Poster Presentations

P01 T cells and immune regulation

P1.01

Systemic lupus erythematosus drives atherosclerosis through CD4+CXCR3+ T cells and plasmacytoid dendritic cells

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Objective. Accelerated atherosclerosis is the leading cause of death in systemic lupus erythematosus (SLE). How SLE promotes accelerated atherosclerosis remains elusive. The purpose of this study was to show that actors of SLE pathogenesis - such as CD4+ T cells and plasmacytoid dendritic cells (pDCs) - contribute to atherosclerosis.
Methods. Internal carotid wall thickness was prospectively assessed, as a measure of atherosclerosis, in 51 SLE patients asymptomatic for cardiovascular disease and 18 controls. The expression of CXCR3, a chemokine receptor involved in tissue migration of T cells, on peripheral blood mononuclear cells was measured. We analyzed *in vitro* the effect of pDCs-derived IFN-α production on CD4+ T cells and on CXCR3 ligands production by endothelial cells. Eventually, the impact of TLR-9 stimulated pDCs on atherosclerosis development was studied in a mouse model.
Results. SLE patients displayed an increased frequency of pro-inflammatory CD4+ T cells expressing CXCR3 that correlates with subclinical atherosclerosis. Furthermore, IFN-α produced by pDCs upon TLR-9 stimulation enhances both CD4+CXCR3+ T cells expansion and CXCR3 ligands production by endothelial cells *in vitro*. Eventually, TLR-9 stimulation of pDCs was shown to accelerate atherosclerosis development in ApoE-/- mice by enhancing the CD4+CXCR3+ T cells recruitment in arterial wall.
Conclusion. In SLE, IFN-α produced by pDCs both expands CD4+T cells expressing CXCR3 and induces endothelial cells to secrete CXCR3 ligands, which drive CD4+T cell migration into the arterial wall and atherosclerosis. Our findings support a multi-step model in which SLE-immune dysfunction is associated with the development of atherosclerosis.

P1.02

Mucosal-associated invariant T cells are numerically and functionally deficient in stemic lupus erythematosus

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Mucosal-associated invariant T (MAIT) cells contribute to protection against certain microorganism infections and play an important role in mucosal immunity. However, the role of MAIT cells remains enigmatic in autoimmune diseases. Here, we examined the level and function of MAIT cells in patients with rheumatic diseases. MAIT cell, cytokine and programmed death-1 (PD-1) levels were measured by flow cytometry. Circulating MAIT cell levels were significantly reduced in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) patients. In particular, this MAIT cell deficiency was more prominent in CD8+ and double-negative T cell subsets, and significantly correlated with disease activity, such as SLE disease activity index (SLEDAI) and 28-joint disease activity score (DAS28). Interestingly, MAIT cell frequency was significantly correlated with natural killer T (NKT) cell frequency in SLE patients. Interferon-γ production in MAIT cells was impaired in SLE patients, but it was preserved in RA patients. In SLE patients, MAIT cells were poorly activated by α-galactosylceramide-stimulated NKT cells, thereby showing the dysfunction between MAIT cells and NKT cells. Notably, an elevated expression of PD-1 in MAIT cells and NKT cells was associated with SLE. In RA patients, MAIT cell levels were significantly higher in synovial fluid than in peripheral blood. Our study primarily demonstrates that MAIT cells are numerically and functionally deficient in SLE. In addition, we report a novel finding that this MAIT cell deficiency is associated with NKT cell deficiency and elevated PD-1 expression. These abnormalities possibly contribute to dysregulated mucosal immunity in SLE.

P1.03

Increased expression of Inducible Costimulator Ligand (ICOSL) on CD4+ T cells in patients with SLE

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Background. ICOSL (Inducible costimulator ligand), which belongs to the B7 family, is crucial for T helper cell and B cell differentiation. Clinical trial of monoclonal antibody targeting ICOSL in SLE is underway. We investigate the expression and function of the ICOSL on T cells in SLE.
Methods. To investigate the expression of the ICOSL on CD 4+ T cells, we evaluated surface ICOSL expression on CD4+ T cells and soluble ICOSL expression in peripheral blood (PB) from 24 lupus patients and 15 controls using flow cytometry. To explore the role of ICOS/ICOSL signaling in CD4+ T cells, we examined CD4+ T cell proliferation after blockade of the ICOS/ICOSL signal from 14 lupus patients. During the proliferation assay, cytokine levels in the CD4+ T cell culture supernatants were assessed.
Results. The proportion of ICOSL+ CD 4+ T cells and soluble ICOSL level was significantly increased in the PB of lupus patients compared to the control group. The level of soluble ICOSL correlated with surface ICOSL expression on the CD4+ T cells. After blocking of the ICOS/ICOSL pathway, the suppression of CD4+ T cell proliferation was not significantly different between the treatment groups and the control group. The expression level of TNF-alpha and IL-17 were significantly depressed in the treatment groups compared to the control group.
Conclusions: ICOSL was significantly up-regulated on CD4+ T cells in the PB in patients with SLE. Blockade of ICOS/ICOSL signaling suppressed the expression of TNF-alpha and IL-17 but it did not affect CD4+ T cell proliferation.

P1.04

Deficient transcriptional regulation of the E3 ligase Cbl-b by early growth response genes 2 and 3 in CD4+ T cells from systemic lupus erythematosus patients

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Background/Aim. T cells from Systemic Lupus Erythematosus (SLE) patients display resistance to anergy induction, which has been related to the deficiency of the E3 ligase Cbl-b. This abnormal peripheral tolerance is characterized by increased IL-2 production, proliferation and expression of activation and costimulatory markers upon anergy-inducing conditions. The transcription factors Early Growth Response (Egr) 2 and 3 have been implicated in the transcriptional regulation of Cbl-b in murine models. However their role in human T cell responses has not been fully addressed. The aim of this study was to evaluate the expression of the transcription factors Egr-2 and 3 and its relationship to Cbl-b in T cells from SLE patients.
Methods. We included 16 SLE patients (8 in remission and 8 with active untreated disease) and 16 healthy controls. PBMCs were isolated and CD4+ cells were purified by negative selection. The expression of Egr-2, 3 and Cbl-b was analysed by qPCR and Western blotting.
Results. CD4+ cells from SLE patients show increased proliferation and IL-2 synthesis after anergy induction. Moreover, upon anergy induction with ionomycin, decreased expression of Egr-2 (0.46 vs 1.89, $p<0.001$); Egr-3 (0.80 vs 2.55, $p<0.001$) and Cbl-b (0.52 vs 0.87, $p=0.028$) was found in lupus T cells in comparison to healthy controls.
Conclusion. Our data suggest that the deficiency in Cbl-b expression in CD4+ T cells from SLE patients, without regarding disease activity, is related to transcriptional defects, mainly, decreased Egr-2 and 3 expression, which is related to the breach in peripheral tolerance.

P1.05

Modulation of p27kip1 by the E3 ligase Cbl-b regulates the interplay between regulatory and effector T cells in patients with systemic lupus erythematosus

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The interplay between effector and regulatory T cells (Tregs) is a key element among peripheral tolerance mechanisms in Systemic Lupus Erythematosus (SLE). Resistance to suppression has been acknowledged as part of the defects shown by lupus T cells. The E3 ligase Cbl-b has been shown to modulate T cell unresponsiveness in SLE. However its role in peripheral Tregs tolerance has not been addressed. The aim of this study was to assess Cbl-b expression and its relationship to the resistance to suppression phenotype in SLE. We included 25 SLE patients and 25 healthy controls. Effector ($CD4^+CD25^-$) and Tregs ($CD4^+CD25^+CD127^-$) were purified by magnetic selection. The expression and interaction of Cbl-b and p27kip1 were analyzed by WB and IP. Proliferative responses were assessed in allogeneic and autologous cocultures by CFSE. We found decreased Cbl-b expression in Tregs from SLE patients in comparison to healthy controls (1.3±1.0 vs 2.8±1.8, p=0.002), which was associated with resistance to suppression in proliferation assays (r=0.553, p=0.041). This phenomenon was related to deficient expression of p27kip1 in T cells from SLE patients when compared to healthy controls. We also found by IP, that p27kip1 interacts with Cbl-b. Our data suggest that Cbl-b is able to regulate the interplay between effector and Tregs, particularly, the resistance to suppression via ubiquitination of p27kip1 in SLE. This is the first study to demonstrate that p27kip1 is able to interact with Cbl-b, which might constitute another mechanism by which this ubiquitin ligase is able to modulate the TCR activation threshold.

P1.06

New insigths into the mechanism of Galectin-1-induced T-cell apoptosis regulation and its relevance to systemic lupus erythematosus

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Background. Secreted, extracellular galectin-1 (exGal-1) is a strong immunosuppressive protein its major activity being apoptosis-induction of activated T-cells, but its mechanism is insufficiently understood. Gal-1 was found to ameliorate lupus in animal models, but its function has not been studied in human SLE.
Methods. Activated T-cells from healthy humans, Gal-1 knock-out and wild-type mice, and Gal-1 transgenic Jurkat (JGal) cells, established in our laboratory, were studied. Furthermore, T-cells were isolated from SLE patients during active disease (n=18), in remission (n=10), and healthy controls (n=20). The expression and localization of Gal-1 were examined with QPCR, Western blotting, cytofluorimetry or confocal microscopy. Apoptosis was studied in co-culture of activated T-cells with Gal-1-expressing HeLa tumour cells.
Results. Gal-1 was de novo expressed by JGal and activated T-cells, and remained intracellularly without secretion. Wild-type mouse and JGal cells were significantly more susceptible to the apoptotic effect of exGal-1 than T-cells from Gal-1 knock-out mice or wild type (Gal-1 non-expressing) Jurkat T-cells. Activated T-cells from SLE patients produced significantly less Gal-1 than controls or patients in remission. T-cells of active SLE patients responded poorly to the apoptotic signal by exGal-1 as compared with healthy controls, but the apoptotic sensitivity was normalized after effective therapy.
Conclusions. We have confirmed in three independent experimental systems that the function of de novo expressed Gal-1 in activated T-cells is the sensitization to the apoptotic effects of environmental exGal-1. Low expression of Gal-1 in SLE T-cells during active disease leads to impaired control of T-cell activity by exGal-1.

P1.07

Monitoring and modulation of follicular helper T cells in lupus

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Follicular B helper T (Tfh) cell is a CD4 T cell subset specialised to regulate high-affinity and long-term antibody responses. The differentiation and function of Tfh cells are regulated by a unique molecular program including transcriptional factors, such as Bcl6, co-stimulators, such as ICOS, signalling molecules, such as SAP and cytokines, such as IL-21. Excessive function of Tfh cells support the production of autoantibodies, leading to the development of autoimmune diseases in animal models.
Using animal models and human samples, we characterised precursor Tfh cells in blood with a CXCR5+CCR7lowPD-1high phenotype. The increase of the early memory Tfh cells in blood represents the active Tfh cell differentiation and correlates with the disease activities of systemic lupus erythematosus (SLE).
Low-dose IL-2 has been recently shown as a promising new therapy for autoimmune diseases by expanding regulatory T (Treg) cells. We carried out an open-label prospective clinical trial of low-dose IL-2 therapy for 40 patients with active SLE. Patients demonstrated broad and rapid responses to low-dose IL-2. Using CXCR5+CCR7lowPD-1high early memory Tfh cells as a reliable marker, we found low-dose IL-2 not only expanded Treg cells but also specifically suppressed Tfh cells.
New knowledge of Tfh cells will help to design new strategies to diagnose and treat lupus.

