symptoms include also fevers, rashes, swelling and pain. Some gastrointestinal symptoms in lupus patients, such as bloating or abdominal pain, could be related to food allergies or intolerance. Gluten intolerance or celiac disease may occur more frequently in lupus patients, which can increase gastrointestinal symptoms. Research even from 1993 shows that people with lupus are at a much higher risk of developing allergies to drugs, skin, and insects. Moreover, family members of individuals with systemic lupus erythematosus are also more likely to experience at least one type of allergy. Aim: To have a closer look on the antibody and autoantibody profile related to lifestyle and nutrition of SLE patients to improve disease management and quality of live.

Methods: Method: A total of 17 patients with a clinical diagnosis of SLE were tested using AESKUBLOTS® Allergy and AESKUBLOTS® Gluten-Related Disorders (GRD) IgA. AESKUBLOTS® Allergy is a membrane-based enzyme immunoassay for quantitative detection of allergen-specific IgE antibodies against allergens/allergen mixtures and total IgE in human plasma or serum. The AESKUBLOTS® GRD IgA is a membrane-based enzyme immunoassay for quantitative detection of IgA subclass antibodies against gliadin, DGP, tTG (tissue Transglutaminase), tTG neo (cross-linking of tTG with gliadin-specific peptides induces the formation of tTG neo-epitopes), TG3 (epidermal Transglutaminase), mTG (microbial Transglutaminase), mTG neo (cross-linking of mTG with gliadin-specific peptides induces the formation of mTG neo-epitopes), Frazer's Fraction in and total IgA in human serum or plasma. The antigens are positioned as parallel lines at precisely defined locations on a nitrocellulose membrane.

Results: A total of 52% of patients exhibited high IgE levels (class 5-6) against allergens such as wheat, spelt, egg white, casein, and various nuts including almond, hazelnut, peanut, pistachio, and cashew. Additionally, 5 out of 17 (30%) patients showed elevated antibodies against gliadin (>3-5x ULN (Upper Limit of Normal)), DGP (>3-5x ULN), mTG-neo (>2-3x ULN) and autoantibodies against tTG (>2x ULN) and tTG-neo (>3-5x ULN) antigens, which are highly associated with gastrointestinal disorders like celiac disease and non-celiac gluten sensitivity. Three SLE patients demonstrated significantly

elevated food allergy-specific IgE levels (≥class 4) along with high levels of autoantibodies related to GRDs.

Conclusions: Even within this small cohort, antibodies and autoantibodies associated with food allergies and GRD are significantly elevated compared to the general population. A comprehensive understanding of SLE epidemiology is urgently needed to gain deeper insights into the disease and better manage healthcare resources. The close interaction between autoimmunity, inflammation, and allergies means that during a lupus flare, both gastrointestinal symptoms and allergic reactions can be exacerbated, which further complicates the treatment and management of SLE patients. Accurate identification, antibody monitoring via multiplex and treatment of gastrointestinal complaints and allergies during a lupus flare are crucial to improving the quality of life for affected patients and preventing complications.

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Poster Topic: ***AS24 - SLE-Treatment***

EFAVALEUKIN ALFA IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A BAYESIAN ADAPTIVE, PHASE 2B, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED DOSE-RANGING STUDY