P1.08

Expression of costimulatory marker on CD134 and PD-1 on T follicular helper cells (Tfh)

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Background. Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by B-cell dependent autoantibody production. T follicular helper cells (Tfh) induce the activation and differentiation of B cells into immunoglobulin (Ig) secreting cells. They are characterized by prodcution of IL-21. Costimulatory markers are important for the B-cell T-cell interaction and potential surface marker of Tfh.
Patients and Methods. Peripheral whole blood of 39 SLE patients fullfilling the ACR criteria of SLE and 19 healthy controls (HC) was stimulated with phorbol myristate acetate (PMA) and calcium ionophore (Ca-Io) for 4 hours. Lymphocytes were stained for CD3, CD8, PD-1 and CD134. Intracellular staining was performed for IFN-γ and IL-21. Patients were assessed for disease activity by systemic lupus erythematodes disease activity index (SLEDAI). Patients were subgrouped into patients with and without lupus nephritis.
Results. The percentages of CD134+ and PD-1+ expressing T-cells which produce IFN-γ is significantly decreased in SLE-patients as compared to HC (18.5±11.5% vs. 29.2 ±19.4 %; p=0.02 and 31.8±15.6% vs. 41.7±14.3%; p=0.03). The percentages of CD134+ and PD-1+ expressing T-cells which produce IL-21 are not significantly different between SLE-patients and HC.
Conclusion. The expression of CD134 and PD-1 is preferable expressed on IFN-γ producing T-cells. According to our data CD134 and PD-1 no reliable marker for Tfh-cells.

P1.09

Mechanisms of Loss of tolerance in systemic lupus erythematous

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The pathogenesis of the systemic lupus erythematosus (SLE) is only partially understood. Our hypothesis concerns a default regulatory mechanism involving anti-inflammatory cytokine the TGF-β,
The aim of our present study was to evaluate the nature of the default and to specify the involved molecular mechanisms.

The functional study of the response to TGF-β1 was conducted on 15 SLE patients in active phase and 18 patients away from peak phases. To target the reply to TGF-β in SLE, the dependent Smad- pathway has been explored by analyzing the transcription of the target genes of TGF-β by RT-PCR.
This study showed a default of transcription of TGF-β target genes in SLE subjects in active phase. Identification of the specific defect on the Smad-dependent pathway was conducted through analysis by flow cytometry, the membrane expression of TGF-β receptor and the phosphorylation of Smad2/3 after activation by TGF -β.
Our results showed a defect of phosphorylation of Smad2/3 in transduction of TGF-β signal. The identification of factors directly responsible for this lack of TGF-β1 signaling in SLE in the phase of activity is underway.

P1.10

Immunomodulator effect of Vitamin D in the mononuclear cells of SLE patients

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Introduction. T helper cell subtypes (Th17 and Th9) seem to participate on SLE pathogenesis. Inhibition of antigen presenting cell and B lymphocytes by 1,25 dihydroxyvitamin D3 (Vit D) has been reported in SLE. However, there are few studies assessing the T lymphocyte cytokine profile.
Objectives. To evaluate immunomodulatory effect of Vit D upon cytokine profile on PBMC from SLE patients.
Methods. Thirty SLE patients and five healthy controls were recruited. PBMCs were incubated with monoclonal antibodies (anti-CD 3 and anti-CD 28), different concentrations of Vit D3 (0.1; 1.0; 10 and 100 nM) and dexametasoen (positive control). After 48 hours, IL-1β, IL-2, IL-4, IL-6, IL-10, IL -12, IL-17A, IL-21, IL-22, IL-23p19, IL-27, IFN-γ,TNF-α and IL-9 was measured by ELISA or Cell Cytometer on culture supernatant.
Results. Twenty-seven SLE patients were included (age 36.2±10.5 years). Vit D induced a significant reduction in IL 17, IL 21 and IL 9 supernatants levels (at 10 and 100 nM) and increased IL 2 level (at 0.1 and 1.0 nM) as well increased IL 10 (at 0.1, 1 and 100 nM), and increased IL 4 level (at all concentration). Vit D did not change the IL-6 and TNF level at any concentration. The serum levels of vit D did not influenced the effect of vit D *in vitro*.
Conclusion. 1,25 Vit D presented inhibitory effect on proinflammatory cytokines and increased anti-inflammatory cytokines. These cytokines are involved in the etiopathogenesis of SLE, reinforcing the necessity to maintain adequate levels of vitamin D in these patients.

P1.11

Environmental Triggers of Lupus Flares: The Roles of Oxidative Stress and Diet

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Lupus flares when genetically predisposed people encounter environmental agents causing oxidative stress, such as ultraviolet light and infections. How oxidative changes cause flares is unknown. Inhibiting T cell DNA methylation with the lupus-inducing drugs procainamide or hydralazine increases expression of genes including CD11a, CD70, CD40L and the KIR gene family, converting antigen specific T cells into autoreactive cells that cause lupus in mice. T cells overexpressing these genes are also found in patients with active lupus. How oxidative modifications inhibit DNA methylation is unclear. T cell DNA methylation patterns are replicated during mitosis by DNA methyltransferase 1 (Dnmt1). Dnmt1 levels are increased by signals transmitted through the ERK pathway. Dnmt1 then binds the replication fork and catalyzes transfer of methyl groups from S-adenosylmethionine (SAM) to dC bases in CpG pairs in the daughter strand where the parent strand is methylated. We found that peroxynitrite (ONOO-) prevents Dnmt1 upregulation in T cells by inactivating PKCδ, and that inducing expression of a negative PKCδ in SJL mouse T cells causes lupus-like autoimmunity. Further, SAM levels depend on dietary micronutrients including methionine and folate. We also found that CD4+ T cells treated with ONOO- cause lupus when injected into syngeneic lupus-prone mice, and that a diet low in transmethylation micronutrients increases lupus severity in lupus-prone mice with low Dnmt1 levels, while a diet enriched in transmethylation micronutrients decreases lupus severity. Together these results suggest that a diet poor in transmethylation micronutrients and anti-oxidants may contribute to lupus flares in genetically predisposed people.

P1.12

A role for interleukin-21 in the pathogenesis of systemic lupus erythematosus

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Background: Interleukin-21 (IL-21) has various effects on a number of immune cells and nonimmune cells. One of the essential roles of IL-21 is to contribute to autoantibody production as a result of promoting hyperactivity of B cells. In this study, we measured serum IL-21 level and IL-21 expression in the kidneys for investigating whether IL-21 participates in the pathogenesis of SLE.
Methods: Serum IL-21 levels were measured in SLE, osteoarthritis (OA) patients and healthy controls (HC). Serum IL-21 levels were analyzed for revealing the correlation with laboratory data or a disease activity index for SLE. Kidney tissues from patients with lupus nephritis and controls were used for evaluating the expression of IL-21 and IL-21R.
Results: Serum levels of IL-21 were increased in the patients with SLE as compared to the patients with OA or HC. Serum IL-21 levels of the patients with SLE were positively correlated with serum levels of IgG, the titers of anti-double-stranded DNA antibodies and the scores of SLE Disease Activity Index. SLE patients with low C4 concentrations had higher serum IL-21 levels than those with normal C4 concentrations. The expression of IL-21 was higher in renal tubular epithelial cells of the patients with lupus nephritis than in those of controls.
Conclusion: This study reveals the association between IL-21 and disease activity in the patients with SLE. We also first demonstrate IL-21 expression in renal tissue of the patients with lupus nephritis. These findings suggest that IL-21 is critically implicated in the pathogenesis of SLE.

P02 B-cells and autoantibodies

P2.01

MiR155 deficient mice show reduced disease severity in pristane-induced lupus (PIL)

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Background. Deregulation of endogenous miR155 was observed in many autoimmune conditions, including SLE. We herein examine the role of miR155 in the development of systemic manifestations in murine PIL.
Methods. MiR155-deficient (miR155-PIL) and C57/Bl6 (WT-PIL) mice were injected with pristane or PBS as control (WT-PBS) and analyzed after 8 months. Glomerulonephritis and pneumonitis were quantified by using the composite kidney biopsy score (KBS) and by analyzing the numbers of affected lung-vessels and the area of the inflammatory lung-infiltrate respectively. Specimens were stained with B220 (B), CD3 (T), Neu7/4 (neutrophils) and F4/80 (macrophages) and analyzed by cell-identification algorithms for nuclear segmentation (HistoQuest®). Anti-dsDNA, anti-histone and anti-chromatin antibodies were measured by ELISA.
For FACS analysis spleen cells were re-stimulated in vivo with anti-CD3 and anti-CD28antibodies.
Results. MiR155-PIL showed significantly decreased perivascular inflammatory area with B cells being the most prominent inflammatory cell. WT-PIL had a more severe renal involvement in the KBS than miR-PIL. Corresponding with reduced organ involvement, miR155-PIL had lower serum levels of measured antibodies, decreased frequencies of $CD4^+$ cells and lower frequencies of activated $CD4^+CD25^+Foxp3^-$ cells. Interestingly, also frequencies of $CD4^+CD25^+Foxp3^+$ regulatory T cells were lower in Mir155-PIL. Upon restimulation, $CD4^+$ cells showed a more pronounced Th2 and Th17 response in WT-PIL, but no significant differences in Th1 phenotype.
Conclusion. MiR155 deficiency in PIL mice did not prevent disease, but was associated with less severe organ involvement, lower serum auto-abs levels and lower Th17 and Th2 frequencies. Thus, antagonisation of miR155 might be a future approach in treating SLE.

P2.02

Altered localization of CD19+ B cells in the splenic germinal centers of IFN-γ-receptor-1 deficient lupus-prone MRL+/+ mice

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It has been reported that IFN-γ or IFN-γ-receptor-1 (IFNGR1) is required for auto-Ab production in murine lupus models. This study aimed to investigate roles for IFNGR1 in auto-Ab production in lupus-prone MRL/*lpr* and MRL+/+ mice.
Flow cytometric analysis showed a significant expression of IFNGR1 on splenic $CD19^{+}CD21^{hi}CD23^{lo}$ marginal zone-B (MZ-B) cells of MRL/*lpr* and MRL+/+ mice compared to their $CD19^{+}CD21^{lo}CD23^{hi}$ follicular-B (FO-B) cells or MZ-B cells of C57BL/6 mice. ELISPOT assay showed significantly increased frequency of anti-dsDNA IgM-producing cells in MZ-B cells of lupus-prone mice compared to their FO-B cells. Next, we generated IFNGR1-KO MRL+/+ mice by backcrossing *Ifngr1*$^{-/-}$ C57BL/6 mice into MRL+/+ mice. ELISA showed that *Ifngr1*$^{-/-}$ MRL+/+ mice had significantly reduced serum anti-dsDNA IgG levels compared to WT MRL+/+ mice. Flow cytometric analysis and ELISPOT assay showed no difference in the population of splenic MZ-B cells or in the frequency of anti-dsDNA IgM-producing MZ-B cells between WT and *Ifngr1*$^{-/-}$ MRL+/+ mice. Immunofluorescence analysis of spleen sections, however, showed significantly reduced frequency of $CD19^{+}$ B cells inside the T-cell zone in splenic germinal centers of *Ifngr1*$^{-/-}$ MRL+/+ mice compared to WT MRL+/+ mice.
These results suggest that IFNGR1 is required for recruitment of MZ-B cells into the T-cell zone in splenic germinal centers in MRL+/+ mice. It is also suggested that reduced serum auto-Ab levels in *Ifngr1*$^{-/-}$ MRL+/+ mice was due to altered localization of autoreactive MZ-B cells that could develop to auto-Ab-producing cells or act as auto-Ag-presenting cells to follicular helper T cells in the splenic germinal centers.

P2.03

Concordance of Increased B1 Cell Subset and Lupus Phenotypes in Mouse and Human Dependent on BLK Expression Levels

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Polymorphisms in the *BLK* gene have been associated with autoimmune diseases, including systemic lupus erythematosus (SLE), with risk correlating with reduced expression of *BLK*. How reduced expression of *BLK* causes autoimmunity is unknown. Using *Blk*$^{+/+}$, *Blk*$^{+/-}$, and *Blk*$^{-/-}$ mice, we show that aged female *Blk*$^{+/-}$ and *Blk*$^{-/-}$ mice produced higher anti-dsDNA IgG antibodies and developed immune complex-mediated glomerulonephritis, compared to *Blk*$^{+/+}$ mice. Starting at young age, *Blk*$^{+/-}$ and *Blk*$^{-/-}$ mice accumulated increased numbers of splenic B1a cells, which differentiated into class-switched $CD138^{+}$IgG-secreting B1a cells. Increased infiltration of B1a-like cells into the kidneys was also observed in aged *Blk*$^{+/-}$ and *Blk*$^{-/-}$ mice. In human, we found that healthy individuals had *BLK* genotype-dependent levels of anti-dsDNA IgG antibodies as well as increased numbers of a B1-like cell population, $CD19^{+}CD3^{-}CD20^{+}CD43^{+}CD27^{+}$, in peripheral blood. Furthermore, we describe the presence of B1-like cells in the tubulointerstitial space of human lupus kidney biopsies. Taken together, our study reveals a previously unappreciated role of reduced *BLK* expression on extraperitoneal accumulation of B1a cells in mice, and the presence of IgG autoantibodies and B1-like cells in human.

P2.04

The significance of Neutrophil Extracellular traps and B lymphocytes in renal tissue of patients with lupus nephritis

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Objective. To investigate the expression of Neutrophil Extracellular traps (NETs) and B lymphocytes in renal tissue of patients with lupus nephritis (LN) and to investigate its pathogenic mechanism.
Methods. Immunohistochemistry was used to detect the expression of NETs (citrullinated histone H3 as the marker) and the infiltration of B lymphocytes (CD19 as the marker)in renal specimens of the three groups (Lupus Nephritis group, n=20; minimal change disease (MCD)group, n=8; normal control group, n=3). Analyze the chronic and the activity index in renal tissues of LN and their relationship with NETs and B lymphocytes.
Results. The expression of NETs was absent in the renal tissues of the normal control group and the MCD group. However, they increased markedly in LN, especially in areas such as glomeruli with moderate and severe mesangial cells proliferation, cellular crescents, and tubulointerstitial areas with inflammatory cell infiltration. Compared with other types of glomeruli, the expression of NETs was significantly increased in glomeruli with moderate and severe mesangial cell proliferation ($p \leq 0.01$). In the glomeruli with moderate and severe glomerular mesangial cell proliferation, the mean number of positive stained cells with NETs (1.418±1.366) was positively correlated with renal pathological active index (r=0.620, p=0.004), the score of SLE-DAI (SLE-disease activity index, SLE-DAI) (r=0.492, p=0.027) and the mean number of positive stained cells of NETs in tubular cells (7.05±7.47) (r=0.558, p=0.011). In renal interstitial areas, the positive stained cells of NETs (0.465±0.451/HPF) were correlated with CD19 positive stained cells of B lymphocytes (6.07±7.70/HPF) (r=0.573, p=0.008) and renal pathological chronic index (r=0.645, p=0.002).
Conclusion. NETs is widely expressed in the renal tissues of lupus nephritis. NETs might play a role in the active damage of glomeruli.

P2.05

B cell derived IL-4 induces proteinuria and foot process effacement

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Background. Lupus nephritis remains the leading cause of mortality for SLE patients, and is associated with proteinuria and foot process effacement. In subsets of LN patients, B cell depletion therapies have been efficacious in lowering disease activity including glomerulopathy. The contributions of B cells to proteinuria and foot process effacement remain unknown. We hypothesized a B cell derived cytokine might be capable of directly inducing podocyte injury.
Methods. B cell model antigen model hen egg lysozyme was biotinylated, complexed to avidin and injected into mice. HEL-specific B cells were adoptively transferred and proteinuria assessed. Podocyte membrane ruffling was assessed with DIC videomicroscopy. IL-4 expression in mice was achieved by hydrodynamically injecting murine IL-4 in the piggyBac vector system. Human kidney biopsies were assessed for phospho-STAT6 by immunohistochemistry.
Results. We identified IL-4 as a B cell derived cytokine capable of stimulating podocyte membrane ruffling. Using a novel model of B cell induced proteinuria, B cells polarized to secrete IL-4 upon activation induced proteinuria without antibody or complement deposition. IL-4 overexpression was sufficient to induce foot process effacement and proteinuria in mice. Inhibition of IL-4 signaling with a JAK1/3 inhibitor markedly reduced proteinuria in these IL-4 overexpressing mice. A subset of patients with steroid-sensitive nephrotic syndromes possessed glomerular STAT6 activation.
Conclusions. These findings suggest a potential explanation for the utility of immunosuppression and more targeted anti-B cell therapy with rituximab in the treatment of proteinuric syndromes. These results support the role of IL-4 in human nephrotic syndromes and a novel therapeutic target.

P2.06

Sjögren's manifestations in aged mice arise from early life germinal centers

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Autoantibodies that arise in autoimmunity such as diabetes, lupus or primary Sjögren's Syndrome (pSS) are present years to decades prior to the onset of disease. This suggests that the initial autoimmune trigger involves a peripheral component which drives disease manifestations in local tissue later in life. NOD.H-2h4 mice are non-diabetic autoimmune mice that develop a disease that closely resembles pSS including linkage to females, characteristic anti-Ro/La autoantibodies and sialadenitis resulting in xerostomia/dry mouth. We have characterized these mice and shown that autoantibodies arise many weeks prior to the onset of salivary gland tertiary lymphoid structures (TLS). Now we demonstrate that removal of spontaneous germinal centers (GC) that arise in spleens of young NOD.H-2h4 mice abolished Sjögren's manifestations later in life. Early, transient blockade of CD40L or splenectomy inhibited TLS neogenesis of aged mice. Moreover, inhibition of CD40/CD40L interactions in young animals by a single injection of anti-CD40L at 4 weeks of age, greatly blunted the formation of key autoantibodies implicated in glandular pathology, such as anti-muscarinic type 3 receptor (anti-M3R) Ab's and restored salivary flow. These data show that early peripheral immune dysregulation gives rise to autoimmune manifestations later in life and that for those diseases that are pre-dated by autoantibodies, early prophylactic intervention with biologics may prove efficacious.

P2.07

Autoantibodies to high mobility group box 1 in patients with Incomplete and Systemic Lupus Erythematosus

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Introduction. High Mobility Group Box-1 (HMGB1) is involved in the pathogenesis of Systemic Lupus Erythematosus (SLE). However, the role of autoantibodies to HMGB1 is unclear. Therefore levels of anti-HMGB1 and their reactivity to HMGB1 BoxA and BoxB were examined in association with disease activity and clinical parameters.
Methods. Eighty-six SLE patients, 34 patients with incomplete lupus (ILE) and 44 age- and sex-matched healthy controls (HC) were included. Anti-HMGB1 levels were measured during quiescent disease (SLEDAI ≤4, n=47), and active disease (SLEDAI ≥5 n=39). Serum IgG, IgM anti-HMGB1 levels and reactivity against Box A and B were measured using ELISA.
Results. Quiescent and active SLE patients had significantly increased anti-HMGB1 IgG levels compared to HC. There was no difference in anti-HMGB1 levels between active and quiescent patients. ILE patients did not have increased anti-HMGB1 levels. Anti-HMGB1 IgM in HC, ILE, quiescent and active SLE patients were comparable. There were no associations between anti-HMGB1 and disease activity, anti-ds DNA. However, patients with arthritis had higher anti-HMGB1 levels, while patients with neurological involvement had lower levels. Anti-HMGB1 levels were similar in active disease and subsequent remission. Patients with antibodies directed against both Box A and B had higher SLEDAI, increased anti-ds DNA, lower complement C3 levels, and higher total anti-HMGB1.
Conclusion. Although anti-HMGB1 IgG levels are increased in SLE patients, no clear relation with disease activity or specific clinical symptoms was found. Therefore, anti-HMGB1 levels do not seem to be a useful biomarker of active disease or organ involvement.

P2.08

Therapeutic implications of the immunostimulatory properties of SLE immune complexes

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Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by formation of autoantibody-containing immune complexes (ICs) that trigger inflammation, tissue damage and premature mortality. SLE ICs often contain nucleic acids that are recognized by numerous innate immune receptors that can initiate pathological mechanisms leading to production of cytokines, interferons and ultimately to immune responses leading to organ damage.

In order to characterize the pathways induced by SLE ICs and identify targets for therapeutic intervention, we have set up an *in vitro* system for evaluation of SLE ICs. Since the analysis of SLE ICs using patient sera is often not feasible (low level of activity, current treatment, etc.), we have isolated total IgG from patients or healthy controls and reconstituted "fully loaded" ICs by mixing IgG with debris from necrotic cells containing autoantigens and nucleic acids. Adding such reconstituted ICs to human PBMCs induces robust interferon and cytokine production. We found that ICs reconstituted from patients expressing anti-RNP antibodies activate type I IFN production. The uptake of these complexes can be inhibited by FcgR-blocking antibodies and is completely dependent on the presence of plasmacytoid dendritic cells. Using a variety of target-specific molecules, we have identified pathways that participate in the inflammatory activity of SLE ICs.
These results broaden our understanding of the immunostimulatory activity of ICs and have implications for selection of targets for treatment of SLE as well as patient stratification.

P2.09

Identification of homogeneous systemic lupus erythematosus (SLE) patient groups using clustered autoantibody reactivities

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In SLE, early diagnosis, differentiation to other autoimmune diseases and prognostic stratification are still great challenges. Hence, SLE represents an enormous challenge for the clinical development of effective therapies.
Aim. Detecting a broad set of SLE-associated autoantibodies (AABs) might help to investigate the number, co-prevalence and similarities of AAB reactivities in SLE patients. Here, we describe the development of a multiplexed AAB array, which enables the analysis of 87 AABs in SLE patients.
Patients and Methods. A Luminex bead-based AAB assay was designed comprising established and novel biomarkers a) for the diagnosis and b) differential diagnosis of SLE, c) associated with disease activity, d) organ involvement, e) interferon type I response genes, and f) for patient subgrouping. AAB reactivity against these antigens was tested in over 700 SLE, healthy controls (n=1000), and AID samples (n=500).
Results. Based on the individual marker pattern, patients either belong to clusters defined by characteristic markers, or are phenotypically more overlapping with other AIDs. The analysis of the AAB reactivity yields at least four different reactivity groups (G1-G4) including patients: G1: a higher disease activity score, broad and homogeneous AAB reactivity; G2: with broad, but heterogeneous AAB reactivity; G3) who have few AABs and G4) with unusual AAB pattern.
Conclusion. The multiplexed analysis of AABs in SLE enables defining an AAB reactivity score and SLE patient clusters. This might support the stratification of SLE patients into more homogenous subgroups in clinical studies thereby increasing the probability of successful drug development.

P2.10

The fluorescence ratio provides a reliable way to study BCR signaling in patients

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Background. B cell receptor (BCR) signaling is central to B cell biology and is the target of therapies for cancer and autoimmunity. We studied whether a flow cytometry-based technique could reliably measure BCR signaling.
Methods. We simultaneously measured four signaling molecules (pSyk, pPLC-g2, pERK1/2, pLYN) in six B cell subsets (IgG and IgM memory, IgG and IgM B1, naïve mature, transitional). Signaling was measured with and without stimulation with polyclonal anti-IgG and IgM. We assayed cells from 102 adults on two days and determined the coefficient of variance (CV) between the two days using three methods to analyze signaling: (1) the raw post-stimulation fluorescence of individual signaling molecules, (2) the stimulated minus unstimulated fluorescence, and (3) the ratio of stimulated divided by unstimulated fluorescence. We compared the ratio with the percent positive cells determined by isotype control. Lastly, we studied cells isolated at different times over 14 months from one individual.
Results. The ratio proved the most robust method. Within the 24 parameters

measured (4 signaling molecules in 6 B cell types), the ratio yielded a CV <11% in 21 of the 24. The ratio correlated strongly with the number of positive cells determined by isotype control. In the subject followed over 14 months, the ratio yielded stable results while the other analysis methods did not.
Discussion. BCR signaling can be measured in a reliable and potentially clinically useful way using the fluorescence ratio. Using this technique, we found that BCR signaling in one adult remained stable over 14 months.