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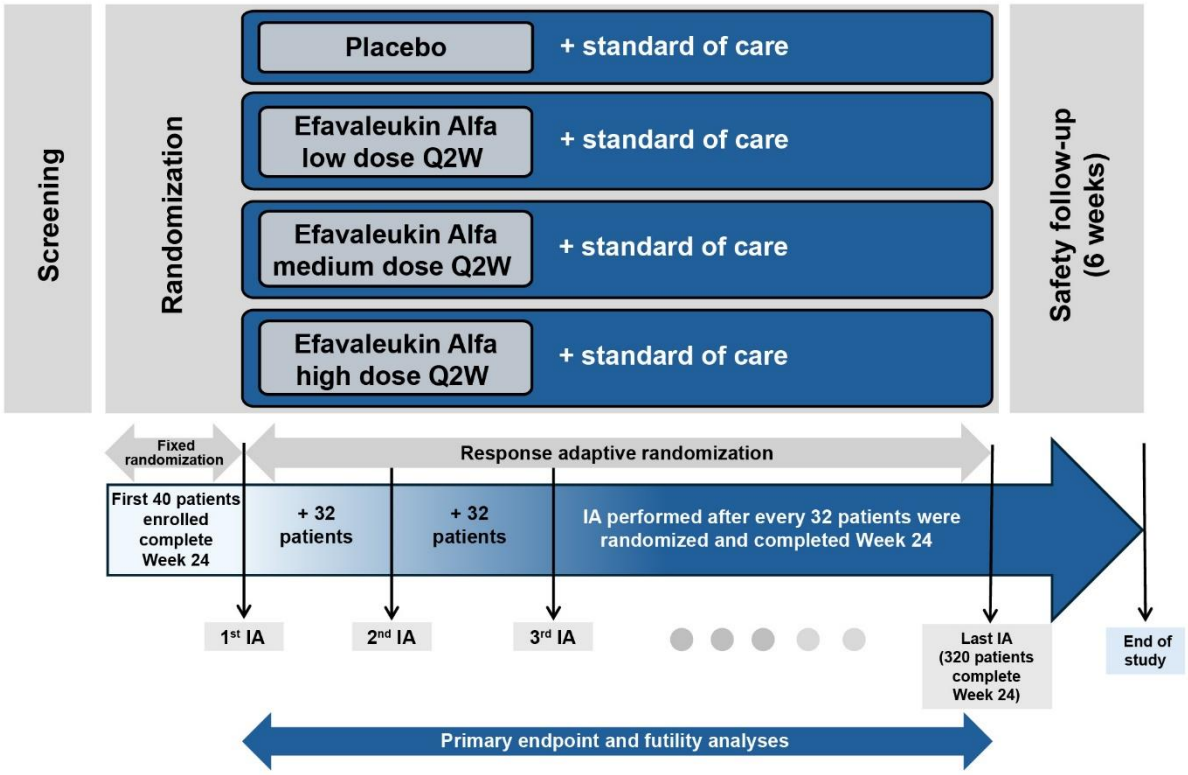
Background/Purpose: SLE is a complex chronic autoimmune disease with diverse clinical manifestations. Impaired regulatory T cell (Treg) function is associated with SLE pathogenesis. Interleukin-2 (IL-2) is a key regulator of Treg homeostasis; decreased levels of circulating IL-2 are associated with aberrant Treg metabolism in SLE. Efavaleukin alfa, an IL-2 mutein Fc fusion protein with superior Treg selectivity, can preferentially expand Tregs in patients with SLE. This study (NCT04680637) evaluated the safety and efficacy of efavaleukin alfa in patients with active SLE.

Methods: This was a Bayesian adaptive phase 2b, randomized, double-blind, placebo-controlled, multi-center, dose-ranging study in adult patients with active SLE with Hybrid Systemic Lupus Erythematosus Disease Activity Index (hSLEDAI) score ≥ 6, clinical hSLEDAI score ≥ 4 and inadequate response to standard of care (SOC) therapies. Patients were randomized to receive either placebo or efavaleukin alfa (low, medium, or high dose) every two weeks and continued SOC treatment for 52 weeks (Figure). The randomization ratio started as 1:1:1:1, then was adapted using Response Adaptive Randomization to allocate more patients to more efficacious doses and fewer patients to less efficacious doses, with a fixed 25% allocation to placebo based on the clinical efficacy at pre-specified interim analyses (IAs) [1]. Futility analyses were conducted using a Bayesian hierarchical model. The primary endpoint was the achievement of SLE Responder Index 4 (SRI-4) response at Week 52, defined as a ≥ 4-point reduction in hSLEDAI score, no new British Isles Lupus Assessment Group (BILAG) 2004 A and no > 1 new BILAG B scores, a < 0.3-point deterioration in Physician's Global Assessment, and no use of more than protocol-permitted therapies. Patients were followed up for at least 6 weeks after the last dose for safety. An adjudication committee was utilized throughout the study to confirm eligibility, endpoints, and clinical outcomes.