P2.11

B1 cell abnormalities in patients with systemic lupus erythematosus

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Background. B1 cells are important in secreting natural antibodies and may play a role in autoimmunity. Markers of human B1 cells have recently been delineated, allowing their study.
Methods. We used flow cytometry to study B1 cell phenotype including B cell receptor (BCR) signaling with and without stimulation in 107 patients with SLE, 15 patients with other autoimmunity, and 24 healthy controls. We correlated signaling with clinical data.
Results. We identified both IgM (CD20+, IgMhigh, CD27high, CD38low, CD43high) and IgG (CD20+, IgGhigh, CD27high, CD43high) B1 cells. B1 cells had higher baseline pERK1/2 levels but a lower increase of pERK1/2 post BCR stimulation than memory cells. There was a trend towards SLE patients having a higher percentage of both IgG and IgM B1 cells. IgM B1 cells from SLE patients had a lower fold post-stimulation increase in pERK1/2 (3.5 fold increase) compared to IgM B1 cells from normal controls (4.7 fold increase), (p<0.0001). IgG and IgM B1 cells had lower surface immunoglobulin levels in SLE patients than the other groups. There was a trend towards an inverse correlation between number of autoantibodies (anti-DNA, ENA, antiphospholipid) and IgM B1 pERK ratio in SLE patients (p=0.056).
Discussion. IgM B1 cells have significantly lower BCR signaling in SLE patients compared to normal controls, and in SLE patients decreased IgM B1 BCR signaling correlates with having more autoantibodies. Given the evidence that polyclonal IgM is protective in SLE, dysfunction of IgM B1 cells may play a role in pathogenesis.

P2.12

Antiphospholipid antibodies in lupus nephritis and their role in long-term renal outcome

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Background. Lupus nephritis (LN) is a severe manifestation of Systemic Lupus Erythematosus (SLE). The role of antiphospholipid antibodies (aPL) in LN is unclear. We investigated aPL levels/positivity as potential biomarkers of severity in LN.
Methods. Serum levels of antibodies to cardiolipin (aCL) and β_2-glycoprotein-I (anti-β_2-GPI) were assessed in 64 patients with biopsy-ascertained active LN before and after induction treatment, and in 286 SLE patients with no history of LN (BioPlex 2200; positivity ≥20 IE/mL). LN patients were followed for a mean time of 10.9 years. Renal outcome was determined by the chronic kidney disease (CKD) stage at the end of follow-up.
Results. Fractions of aPL positive patients were similar in active LN and in non-renal SLE, whereas the majority of them declined following induction therapy for LN (Table I). Moreover, aPL levels decreased following treatment.

Table I. Fractions of aPL positive patients (%) and aPL levels (median, IE/mL). Comparisons between active and treated LN.

aPL isotype	Non-renal SLE	Active LN	Treated LN	p-value
IgG aCL	18.6%; 1.0	12.5%; 1.95	9.4%; 0.8	0.317; **<0.001**
IgM aCL	8.1%; 1.0	9.4%; 0.75	1.6%; 0.65	**0.025**; **<0.001**
IgG anti-β_2-GPI	19.7%; 1.4	20.3%; 2.0	10.9%; 0.7	**0.034**; **<0.001**
IgM anti-β_2-GPI	8.1%; 1.1	9.4%; 1.0	3.1%; 0.75	**0.046**; **<0.001**

Subgroup analyses revealed that in patients with proliferative LN (n=52), IgM titers decreased in responders, but not in non-responders. IgG titers decreased in all response groups. In membranous LN patients (n=12), aPL levels remained unchanged regardless of treatment outcome.
Neither aPL levels nor aPL positivity predicted long-term renal outcome, but we noted a significant correlation between CKD stage and duration of follow-up.
Conclusions. In this study, aPL did not predict long-term renal outcome. Following immunosuppression for proliferative LN, IgG and IgM isotypes were affected differently with regard to treatment outcome.

P2.13

Decreased IL-10+ regulatory B-cells (Bregs) in lupus nephritis patients

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Background. Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by B-cell dependent autoantibody production. Recently, a new B-cell subset was discovered which have a regulatory capacity. The aim of this study was to analyse regulatory B-cells in SLE patients.
Patients and Methods. Peripheral mononuclear blood cells (PBMCs) of 34 SLE patients fullfilling the ACR criteria of SLE and 21 healthy controls (HC) were included. PBMCs were stained for CD19, CD24 and CD38 and analysed by flow cytometry. In vitro stimualted PBMCs with CPG and restimulated with PMA and ionomycin were investigated for IL-10+ regulatory B-cells.
Results. The percentages of circulating CD19+CD24hiCD38hi cells in HC is not different from SLE patients. The percentages of IL-10+ regulatory B-cells (Bregs) are significantly decreased in SLE patients, in particular with lupus nephritis, compared to HC. The proportion was independent of disease activity.
Conclusion. This is the first study demonstrating a decrease of IL-10 producing B-cells in lupus nephritis patients as compared to HC reflecting an impaired regulatory function. This might contribute to the development of lupus nephritis.

P2.14

IL-21 dependent Granzyme B production of B-cells is decreased in patients with systemic lupus erythematosus (SLE)

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Background. B-cells play a pivotal role in the pathogenesis of systemic lupus erythematosus. They are a source of characteristic autoantibodies and act as antigen-presenting cells. Recently, B-cells have been shown to produce Granzyme B. This study aimed to investigate the ability of Granzyme B production by B cells in SLE.
Patients and Methods. Peripheral mononuclear blood cells (PBMCs) of 18 SLE patients fullfilling the ACR criteria of SLE and 11 healthy controls (HC) were included. PBMCs were stimulated *in vitro* with CpG, IL-21, IgG+IgM, IL-21 and a combination of IgG+IgM and IL-21 for 20 hours. Next, cells were stained for CD19, IL-10 and Granzyme B. Patients were assessed for disease activity by systemic lupus erythematodes disease activity index (SLEDAI).
Results. B-cells of SLE-patients and HC have relatively low proportion of IL-10 expression about 1-2 % independent of the stimulus. The Granzyme B production is significantly increased after stimulation with IL-21 and even more after a combination with IgG+IgM an IL-21. In SLE patients the proportion of Granzyme B expressing B cells is lower as compared to HC (17.56±3.92% vs. 32.48±8.34%; p<0.005). No correlation could be found between the proportion of Granzyme B expression and disease activity.
Conclusion. These data show that B cells of patients with SLE are able to produce Granzyme B. Especially IL-21 seems to be important to induce this B-cell development.

P2.15

Pristane induced lupus and models for other CTD

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Along with end-organ damage, SLE patients develop high levels of Type I interferon (IFN) and autoantibodies against Sm/RNP, DNA, and other antigens. Impaired phagocytosis of apoptotic cells by lupus macrophages may contribute to the pathogenesis of these immunological and clinical manifestations by promoting chronic inflammation. Pristane-induced lupus in mice closely mimics the clinical and immunological features of SLE. Pristane-treated mice develop anti-Sm/RNP/DNA autoantibodies, lupus nephritis, anemia, erosive arthritis resembling rheumatoid arthritis, and pulmonary vasculitis with diffuse alveolar hemorrhage (DAH). We have shown that autoantibody production and nephritis are TLR7 and IFN dependent whereas anemia (and probably arthritis) are TLR7 and TNF-α dependent but IFN-independent. More recently, we found that pristane-induced hematological manifestations and DAH are absent in immunoglobulin-deficient, C3-deficient, and complement receptor 3-deficient mice and that DAH does not develop in wild-type mice treated with cobra venom factor to deplete C3. In addition, we found that intraperitoneal pristane injection causes a generalized phagocytosis defect similar to that in SLE patients, resulting in the accumulation of dead cells in the lung, bone marrow, and other tissues. Taken together, these data suggest that pristane-induced lupus is caused by an acquired phagocytosis defect, resulting in the accumulation of dead cells in tissues, opsonization by immunoglobulin and complement, and phagocytosis of apoptotic/necrotic cells by complement receptors, resulting in TLR7 engagement by endogenous nucleic acids, proinflammatory cytokine production, and ultimately the clinical manifestations of lupus. Pristane-induced lupus is a useful model for understanding how unremitting inflammation in humans progresses to autoimmune disease.

P2.16

Study of serum anti-nucleosomal antibodies as marker of renal affection in a cohort of Egyptian SLE patients

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Objective: evaluate the role of anti-nucleosome antibodies in lupus patients, its diagnostic and predictive value.
Methods: Group I, 40 SLE patients divided into: group I A (20 SLE patients with no renal disease), and group I B (20 SLE patients with lupus nephritis). Group II: 20 healthy subjects as control. Serum anti-nucleosome antibodies titer was evaluated by ELISA.
Results: For group IA 35% had mild disease activity, 35% had moderate and 30% had severe activity. For group IB, 20% had moderate activity and 80% had severe activity, with a statistical significant difference, p<0.001. Renal biopsy was done for patients in group IB, 6 had class III lupus nephritis, 4 had class IV lupus nephritis, 8 had combined class IV and V lupus nephritis. Concerning serum Anti- nucleosome antibodies level, it was significantly higher in group I (A&B) (156.43±73.69) u/ml than in group II (6.50±1.85) u/ml, p<0.001. Serum anti-nucleosome antibodies in group IB was significantly higher than the mean value of group IA, p<0.001. Roc curve of serum anti-nucleosome antibodies shows that it can significantly discriminate between normal persons and SLE patient at cut off level >20u/ml. Also, Roc curve shows that serum anti-nucleosome antibodies can significantly discriminate between lupus patients with and without lupus nephritis at cut off level >160u/ml as a diagnostic of renal involvement in SLE.
Conclusions: Serum anti-nucleosome antibodies can significantly discriminate between normal and SLE patients with a very high sensitivity and specificity and can significantly discriminate between SLE patients with and without lupus nephritis.

P2.17

Evidence for the waste disposal hypothesis: CR3 polymorhism SNP1143679 is associated with enhanced class switching of nucleic acid-specific antibodies and multi-organ involvement in SLE

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Objective: Defective apoptotic waste disposal is thought to contribute to SLE pathogenesis. To clarify the role of complement in these events we examined the relationships among autoantibody isotype, complement activation, complement receptor 3 polymorphism and organ involvement.
Design: We recruited patients with SLE (n=211), with other systemic autoimmune disease (n=65) and non-autoimmune control subjects (n=149). The genotype of SNP rs1143679 in the ITGAM gene was determined. Ex vivo formation of immune complexes was examined using serum-treated autoantigen microarrays. The amount of antigen-bound IgM, IgG and complement C4 and C3 was quantified on autoantigens comprising nucleic acids, proteins and lipids.
Results: The non-synonymous variant rs1143679 in complement receptor type 3 was associated with an increased production of anti-dsDNA IgG antibodies. Homozygous carriers of the previously reported susceptible allele (AA) had significantly lower levels of dsDNA specific IgM than SLE patients with GG genotype. Carriers of the susceptible allele were more likely to develop nephritis (odds ratio=2.0, p<0.05) and to have triple organ involvement (kidney, joints, skin) versus single organ involvement (odds ratio=1.9, p<0.05). The presence of a high ratio of nucleic acid specific IgG/IgM was associated with the involvement of these organs in the complete SLE cohort.
Conclusion: Polymorphism in the ITGAM gene is associated with susceptibility to produce anti-nucleic acid antibodies and with increased anti-nucleic acid IgG/IgM ratio in SLE patients. Complement receptor 3 dysfunction may be responsible for complement-mediated apoptotic debris removal deficiency, promoting the development of class-switched autoantibodies targeting nucleic acids.

P03 (Auto-)immunity (misc.)

P3.01

In vitro induced regulatory T-Cells reduce organ involvement in a murine model of Systemic Lupus Erythematosus

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Background/Purpose. Regulatory T cells (Treg) are crucial for maintaining peripheral tolerance. In Systemic Lupus Erythematosus (SLE), theyare reduced in their number and function. The aim of this study was to characterize organ involvement in a murine model of SLE and analyze the effect of intravenously applied *in vitro* induced Treg(iTreg).
Methods. Lupus was induced in female BALB/c mice by a single i.p. injection of 0.5ml pristane; 6 control mice received PBS. 21 mice served as a positive control (PIL). ITreg ($CD4^+CD25^+Foxp3^+$) were injected intravenously either once at the beginning of the experiment (iTreg-boost, 8 mice) or monthly (iTreg-rep, 6 mice). Mice were monitored for clinical signs of arthritis and sacrificed after 8 months. Arthritis and lung involvement (perivascular inflammation) were quantified by an image analysis system (Osteomeasure®). Kidneys were analyzed by an experienced pathologist (kidney biopsy score).
Results. PIL presented with involvement of the lungs (100%), joints (62%) and kidneys (29%).

results		
Perivascular inflammatory area		
PIL	iTreg-rep	iTreg-boost
0.007 ± 0.001 mm2/ mm2	0.003 ± 0.001 mm2/ mm2 p<0.05	0.006 ± 0.003 mm2/ mm2
Kidney Biopsy Score		
PIL	iTreg-rep	iTreg-boost
3.286 ± 0.535	1.833 ± 0.601 p=0.092	2.25 ± 0.526
Paw inflammatory area		
PIL	iTreg-rep	iTreg-boost
0.688 ± 0.113 mm2/ mm2	0.188 ± 0.0574 mm2/ mm2 p<0.001	0.598 ± 0.082 mm2/ mm2
Mean paw swelling		
PIL	iTreg-rep	iTreg-boost
0.360 ± 0.069	0.044 ± 0.020 p<0.01	

ITreg-rep showed significantly decreased histological signs of lung involvement and clinical and histological signs of arthritis. The mean kidney biopsy score of PIL was almost twice as high as iTreg-rep. ITreg-boost did not significantly differ from PIL however showed less inflammation.
Conclusion. Repeated injections of iTregs were able to prevent the development of severe pneumonitis and arthritis. A single injection before the development of PIL was not effective, however, it still showed a trend towards a less severe disease.

P3.02

Estrogen-mediated TLR8 expression via STAT1 facilitates endogenous miRokine ligand activation through miR-21-containing exosomes: a novel innate inflammatory pathway in systemic lupus erythematosus

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While the adaptive immune response has been investigated extensively in systemic lupus erythematosus (SLE), recent work suggests that innate immunity plays an important pathological role. We have demonstrated that estrogen lowers the threshold of immune cell activation and enhances TLR8 expression with agonist stimulation; a response that was more robust in females. TLR8 is an innate immune system receptor that binds to single-stranded RNA sequences present in viruses. In this study, we investigated this pathway more comprehensively to better understand innate immune responses via TLR8 in SLE. Estrogen treatment of primary cells significantly up-regulated the expression of many genes, including STAT1 and TLR8. CHiP-seq and EMSA analysis in cells stimulated with estrogen identified and validated a putative estrogen response element that promotes STAT1 expression. Subsequently, EMSA analysis confirmed STAT1-mediated transcriptional activation of TLR8 with estrogen stimulation. In lieu of viral RNA to activate TLR8, we explored the potential role of miR-21, which has been suggested to be an endogenous ligand activator in carcinogenesis via exosome signaling. miR-21 was detected in exosomes isolated from SLE serum and TLR8 expression was induced in vitro by stimulating cells with exosomes that were synthesized to contain fluorescently labeled miR-21. Thus, just as a cytokine or chemokine, exosome-encapsulated miR-21 can act as an inflammatory signaling molecule, or miRokine, between cells by virtue of being an endogenous ligand of TLR8. Collectively, our data elucidate a novel innate inflammatory pathway in SLE where estrogen-mediated expression of STAT1 promotes TLR8 expression, which can also be activated by miR-21.

P3.03

Interferon regulatory factor 5 promotes disease in the FcγRIIB-/- mouse model of lupus through TLR7-dependent and -independent pathways

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Background. Polymorphisms in interferon regulatory factor 5 (IRF5) are strongly associated with an increased risk of developing systemic lupus erythematosus. We previously demonstrated that IRF5 is required for disease development in the FcγRIIB-/- lupus mouse model. The exact pathways through which IRF5 acts to promote disease in this model are not known. As IRF5 plays a central role in signaling through TLR7, a TLR involved in pathogenesis in other lupus models, we investigated the relative effects of TLR7 deficiency, and combined TLR7 and IRF5 deficiency in the FcγRIIB-/- mouse model.
Methods. We generated the following experimental groups of FcγRIIB-/- female mice: TLR7+/+IRF5+/+ mice, TLR7-/-IRF5+/+ mice and TLR7-/-IRF5-/- mice. Mice were analyzed at the age of 8 months. Experimental groups were compared for disease manifestations including autoantibody production, serum IgG levels, and kidney disease severity.
Results. We found that TLR7 deficiency reduces disease severity and that TLR7 is required not only for the production of autoantibodies against RNA-containing autoantigens but also for autoantibodies against double-stranded DNA. FcγRIIB-/- mice deficient in both TLR7 and IRF5 developed less disease than mice deficient in TLR7 alone, with lower titers of anti-RNA autoantibodies, lower levels of the pathogenic IgG isotypes, and less severe renal disease.
Discussion. We have identified TLR7-dependent and TLR7-independent roles for IRF5 in the development of lupus autoimmunity. This suggests that therapies targeting IRF5 may offer some additional benefit compared to therapies targeting only TLR7 for the treatment of lupus.

P3.04

Regulatory haplotypes in HLA-D modulate transcription of multiple genes in the antigen presentation pathway and potentiate systemic autoimmunity

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Genetic predisposition is key for SLE susceptibility, however little is known about the nature or functional properties of causal genetic variants. We used targeted population sequencing to comprehensively characterize genetic variability at 28 risk loci for SLE in cases (773) and controls (576). The HLA-D region contains the strongest risk loci identified for SLE, with multiple alleles of both HLA-DR and -DQ showing strong associations. Sequence analysis of the BTNL2-DR-DQB2 region identified 15,261 common (MAF >0.05) genetic variants. Disease-associated variations are imbedded in stable haplotypes formed by multiple, ENCODE and eQTL-defined functional variations impacting the transcription of more than 20 genes that encode components of the antigen processing and presentation (APP) pathways of HLA class I and class II genes. Median neighbor joining analyses identified regulatory haplotypes strongly associated with SLE, all of which contained eQTL variants that increased the transcription of HLA-DR, DQ, DP, and other elements of the APP pathway in multiple myeloid and lymphoid cell lineages. This risk clade contains all of the classical HLA-D alleles previously associated with SLE, indicating that the systemic up-regulation of the APP pathway is a consistent feature of all SLE-associated HLA-D alleles. Our analyses demonstrate that such regulatory haplotypes have increased disease-associated odds ratios in comparison to the disease odds for maximal GWAS tagging SNPs in these loci. These findings show that functional variations underlying many common disease alleles form regulatory haplotypes modulating the transcription of multiple genes in immune system pathways and that their functional phenotypes are potent and complex.

P3.05

RGC-32 enhances suboptimal CD8 cytotoxic T cell effector function in acute graft versus host disease and promotes lupus-like disease in chronic graft versus host disease

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Response Gene to Complement (RGC)-32 is an intracytoplasmatic protein expressed in a variety of cells in response to sublytic complement activation, TGFb and other cytokines. It plays a role in cell growth, fibroblast activation and renal fibrosis, Th17 and plasma cell differentiation. To assess whether RGC-32 expression promotes lupus-like disease, we used WT and RGC-32 KO mice to investigate whether lack of RGC-32 in B cells affects parameters of chronic (c) GVHD in the Bm12→B6 model and whether lack of RGC-32 in T cells affects parameters of acute (a)GVHD in the P→F1 model. In F1 mice injected with RGC-32 KO splenocytes, an attenuated phenotype of aGVHD was observed at suboptimal (30 $x10^6$) but not optimal (50 $x10^6$) donor cell doses as indicated by a significant decrease in donor CD8 engraftment, proliferation and host B cell elimination. Bm12→B6 cGVHD induced in RGC-32 KO hosts displayed an attenuated phenotype as indicated by decreased number of germinal center B cells and plasmablasts, mRNA expression of Prdm1, IRF-4 and Aicda and anti-dsDNA Ab production. These results suggest that RGC-32 expression in host B cells promotes autoimmune parameters in cGVHD while its expression in T cells enhances suboptimal CD8 cytotoxic T cell effector function thus preventing humoral autoimmunity in aGVHD. These data support the idea that RGC-32 blockade has the potential to reverse abnormalities in the CD8 T cell and B cell pathways that contribute to lupus pathogenesis.

P3.06

Lupus-Associated Functional Polymorphism in PNP Causes Cell Cycle Abnormalities in Human Immune Cells

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Systemic lupus erythematosus (SLE) is a multi-system, autoimmune disease characterized by autoantibodies to nucleic acids and nucleosomal proteins. The type I interferon pathway is dysregulated in SLE and IFN-α levels are high in patients. We performed a genome-wide association study and found that a missense SNP in the purine nucleoside phosphorylase (PNP) gene associates with high serum IFN levels in SLE (rs1049564, p=1.24 x10-7). PNP is a key enzyme of purine metabolism. PNP deficiency leads to dysregulated levels of deoxynucleotides, a slowing or inhibition in DNA synthesis, and defective T-cell and variable B-cell immunity. We find that the rs1049564 variant of PNP induces an S phase block in lymphoblastoid cells. Cell lines with homozygous variant (TT) had ~2 fold increases in S phase block as compared to cells lines with homozygous non variant (CC). We further showed that rs1049564 variant induced S phase block can be pharmacologically reversed, and similar findings were observed in SLE patient cells. These results suggest that the rs1049564 PNP polymorphism is a loss of function variant, and the C to T substitution in PNP alters PNP function results in S-phase block in select cell subsets within the lymphocyte compartment. This may result in an increase in circulating apoptotic lymphocytes, and higher type I IFN in human SLE. These findings have pharmacogenomic implications, as the S-phase block can be rescued in our in vitro experiments, suggesting a potential for personalized therapeutics.

P3.07

IRF5 deficiency ameliorates lupus but promotes atherosclerosis and metabolic dysfunction in a mouse model of lupus-associated atherosclerosis

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Premature atherosclerosis is a severe complication of lupus and other systemic autoimmune disorders. Gain-of-function polymorphisms in interferon regulatory factor 5 (IRF5) are associated with an increased risk of developing lupus and IRF5 deficiency in lupus mouse models ameliorates disease. However, whether IRF5 deficiency also protects against atherosclerosis development in lupus is not known. Here we addressed this question using the *gld.apoE*$^{-/-}$ mouse model. IRF5 deficiency markedly reduced lupus disease severity. Unexpectedly, despite the reduction in systemic immune activation, IRF5-deficient mice developed increased atherosclerosis and also exhibited metabolic dysregulation characterized by hyperlipidemia, increased adiposity and insulin resistance. Levels of the atheroprotective cytokine IL-10 were reduced in aortae of IRF5-deficient mice and in vitro studies demonstrated that IRF5 is required for IL-10 production downstream of TLR7 and TLR9 signaling in multiple immune cell types. Chimera studies showed that IRF5 deficiency in bone marrow-derived cells prevents lupus development and contributes in part to the increased atherosclerosis. Notably, IRF5 deficiency in non-bone marrow-derived cells also contributes to the increased atherosclerosis through the generation of hyperlipidemia and increased adiposity. Together, our results reveal a protective role for IRF5 in lupus-associated atherosclerosis that is mediated through the effects of IRF5 in both immune and non-immune cells. These findings have implications for the proposed targeting of IRF5 in the treatment of autoimmune disease as global IRF5 inhibition may exacerbate cardiovascular disease in these patients.