Figure. Clinical trial design utilizing response adaptive randomization



IA, interim analysis; Q2W, every two weeks

Results: A total of 168 participants (94.0% female; 56.0% White) from 13 countries across 4 continents were enrolled (mean [SD] age: 44.1 [11.8] years). The trial was discontinued due to meeting predefined futility criteria at its third IA. At the date of termination, 16, 17, and 14 patients in the low, medium, and high dose efavaleukin alfa groups, respectively, and 15 patients in placebo had completed the Week 52 visit. Among these, a lower percentage of patients achieved an SRI-4 response at Week 52 in the 3 efavaleukin alfa groups (25-35.7%) compared to placebo (53.3%). All 168 patients who received at least one dose of study drug were included in the safety analysis (Table). Treatment-emergent adverse events (AEs) occurred in the efavaleukin alfa groups (82.9-100%) and placebo (70.7%). Incidences of serious AEs across efavaleukin alfa groups (5.1%-12.1%) were comparable with placebo (9.8%). The most frequent AEs (≥ 10.0%) in the overall efavaleukin alfa group were injection site erythema, injection site pruritus, injection site pain, injection site rash, injection site swelling, COVID-19, and headache. All injection site reactions were grade 1 or 2. No serious treatment-related AEs were observed.

Table. Safety of efavaleukin alfa in patients with active SLE

	Placebo (N=41) n (%)	Efavaleukin Alfa Overall (N=127) n (%)
All TEAEs	**29 (70.7)**	**117 (92.1)**
Grade 1	**6 (14.6)**	**25 (19.7)**
Grade 2	**18 (43.9)**	**79 (62.2)**
Grade 3	**4 (9.8)**	**12 (9.4)**
Grade 4	**0 (0)**	**1 (0.8)**
SAEs[a]	**4 (9.8)**	**10 (7.9)**
Fatal AEs, n (%)	**1 (2.4)**	**0**

[a] None of the reported individual SAE exceeded 5% prevalence.
Severity of each adverse event is graded using CTCAE version 5.0 criteria.
AE, adverse event; SAE, serious adverse event

Conclusions: CONCLUSION: The study was terminated as it met predefined futility criteria and not because of safety concerns. Treatment with efavaleukin alfa did not result in improvements of the efficacy endpoints over placebo in patients with active SLE. The safety profile observed in this study was consistent with the known profile of efavaleukin alfa. **Reference:** [1.] Garces S, et al. Lupus Sci. Med 2023;10:e000890. doi:10.1136/lupus-2022-000890

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Poster Topic: ***AS24 - SLE-Treatment***

FACTORS ASSOCIATED WITH EFFICACY OF BELIMUMAB IN DIFFERENT JOINT AND SKIN PHENOTYPES OF SYSTEMIC LUPUS ERYTHEMATOSUS: PRELIMINARY DATA FROM THE MULTICENTER BERLISS-NEJS STUDY

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Background/Purpose: To evaluate factors associated with belimumab's efficacy on different skin and joint manifestations in a nationwide multicenter cohort (BeRLISS-NeJS) of patients with systemic lupus erythematosus (SLE).

Methods: In this retrospective observational study, adult SLE patients treated with belimumab (10 mg/kg/month IV or 200 mg/week SC) were stratified by joint (non-deforming non-erosive arthritis (NDNE), Jaccoud's arthropathy, rhupus) and skin phenotypes (acute-ACLE, subacute-SCLE, chronic cutaneous lupus erythematosus-CCLE). We analyzed DAS28, CLASI-A, CLASI-D scores as well as DAS28 and CLASI-A remission rates (respectively DAS28<2.6 and CLASI-A=0) at 6, 12, 24, 36 months from baseline. Parametric and non-parametric tests were used according to data distribution.

Results: A total of 443 patients (88.9% female, mean treatment duration 30 months (range 12-60) were enrolled. At belimumab initiation, 272 patients (61.4%) had joint manifestations: 221 NDNE (50.7%), 30 Jaccoud's arthropathy (6.9%), and 21 rhupus

(4.8%); 231 patients (52.1%) had skin manifestations: 112 ACLE (25.3%), 54 SCLE (12.2%), 18 CCLE (4.1%), and 47 aspecific skin manifestations (10.6%). Patients with Jaccoud's arthropathy or rhupus had a longer disease duration before belimumab initiation compared to NDNE patients. The NDNE subtype was associated with higher DAS28 remission rates than Jaccoud's and rhupus at 6 and 36 months (Figure).

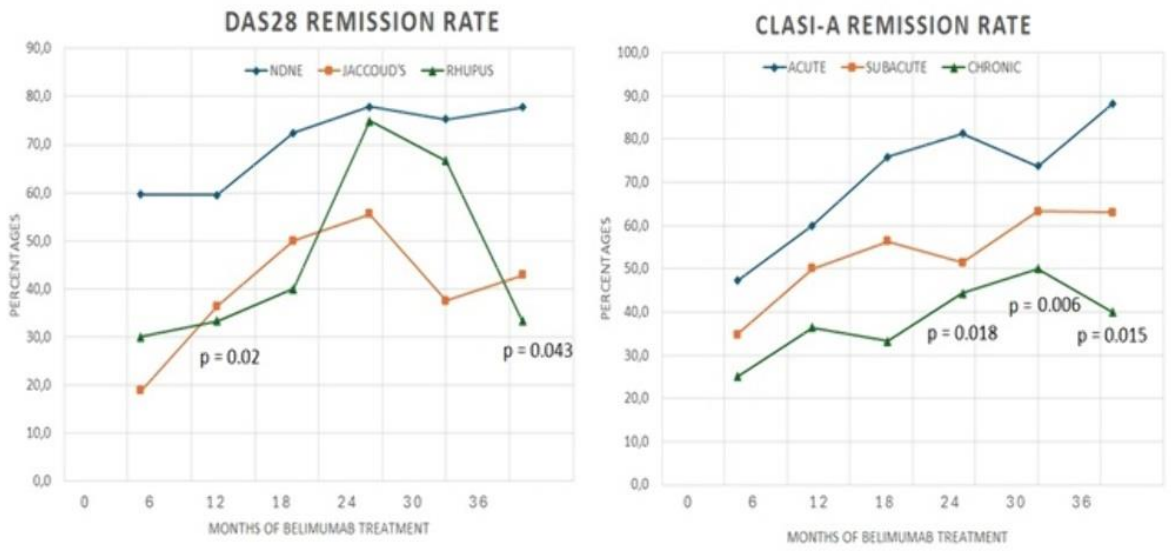

Figure. DAS28 and CLASI-A remission stratified for different joint and skin phenotypes, respectively. P values were assessed by Chi-squared test with Bonferroni correction (α=0.05). Please note that the p-values shown refer to the comparison in remission rates among different phenotypes for that given timepoint.

Higher baseline DAS28 in NDNE patients correlated with lower remission rates at 6 and 12 months (p<0.001 and p=0.003). Smoking was associated with less probability to achieve remission at 12 months (p=0.003), while higher baseline prednisone intake was associated with higher remission rates at 12 months (p=0.046). Prior methotrexate treatment was negatively associated with remission at 6 and 24 months (p=0.006 and p=0.027), but concurrent methotrexate treatment did not affect remission rates. In Jaccoud's patients, baseline DAS28 was not associated with remission rates. Prior methotrexate use was associated with lower remission rates at 12 months (p=0.027) and 36 months (p=0.022). In rhupus patients, higher baseline DAS28 was associated with lower remission rates at 6 months (p=0.016). Concurrent and prior methotrexate use did not influence remission rates. When considering remission in patients with skin manifestations, ACLE showed higher CLASI-A remission rate compared to the SCLE and CCLE at 18, 24, and 36 months (Figure). In ACLE patients, older age at belimumab initiation negatively correlated with CLASI remission at 6 (p=0.047) and 12 months (p=0.015). High baseline CLASI-A negatively impacted on remission at 6 (p<0.001), 12 (p=0.003), and 24 months (p=0.002), but not at 36 months (p=0.082). High baseline CLASI-D was associated with lower remission at 6 (p=0.002), 12 (p=0.030), and 24 months (p<0.001). In SCLE patients, high baseline CLASI-A was negatively associated with remission at 6 (p<0.001), 12 (p=0.001), and 24 months (p<0.001). High baseline CLASI-D correlated with lower remission rates at 6 (p=0.049), 12 (p=0.005), and 24

months (p=0.026). Anti-SSB antibodies at baseline negatively impacted on remission at 6 (p=0.025) and 24 months (p=0.012). In CCLE patients, high baseline CLASI-A negatively impacted remission at 24 months (p=0.016). Baseline CLASI-D did not affect remission; however, this subset had few patients.