P3.08

Surface expression of Stabilin-2 in peripheral blood mononuclear cells in patients with systemic lupus eryhematosus

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Background. The efficient clearance of apoptotic cells by phagocytosis is critical for the maintenance of cellular homeostasis and for the resolution of inflammation to protect tissue from the inflammatory and immunogenic components of dying cells.Stabilin-2, one of the phosphadylserine receptors, mediates rapid cell corpse engulfment through interaction with intergrin. In this study, we preliminarily investigated surface expression of stabilin-2 in peripheral blood mononuclear cells(PBMCs) in patients with systemic lupus erythematosus (SLE) patients, and compared it with other autoimmune disease and healthy contols.
Patients and Methods. PBMCs (1x105 cells) from 5 SLE, 5 rheumatoid arthritis, 5 other diseases (lymphoma, Behçet's disease, systemic sclerosis, pyelonephritis), and 5 healthy controls were incubated in a 20 ml cocktail of FITC-conjugated anti-human CD14 antibody and PE-conjugated anti-stabilin-2 antibody. The stained cells were analyzed by fluorescence-activated cell sorter (FACS) analysis (BD bioscience). Nonparametric Kruscal-Wallis and the Wilcoxon Rank-Sum test was used to compare stabilin-2 positive populations in each group of patients.
Results. The percentage of stabilin-2 expressing monocytes and lymphocytes in the PBMCs of SLE patients was 1.25±0.70% (monocyte, median, standard error), 6.99±2.54% (monocyte), which was significantly lower than in healthy controls (26.35±4.39% monocyte, p=0.023, 26.59±3.94% lymphocyte, p=0.016). The difference between SLE and rheumatoid arthritis was not statistically different (p=0.057 monocyte).
Conclusion. The percentage of CD14+stabilin-2+ monocyte and lymphocyte in SLE and rheumatoid arthritis patients was lower than healthy control group. Considering the role of stabilin-2 in regulation of apoptosis and autoimmune function, further large-scale investigations are warranted.

P3.09

Lupus nephritis is characterized by unique DNA methylation changes in naïve CD4$^+$ T cells

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Objective. To characterize DNA methylation changes in naïve CD4$^+$ T cells in lupus patients with renal involvement.
Methods. Genome-wide DNA methylation changes in naïve CD4$^+$ T cells were identified and compared between two sets of lupus patients with and without a history of renal involvement. A total of 56 lupus patients, and 56 age-, sex-, and ethnicity-matched healthy controls were studied.
Results. We identified 191 CG sites and 121 genes that were only differentially methylated in lupus patients with but not without a history of renal involvement. The tyrosine kinase gene *TNK2* involved in cell trafficking and tissue invasion, and the phosphatase gene *DUSP5* which dephosphorylates and inhibits ERK signaling pathway, are among the most hypomethylated. Renal involvement is characterized by more robust demethylation in interferon-regulated genes in lupus patients. The type-I interferon master regulator *IRF7* is only hypomethylated with renal involvement. IRF-7 is an upstream transcription factor that regulates several loci demethylated only with renal involvement such as *CD80, HERC5, IFI44, ISG15, ISG20, ITGAX,* and *PARP12* (p=1.78X10^{-6}). Among the CG sites only hypomethylated with renal involvement, CG10152449 in *CHST12* has a sensitivity of 85.7% and a specificity of 64.3% for detecting renal involvement in lupus patients (p=0.0029).
Conclusions. We identified novel differentially methylated targets in the presence of renal involvement in lupus. These identified targets will help to better understand lupus nephritis, and provide a proof of principle for the potential applicability of specific methylation changes as predictors for specific organ involvements in lupus.

P3.10

Myxovirus resistance protein 1 (Mx1) levels are elevated in T cells of the patients with SLE and serum Mx1 is a marker of Neuropsychiatric SLE

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Background. Type I interferon signature has been known as a prominent feature in patients with systemic lupus erythematosus (SLE), but correlation with disease activity is still controversial. Nervous system disease is one of the most common manifestations in patients with SLE that significantly affects morbidity and mortality. Due to the complexity of clinical presentation of neuropsychiatric lupus (NPSLE), there are no specific markers for the diagnosis.
Methods. Two-sets of microarray were introduced in T cells from active lupus patients and quiescent lupus patients, both compared with healthy controls. Mx1 mRNA levels were determined in T cells from 34 lupus patients and 22 healthy controls using real-time qPCR. Serum levels of Mx1 were measured by sandwich ELISA in 27 patients with NPSLE, 20 with non-NPSLE, 28 with other neurodegenerative diseases and 15 healthy controls. Disease activities in lupus patients were evaluated using BILAG or SLEDAI.
Results. Mx1 and RGS1 were the only genes elevated in both sets of microarray more than 3-fold change. MX1 mRNA/protein levels were significantly higher in T cells from lupus patients compared with healthy controls, but mRNA levels were not correlated with BILAG. The levels of serum Mx1 were significantly higher in patients with NPSLE than in non-NPSLE and other investigated groups, with no correlation with SLEDAI.
Conclusion. Mx1 was highly expressed in T cells as well as in sera from lupus patients, regardless of disease activity. Serum Mx1 was significantly correlated with NPSLE, suggesting that serum Mx1 is one of the biomarkers for NPSLE.

P3.11

Blood-brain barrier damages in the pathogenesis of acute confusional state in systemic lupus erythematosus

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Objective. Although neuropsychiatric systemic lupus erythematosus (NPSLE) is one of the recalcitrant manifestations of SLE, its pathogenesis remains unclear. The present study was performed in order to elucidate the roles of blood-brain barrier (BBB) function and intrathecal synthesis of autoantibodies In NPSLE.
Methods. Paired serum and cerebrospinal fluid (CSF) samples were obtained from 84 SLE patients when they presented active neuropsychiatric manifestations (58 patients with diffuse psychiatric/neuropsychological syndromes [diffuse NPSLE] and 23 patients with neurologic syndromes or peripheral nervous system involvement [focal NPSLE]) and from 22 non-SLE control patients with non-inflammatory neurological diseases. IgG anti-NR2, anti-Sm, anti-RNP and albumin were measured by ELISA.
Results. CSF levels of anti-NR2 and anti-Sm, but not anti-RNP, were significantly higher in acute confusional state (ACS) than in non-ACS diffuse NPSLE (anxiety disorder, cognitive dysfunction, mood disorder and psychosis) or in focal NPSLE. There was no significant difference in CSF anti-NR2 index or CSF anti-Sm index among the 3 groups. Of note, Q albumin was significantly elevated in ACS compared with focal or non-ACS diffuse NPSLE. CSF anti-NR2 levels were significantly correlated with CSF anti-Sm levels in NP SLE, whereas there was no significant correlation between serum anti-NR2 and serum anti-Sm. Both CSF anti-NR2 and anti-Sm levels were significantly correlated with Q albumin.
Conclusion. These results demonstrate that the severity of BBB damages, but not the intrathecal synthesis of anti-NR2 or anti-Sm, plays a crucial role in the development of ACS, the severest form of diffuse NPSLE.

P3.12

Association study of LILRA4 with systemic lupus erythematosus in a Japanese population

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Objectives. Leukocyte immunoglobulin (Ig)-like receptor (LILR) multigene family are clustered within the human leukocyte receptor complex on chromosome 19q13.4. We previously reported association of LILRA2 and LILRB1 polymorphisms with systemic lupus erythematosus (SLE) and rheumatoid arthritis, respectively. LILRA4 is considered to negatively regulate type I interferon production. Type I interferons play a crucial role in the pathogenesis of SLE. In this study, we examined whether LILRA4 polymorphisms contribute to susceptibility to SLE.
Methods. Twelve tag SNPs in the LILRA4 region were selected based on the HapMap JPT data (MAF>0.05, R-squared>0.8). Association of the tag SNPs were examined in 501 Japanese patients with SLE and 551 healthy controls. A replication study was carried out for the associated SNP in Japanese 338 SLE and 265 healthy controls. Subsequently, a meta-analysis was conducted by the Mantel-Haenszel method.
Results. Among the 12 tag SNPs, rs7259036, located approximately 3kb downstream of the LILRA4 gene, showed the strongest association with SLE (A allele, p=3.8X10-4, odds ratio [OR]: 1.61). We next examined the association of rs7259036 using an independent SLE and control set. Although significant association of rs7259036A was not observed in the replication set (p=0.73, OR: 1.06), rs7259036A was slightly increased in SLE (p=0.0030, OR: 1.38) when the two studies were combined by a meta-analysis.
Conclusion. Our observation suggested a possible contribution of LILRA4 to SLE susceptibility. Further studies are required to confirm the association.

P3.13

An Estrogen Receptor alpha functional mutant is protective in murine lupus

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Systemic lupus erythematosus is a disease that disproportionately affects females. The etiology of this sex bias is unclear. We previously showed that a functional knockout of estrogen receptor alpha (ERαKO) resulted in significantly reduced renal disease and increased survival in murine lupus. Dendritic cell (DC) development, which requires both estrogen and ERα, is impacted as is activation status and cytokine production. Due to altered hormonal feedback loops, ERαKO mice have hypergonadism and partial endocrine sex reversal. Elevated estrogen (E2) and testosterone levels may have immunomodulating effects. We investigated the phenotypes of lupus-prone ERαKO (functional ERα mutant) vs. Ex3a (deletional ERα mutant) following ovariectomy (OVX) ± E2 replacement (to preserve a physiologic hormonal state). We found that NZM ERαKO mice were protected from lupus disease expression (no early deaths; no proteinuria) if they were unmanipulated, or if they were both ovariectomized *and* E2-repleted. These mice had fewer activated cDCs isolated from Flt3L-cultured bone marrow, *ex vivo* spleen or kidney. Protection was lost after OVX if no E2 pellet was administered, suggesting that the protective effect actually requires E2 (despite the lack of a functional ERα). A protective effect was *not* observed in NZM Ex3a mice (ERα-/-) when they were similarly OVX and estrogen-repleted. These data suggest that it is the *presence* of the truncated ERαKO mutant plus E2, rather than the *absence* of full length ERα or elevated testosterone, that impacts DC development/function and modulates disease to confer protection in this lupus model.

P3.14

Alternatively activated dendritic cells derived from systemic lupus erythematosus patients have tolerogenic phenotype and function

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Background. Tolerogenic dendritic cells (DCs) are increasingly explored as cell-based therapy in murine model of autoimmune diseases and may have potential therapeutic implications in the treatment of systemic lupus erythematosus (SLE) that is characterised by dysregulated innate and adaptive immune responses.
Objectives. In this study, we generated alternatively activated DCs (aaDCs) from SLE patients and healthy subjects and examined their immunoregulatory properties *in vitro*.
Methods. aaDCs were generated by treating monocyte-derived DCs by combination of 1,25 dihydroxyvitamin D(3) (vitD3) and dexamethasone followed by lipopolysaccharide-induced maturation.
Results. Lupus aaDCs were found to acquire semi-mature phenotype that remained resistant to immunostimulatory effect of sCD40L, CpG-DNA and SLE serum. These cells produced low level of IL-12 but high level of IL-10. They had attenuated allostimulatory effect on T cell activation and proliferation comparable to normal aaDCs and demonstrated differential immunomodulatory effects on naïve and memory T cells. These aaDCs were capable of inducing IL-10 producing regulatory T effectors from naïve T cells whereas they modulated cytokine profile with suppressed production of IFN-γ and IL-17 by co-cultured memory T cells with attenuated proliferation. The tolerogenicity of aaDCs was shown to be superior than those generated using vitD3 alone in lupus patients. aaDCs expressed lower level of RelB but apoptosis of DCs and IL12/IL-10 imbalance were not found to account for their tolerogenicity.
Conclusions. Combination of vitD3 and dexamethasone represented a feasible method in the generation of tolerogenic DCs from SLE patients.