Conclusions: Patients with NDNE arthritis and ACLE more frequently achieved DAS28 and CLASI-A remission, respectively. Univariate analyses indicated that active disease (high DAS28 and CLASI-A) and damage (high CLASI-D) at baseline were associated with lower remission rates, particularly in NDNE and ACLE patients. Prior methotrexate use was associated to lower remission rates, suggesting that methotrexate-refractory patients may benefit less from belimumab.

PV279 / #686

Poster Topic: ***AS24 - SLE-Treatment***

REAL-WORLD EFFICACY AND SAFETY DATA OF ANIFROLUMAB FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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Background/Purpose: Anifrolumab (ANI), an anti-type 1 interferon alpha receptor antibody, has recently been approved for SLE treatment, following the positive results in two phase III randomized controlled trials. The purpose of this work is assessing the efficacy of Anifrolumab in active non-renal SLE, focusing on cutaneous and musculoskeletal manifestations.

Methods: Data of SLE (ACR/SLICC or EULAR/ACR classification criteria) patients (pts) treated with ANI were prospectively collected. Disease activity measures, including SLE Disease Activity Index 2000 (SLEDAI-2K), SLE Disease Activity Score (SLEDAS), swollen joint count (SJT), tender joint count (TJC) and Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) were assessed at baseline and every 3 months thereafter. Platelet count (PC), lymphocyte count (LC), complement levels, anti-dsDNA titers, and prednisone dose were also assessed at same timepoints. SLICC/ACR Damage Index (SDI) was collected at baseline and after 6 months of treatment. T-test and Wilcoxon test for paired data were used to assess differences across different timepoints.

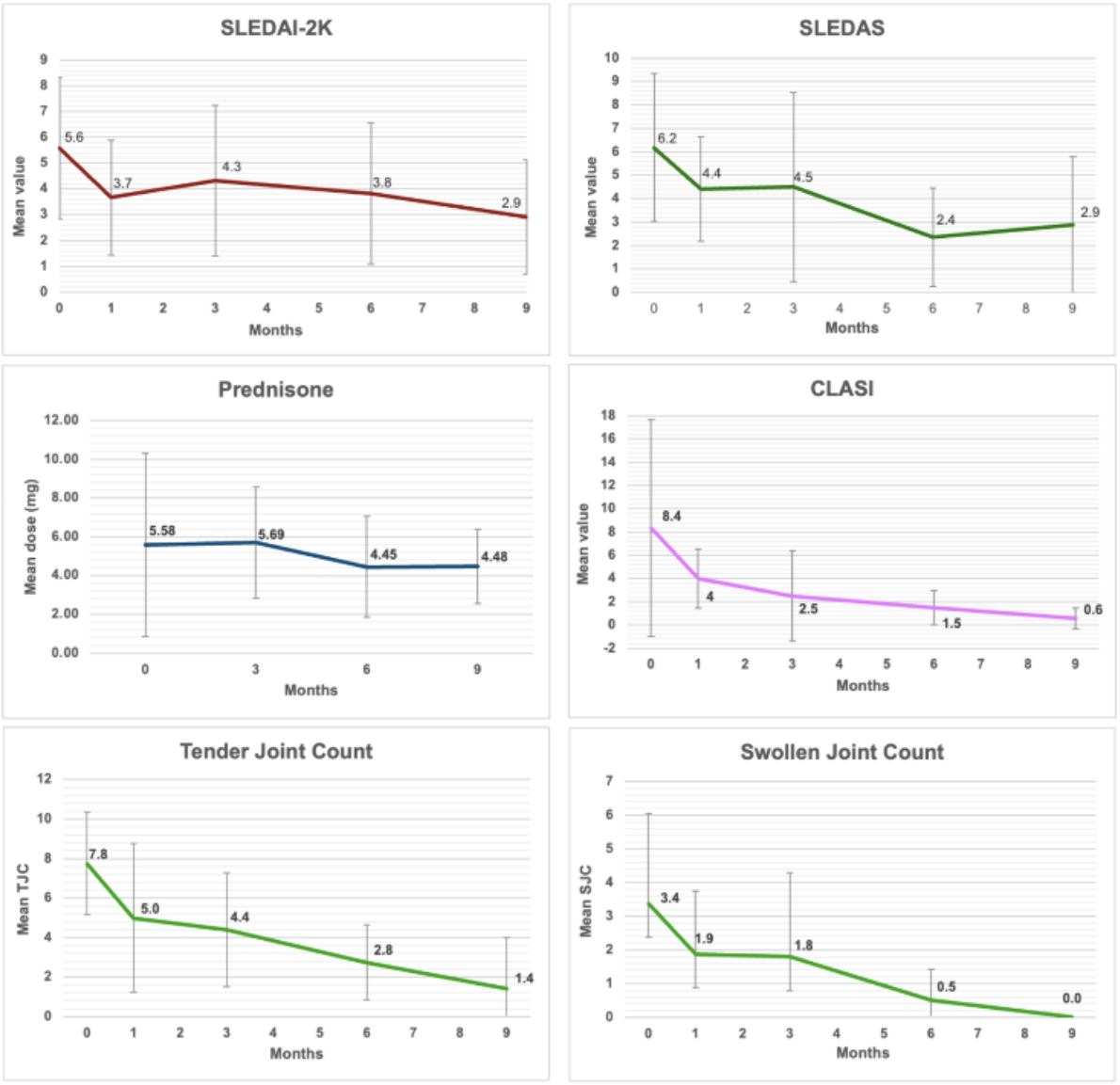
Results: Since September 2023, 22 SLE pts have been treated with ANI. ANI was prescribed for active cutaneous involvement in 11/22 (50%), joint involvement in 10/22 (45%), hematological involvement in 4/22 (18%), and serosal involvement in 2/22 (9%). In 8/22 pts (36%), ANI was administered prior to any conventional immunosuppressants (IS) (including 2 pts in which it was administered after belimumab only). At 6 months, significant reductions from baseline of mean SLEDAI-2K ($p=0,016$), SLEDAS ($p<0.001$), CLASI ($p=0,008$), TCJ ($p=0,009$), SJC ($p=0,023$), and LC ($p=0,021$) were observed (Images 1 and 2). At 9 months, improvements were confirmed in all previous endpoints (Images 1 and 2). Efficacy was similar between conventional IS experienced vs. naïve pts. Of note, a trend towards reduced prednisone use was observed. At 6 and 9 months, no significant changes in PC, rates of hypocomplementemia and proportion of patients with positive anti-dsDNA antibodies were detected. SDI did not vary after 6 months of follow-up. Treatment was discontinued for inefficacy in 2 pts (1 joint and 1 hematological involvement) and for safety reasons in 1 pt (sepsis).