P3.15

High Interferon GeneSignature is associated with increased disease activity and oral corticosteroiduse in lupus

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Background. Increased expression of genes inducible by Type 1 interferons has been observed in a subset of patients with lupus. Oral corticosteroids (OCS) are used to manage the signs and symptoms of lupus, with higher doses needed for more severe disease. We explored whether patients with SLE who have elevated expression of Type I interferon inducible genes (IFIG Dx) in their blood have worse disease activity and increased use of OCS.
Methods. Baseline disease activity data from two randomized controlled trials of sifalimumab (NCT01283139) and anifrolumumab (NCT01438489)was pooled. An investigative use only assay was used to determine IFIG Dx. Association between disease activity scores (SLEDAI and CLASI <10 or ≥10), OCS dose (< 10 or ≥10 mg/day) and IFIG Dx was assessed using chi-square tests.
Results. Pooled data from 739 subjects was available for analysis. Mean age was 39.6±11.9. Ranges of SLEDAI and CLASI scores were 4-29 and 0-53, respectively and 61% and 28% had SLEDAI or CLASI scores ≥10. 57% were on OCS doses ≥10 mg/day. 79% were IFIG Dx and had significantly greater disease activity: Odds ratios of 1.63 (95% C.I. 1.14-2.32; p=0.007) for SLEDAI ≥10; 2.84 (95% C.I. 1.75-4.61; p≤0.001) for CLASI ≥10. IFIG Dx subjects were significantly more likely to be on OCS ≥10 mg/day (odds ratio 1.58; 95% C.I 1.11-2.25; p value = 0.011).
Conclusions. IFIG Dx lupus patients had worse disease activity and were on higher doses of OCS.

P3.16

Utilization of a combined family-based/case-control cohort for the ImmunoChip identifies SLE loci not previously seen in standard case-control studies

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While family-based genetics studies have been around for decades, the GWAS era using large independent case-control cohorts has in essence superseded their utilization. While these screens of the genome have been successful in identifying SLE risk loci, it is not known if the genetic architecture of families significantly differs from independent case-control populations in such a way that favors identification of specific risk loci. We conducted a combined SLE family-based/case-control association study of the ImmunoChip in a multi-racial collection of multiplex (n=584) and simplex (n=713) families, as well as isolated cases (n=524). Our European-American sample consisted of 1801 SLE cases, 2213 unaffected family members, and 764 population-based controls; the African-American sample consisted of 1063 SLE cases, 865 unaffected family members, and 410 population-based controls; and the Hispanic sample consisted of 381 SLE cases, 213 unaffected family members, and 461 population-based controls. We utilized the PLINK DFAM procedure, which combines discordant sibship data, parent-offspring trio data, and unrelated case-control data in a single analysis via a clustered analysis using the CMH statistic. While we observed significant ethnic-specific associations with known SLE risk loci, we identified novel significant associations not seen (or only suggestively associated) in a SLE case-control study of the ImmunoChip in many thousands of more samples. Trans-racial mapping will allow for refinement of shared genetic regions and confirmation assays are underway. These results demonstrate the value of family studies in revealing the genetics of complex diseases and their ability to detect risk loci previously missed by population-based case-control designs.

P3.17

Engagement of BAFF with its receptor and its regulation by prednisone treatment in patients with System Lupus Erythematosus

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Background. B cell-activating factor (BAFF/Blys) is a critical survival factor for B cells, and known to contribute to B cell-mediated autoimmunity. Over-expression of BAFF leads to B cell expansion and lupus-like syndrome in NZB/W mice whereas inhibition of BAFF delays SLE onset. Elevated levels of serum BAFF and occupancy of BAFF receptor (BAFF-R) were observed in SLE patients and may be involved in SLE pathogenesis. We investigated the regulatory role of prednisone on BAFF-R expression and B cell responsiveness to BAFF in SLE patients.
Methods. Peripheral blood was collected from 4 healthy donors and 10 SLE patients meeting ACR 1997 revised criteria. Binding capacity of BAFF-R to BAFF on B cells was measured by flow cytometry. Peripheral B cells (PBB) were isolated and cultured to examine their response to exogenous BAFF *in vitro*, which was measured by ^{3}H-TdR incorporation.
Results. BAFF-R expression on PBB was significantly increased in SLE patients (p<0.005). BAFF binding to BAFF-R was not increased in SLE B cells. Exogenous BAFF-induced B cell proliferation was equivalent in SLE patients on >20mg/day prednisone and healthy donors, but was decreased in SLE patients on <5mg/day prednisone.
Conclusions. BAFF-R expression is increased in SLE patients and likely contributes to SLE pathogenesis. Decreased BAFF binding suggests BAFF-R is occupied by endogenous BAFF in SLE patients. This may explain the poor proliferation response to exogenous BAFF in the low-dose prednisone patients. The normal proliferation response by SLE patients on high-dose prednisone suggests other mechanisms of response or signal pathway to BAFF.

P3.18

SLE-Key™ rule-out serlogic test for SLE using the immunarray ICHIP™

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Background. SLE is associated with a broad spectrum of autoantibodies, but currently there is no single adequate serologic test. Lupus diagnosis is based on multiple criteria, and the disease can take years to evolve.
Objectives. We developed the previously described iCHIP™ as an effective SLE rule-out diagnostic test by profiling SLE patients compared to healthy controls to rule out a diagnosis of SLE. An initial set of 200 antigens associated with SLE was augmented with sets of proprietary markers developed by ImmunArray. Here we report verification and validation of our SLE-Key™ Rule-Out Serologic Test.
Methods. We collected serum samples from 250 SLE patients and compared them with sera of 250 healthy control samples, all independently sourced. We tested these samples using the ImmunArray iCHIP™ . Training was performed on a subset of 150 SLE patients and 150 healthy controls using 4 independent classification methods. Verification and validation were performed on an additional sets of 50 SLE patients and 50 healthy control samples each.
Results. All 4 classification methods differentiated SLE patients from healthy subjects. Validation of the different classification methods was performed on the remaining set of 50 SLE patients and 50 healthy controls showing sensitivity of greater than 90% and specificity of greater than 70% using a selected subset of auto-antigens.
Conclusions. The SLE-Key™ multiplex test can be used to assist physicians in ruling out serologically a diagnosis of SLE with a sensitivity of >90%. Work comparing this testing performance in direct comparison to standard serologic testing is ongoing.

P3.19

Infiltrating CD16+ are associated with a reduction in peripheral CD14+CD16+ monocytes and severe forms of lupus nephritis

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The role of monocytes (Mo) in lupus nephritis (LN) is not well understood. Our aim was to characterize glomerular Mo infiltration and to correlate them with peripheral circulating Mo levels, SLE clinical manifestations and severity of LN.
Methods. We evaluated 48 LN biopsy samples at Hospital San Vicente Fundación at Medellin, Colombia (2000-2011). Recognition of Mo cells was done using microscopic view and immunohistochemistry stain with CD14 and CD16. Based on the number of cells, we classified LN samples as low degree of diffuse infiltration (<5 cells) and high degree (≥5 cells). Immunophenotyping of peripheral Mo subsets was done using flow cytometry. We classified Class III and IV as severe LN.
Results. Mean age was 33.5±13 years and the mean SLEDAI was 17.5±6.9. The most common SLE manifestations were proteinuria (91%), hypocomplementemia (75%) and hematuria (66%). Severe LN was found in 69% of patients (Class III 26%, Class IV 43%). Severe LN patients and patients with higher grade of CD16 infiltration had lower levels (non significant) of non-classical Mo in peripheral blood (Table). High degree of diffuse infiltration was significantly associated with a higher SLEDAI and hypocomplementemia.

Table. Levels of peripheral blood Mo subsets according the severity of LN

	Severe LN	Non-severe LN	*p* value	High degree of diffuse CD16 infiltrates (>5 cells)	Low degree of diffuse CD16 infiltrates (< 5 cells)	*p* value
Classical (CD14++CD16-)	485.80±345.81	393.63±239.20	0.56	496.35±443.38	543.71±368.67	0.81
Intermediate (CD14++CD16-)	18.32±18.11	14.84±10.10	0.66	9.65±7.35	17.06±18.79	0.43
Non-classical (CD14+CD16++)	7.14±7.22	17. 47±25.32	0.15	3.95±2.32	11.70±10.37	0.13

Conclusion. Our results might suggest than those patients with more severe forms of LN had lower peripheral levels of non-classical (CD14+CD16++) Mo and might reflect a recruitment process in renal tissues.

P3.20

Circulating hsa-miR-30e-5p, hsa-miR-92a-3p and hsa-miR-223-3p may be novel biomarkers for Systemic lupus erythematosus

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Background. MicroRNAs (miRNAs) are short, noncoding RNAs that regulate gene expression on the posttranslational level and emerging as biomarkers in various diseases. However, a systematic analysis of circulating miRNAs in patients with SLE has been rarely addressed.
Objective. We attempted to identify plasma miRNAs associated with the susceptibility to SLE in Koreans, and to elucidate their significance in clinical manifestations of SLE.
Materials and Methods. Blood samples were collected from SLE patients (n = 70) and normal controls (NC, n = 40). For the microRNA PCR arrays, we isolated total RNA from plasma samples of 10 SLE patients and 10 NC. A miRNA expression profiling analysis was performed and compared between the SLE and the NC. To verify the microRNA PCR arrays results, we performed the quantitative real-time PCR in samples from SLE patients and NC.
Results. Nine miRNAs were differentially expressed in plasma between the SLE and the NC by miRNA PCR array. The plasma expression level of hsa-miR-17-5p, hsa-miR-19a-3p, hsa-miR-21-5p, hsa-miR-25-3p, hsa-miR-92a-3p, hsa-miR-223-3p, and hsa-miR-30e-5p were up-regulated in the SLE compared to the NC. The plasma expression level of hsa-miR-26b-5p and hsa-miR-150-5p were down-regulated in the SLE. The hsa-miR-30e-5p, hsa-miR-92a-3p and hsa-miR-223-3p were significantly up-regulated in SLE patients by quantitative real-time PCR. Especially, the hsa-miR-223-3p was significantly associated with oral ulcer (p<0.001) and lupus anticoagulant (p=0.031).
Conclusion. Our data suggest that plasma hsa-miR-30e-5p, hsa-miR-92a-3p and hsa-miR-223-3p may be novel biomarkers in the diagnosis of SLE. These promising markers warrant validation in larger prospective studies.

P3.21

Decreased free protein S can be biomarker of disease activity, but not associated with subclinical atherosclerosis in SLE

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Background. Protein S plays a role not only in coagulation pathway, but also in removal of apoptotic remnants. Free protein S was investigated whether it could represent as a disease related marker in systemic lupus erythematosus (SLE).
Methods. We checked free protein S, and carotid artery intima media thickness (cIMT) and plaque in 110 SLE patients.
Results. The free protein S in SLE patients was 67.4±19.7%, and 21 patients had low level of free protein S, defined as less than 50%. Hemoglobin and lymphocyte count were lower (11.4±1.4 vs 12.5±1.4, p=0.002 and 1, 221±609 vs 1,720±1,097, p=0.047), erythrocyte sedimentation rate (ESR) was higher (30.1±20.6 vs 20.8±17.8, p=0.033), C3 and C4 were lower (80.8±27.6 vs 103.4±25.8, p=0.001 and 15.6±10.4 vs 21.5±7.6, p=0.005, respectively) in SLE patients with low protein S level compared to those were not. However, the mean cIMT and the proportion of patients with carotid plaque were similar. On univariate logistic analysis, free protein S was correlated with hemoglobin, lymphocyte, ESR, C3, and C4, but not with cIMT and plaque. With adjustments, low free protein S was independently associated with hemoglobin (OR 0.57, p=0.023) and C3 (OR 0.94, p=0.017).
Conclusion. Decreased free protein S was associated with hemoglobin and complement 3. However, free protein S was not related with subclinical atherosclerosis.