IMAGE 1

	Baseline	6 months		9 months	
	Mean value (SD)	**Mean value (SD)**	**p value**	**Mean value (SD)**	**p value**
SLEDAI-2K	5.59 (2.74)	3.81 (2.74)	**0.016**	2.91 (2.21)	**0.007**
SLEDAS*	6.18 (3.16)	2.36 (2.09)	**<0.001**	2.88 (2.90)	0.059
Swollen Joint Count	3.37 (2.67)	0.5 (0.93)	**0.023**	0 (0)	0.161
Tender Joint Count	7.75 (2.60)	2.75 (1.91)	**0.009**	1.4 (2.61)	**0.033**
CLASI	8.36 (9.32)	1.5 (1.51)	**0.008**	0.6 (0.89)	**0.043**
prednisone equivalent (mg/day)	5.58 (4.72)	4.45 (2.61)	0.283	4.48 (1.93)	0.432
Platelet (n°x10^3/mmc)	221.29 (110.55)	225.37 (100.47)	0.744	238 (119)	0.156
Lymphocites (n°x10^3/mmc)	1.14 (0.56)	1.42 (0.43)	**0.021**	1.59 (0.34)	**0.007**
Neutrophils (n°x10^3/mmc)	3.93 (1.88)	//		//	
	Median (Max. min)	**Median (Max. min)**			
SLICC	0 (2. 0)	0 (2. 0)	ns	//	//

*Statistically significant reduction in SLEDAS was seen also at 1 month (p= 0.022)

IMAGE 2



Conclusions: In our cohort, ANI showed promising results, reducing overall and organ-specific disease activity, confirming its efficacy in cutaneous and joint manifestations. Further data are needed to evaluate its steroid-sparing effect and its impact on hematological manifestations.