P3.22

Depletion of sCD40L and VEGF is associated with thrombotic thrombocytopenic purpura (TTP) in SLE patients

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Background. CD40L is a costimulatory molecule expressed by lymphocytes and activated platelets. Soluble CD40L (sDC40L) levels have positively correlated with SLE activity. The aim of this study was to correlate sCD40L and vascular endothelial growth factor (VEGF) levels in patients with SLE-associated TTP at diagnosis (dx), after plasmapheresis (ap) and at remission (rem).
Material and Methods. We included 81 subjects (19 healthy controls, 14 SLE patients in remission, 13 patients with active hematological SLE, 14 patients with non-hematological active SLE and 21 SLE/TTP patients). We obtained serum samples, including serial samples for SLE/TTP patients (dx, ap and rem). ELISA for sCD40L and VEGF was performed.
Results. We found a positive correlation between sCD40L and VEGF levels in SLE/TTP (r=0.62, p=0.004). Both sCD40L and VEGF levels were lower in SLE/TTP^{dx} vs healthy controls (mean 1131 vs 5709 pg/ml and 54 vs 558 pg/ml; p=0.0001 and 0.007 respectively). Also, sCD40L levels were higher in active hematological SLE than SLE/TTP^{dx} (1131 vs 3397 pg/ml, p=0.021), but there were no differences with SLE/TTP^{rem} (3044 vs 3397 pg/ml, p=0.77). Mean sCD40L levels progressively increased in treated SLE/TTP patients (dx=1131, ap=1515, rem=3044 pg/ml; p=0.012). Other results are shown in Table I.
Conclusion. SLE/TTP patients display sCD40L depletion at diagnosis, which differs from findings in active hematological SLE. This costimulatory molecule may have a physiopathogenic role in microangiopathy-associated endothelial dysfunction.

Table I

Groups (n)	Age, years (mean ± SEM)	Hemoglobin g/dl (mean ± SEM)	Platelets cells/µl x10^3 (mean ± SEM)	Leukocytes cells/ mm^{3}x10^3 (mean ± SEM)	VEGF pg/ml (mean ± SEM)	CD40L pg/ml (mean ± SEM)
Healthy controls (19)	31±2	N/A	N/A	N/A	558±163	5709±840
SLE remission (14)	39±4	14.4±0.19	248±13	5.56±0.42	26 1± 93	3754±650
Active SLE						
Hematological (13)	31±3	8.80±0.45	106±13	7.31±1	119±69	3397±708
Non hematological (14)	28±2	10.1±0.23	296±37	8.33±1.27	268±131	4138±667
SLE / TTP (21)						
At diagnosis	32±5	7.00±0.37	66±8	5.83±1.24	54±41	1131±410
Postplasmapheresis		8.00±0.57	102±25	7.25±0.70	89±30	1515±440
Remisson		9.17±0.53	223±34	7.68±0.80	187±76	3044±403

P3.23

Epidermal injury promotes activation of nephritis in lupus-prone mice

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Systemic lupus erythematosus is clinically characterized by episodes of flare and remission. In patients, cutaneous exposures have been proposed as a flare trigger. Here, we describe a system in which epidermal injury is able to trigger the development of a lupus nephritis flare in New Zealand Mixed (NZM) 2328 mice. Following removal of the stratum corneum via duct tape, 20-week old NZM2328 female mice developed rapid onset of proteinuria when compared to sham-stripped littermate control NZM2328 mice. Histology of proteinuric mice demonstrated hypercellular glomeruli with inflammatory infiltrate and tubular protein casts suggestive of glomerulonephritis. To determine changes occurring in the kidney prior to the onset of nephritis, a time course was performed following tape stripping. By day 15 post injury, enhanced immune complex deposition was noted in the glomeruli. Recruitment of CD11b$^+$CD11c$^+$F4/80^{low} dendritic cells and CD11b$^+$CD11c^{int}F4/80^{high} macrophages into the kidney was the first detectible change noted in pre-proteinuric mice. Transcriptional changes within the kidney suggest a burst of type I IFN-mediated and inflammatory signaling which is followed by upregulation of CXCL13. Thus, we propose that tape stripping of lupus-prone NZM2328 mice is a novel model of lupus nephritis induction that will allow for the study of the role of cutaneous inflammation in lupus development and how crosstalk between dermal and systemic immune systems can lead to lupus flare.

P3.24

Profile of cytokines and chemokines in peripheral blood in Colombian patients with lupus nephritis

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Introduction. Systemic lupus erythematosus(SLE) is an autoimmune disease in which the innate and adaptive response plays a significant roll, mainly mediated by cytokines. Lupus nephritis-LN-is the most severe complication associated with SLE.
Objective. To identify differential expression of cytokines profiles and circulating chemokines in plasma of SLE patients with different degrees of renal compromise compared to SLE patients without LN, from a reference center in the Colombian Caribbean region.
Methods. This was a case-control-study. Plasma-samples from 10 patients with NL-class-II and 10 patients with NL-class-III, and 30 patients with NL-class-IV were analyzed. As a control plasma from 30 SLE patients without nephritis were used. Plasma samples were analyzed using the Luminex technology of 38 analytes (EGF, Eotaxin, FGF-2, Flt-3 ligand, Fractalkine, G-CSF, GM-CSF, GRO, IFN-α2, IFN -γ, IL-10, IL-12 (p40), IL -12(p70), IL-13, IL-15, IL-17, IL-1Rα, IL-1α, IL-1β, IL-2, IL -3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IP-10, MCP-1, MCP-3, MDC (CCL22), MIP-1α, MIP-1β, TGF-α, TNF-α, TNF-β, VEGF, sCD40L, RIL-2Ra) using MILLIPLEX®-MAP-Human Cytokine/Chemokine-Magnetic-Bead-Panel-Premixed 39 Plex.
Results. Significant differences($p<0.05$) was found between concentrations of the cytokines EGF, G-CSF, GM-CSF, GRO, IFN, IL4, IL8, IP10, MCP, MDC, MIP.1a, sIL2Ra,TNFb when SLE-patients with LN vs SLE-patients without LN were compared.
Conclusion. These preliminary data suggest that there are differences in the LN plasma patients level of some chemokines and proinflamatory cytokines. Our results support the hypothesis that circulating levels in plasma samples of these molecules may be considered, in the future, as a damage biomarkers in LN of SLE patients.

P3.25

Role of pSYK in inflammatory skin diseases

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Background. Spleen tyrosine kinase (Syk) is activated via phosphorylation (pSyk) and known to mediate diverse inflammatory functions. Recent studies suggested that Syk-phosphorylation plays a crucial role in systemic autoimmune disorders. Aim of our study was to investigate a potential role of pSyk in inflammatory skin diseases, particularly cutaneous LE (CLE).
Patients & Methods. Skin samples of patients with inflammatory skin disorders (CLE, atopic dermatitis, psoriasis, lichen planus) and healthy controls were included. They were sourced ethically and their research use was in accord with the terms of the informed consents. Gene expression analysis of lesional skin samples was performed to determine the activation of Syk-associated proinflammatory pathways in CLE. Immunohistochemistry was applied to analyse the lesional expression of pSyk in LE and other inflammatory diseases.
Results. Gene expression analyses revealed a strong enrichment of the interferon responsive gene signature in CLE samples with an activation of several proinflammatory pathways. We found pSyk mediated genes (OAS2, CCL5, BLNK, PLCG2 and IL21) to be strongly upregulated. pSyk was strongly expressed by immune cells and keratinocytes within CLE skin lesions.
Discussion. Our results demonstrate the expression of pSyk and several Syk-associated proinflammatory cytokines in inflammatory skin diseases, particularly CLE. We believe that pSyk might provide a potential future drug-target for the treatment of patients who suffer from CLE and related skin disorders.

P3.26

Heart rate variability is associated with TNF and INF I mediated signaling in SLE

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Introduction. Decreased heart rate variability (HRV), associated with adverse outcomes in cardiovascular diseases, characterizes patients with SLE. The LF/HF ratio, an HRV measure, reflects sympathovagal balance. We examined associations of HRV with SLE activity and cytokine expression.
Methods. 53 SLE patients were evaluated at 2 visits with BILAG, SLEDAI, PGA and SFI (SELENA flare index). Caffeine, tobacco and medications were recorded. HRV (RMSSD, pNN50, HF, LF/HF ratio) was measured using a 5-minute ECG. Plasma cytokines were assessed by ELISA or a multiplex immunoassay.
Results. Baseline HRV was inversely related to disease activity and flare (table). Changes in HRV between visits were inversely related to changes in SLEDAI and PGA. Hydroxychloroquine dose was associated with increased HRV. Age, caffeine, tobacco and other medications had no impact. Plasma TNFRII and MIG inversely correlated with baseline HRV, and similar trends were observed for BLyS, IL1A, INFα and IP-10. Using multivariate regression with backward elimination, only TNFRII remained an independent predictor of baseline HRV after adjusting for hydroxychloroquine dose and plasma BLyS, IL1A and INFα. In a separate model, MIG also remained significant among the same variables.
Conclusions. Impaired HRV, particularly the LF/HF ratio, is associated with lupus disease activity and several cytokines related to TNF and INF I pathways. The strongest association was with TNFRII and MIG, confirming and expanding previous immune connections of vagal signaling.

p values		Univariate linear regression				Multivariate linear regression			
		Dependent variables at baseline				Dependent variables at baseline			
		RMSSD	pNN50	HF	LF/HF	RMSSD	pNN50	HF	LF/HF
Independent variables at baseline	BILAG	ns*	**0.019**	**0.02**	**0.024**				
	SLEDAI	ns	ns	ns	0.073				
	PGA	ns	**0.014**	ns	0.062				
	Flare (SFI)	ns	ns	**0.047**	**0.008**				
	HCQ dose	**0.038**	ns	ns	ns	ns	ns	ns	ns
	BLyS	ns	ns	ns	0.071	ns	ns	ns	ns
	IL-17A	ns	ns	ns	ns				
	TNF alpha	ns	ns	ns	ns				
	TNFRII	**<0.001**	**0.01**	**0.039**	**0.024**	**<0.001#**	**0.01#**	**0.039#**	**0.024#**
	IL-1A	0.089	0.099	ns	ns	ns	ns	ns	ns
	INF alpha	ns	0.076	ns	ns	ns	ns	ns	ns
	MIG	**0.007**	**0.015**	**0.018**	**0.026**	**0.007#**	**0.015#**	**0.018#**	**0.026#**
	IP-10	ns	0.088	ns	ns				

*nonsignificant ($p>0.1$)
TNFRII and MIG were included in separate multivariate models, each adjusting for HCQ dose, plasma BLyS, IL-1A and INF alpha.

P3.27

Neutrophil extracellular traps from systemic lupus erythematosus patients elicit a proinflammatory response in macrophages

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Neutrophil extracellular traps (NETs) have been linked to systemic lupus erythematosus (SLE) pathogenesis. Decreased NET degradation has been shown to correlate with disease activity. Macrophages were shown to participate in NET clearance without eliciting an inflammatory response. However, this has not been addressed in SLE patients. The aim of this study was to analyze whether NETs derived from SLE patients are able to induce a pro-inflammatory response in macrophages.
Monocyte-derived macrophages from SLE patients and healthy controls were studied. SLE and control neutrophils were isolated by density gradient. NETs were induced by neutrophil incubation with LPS stimulation (SLE and controls) or without any stimulus (SLE). Macrophages were incubated with SLE and control-derived NETs for 6 hours. IL-6, IL-10 and TNF-α production was measured by ELISA.
NETs from 7 patients and 7 controls were analyzed. IL-6, IL-10 and TNF-α were induced upon macrophage incubation with NETs. After incubation with LPS-stimulated SLE NETs, SLE macrophages had a significantly higher synthesis of IL-6 and TNF-α than control macrophages (892 vs 237 pg/ml, p=0.017 and 1033 vs 115 pg/ml, p=0.021, respectively). IL-6 levels were higher when macrophages were cultured with LPS-stimulated NETs than with spontaneous SLE NETs (p=0.039), but this effect was not seen with TNF-α or IL-10.
Macrophages synthetize IL-6, IL-10 and TNF-α in response to NETs, which suggests that NET clearance is not a completely silent process. Moreover, we found a differential proinflammatory response characterized by the predominant induction of TNF-α after NET stimulation of SLE macrophages compared with controls.

P3.28

Suppression of lupus development by manipulating microRNA Activity

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MicroRNAs (miRNAs), as a novel epigenetic regulator play a crucial role in regulation of immune response and involvement in autoimmunity. We first revealed that genetic and epigenetic mediated abnormal expression of miRNAs can contribute to activation of several inflammatory pathways linked to the development of SLE. More importantly, in vitro manipulation of these miRNAs in patients' immune cells can alleviate the coordinate activation of the relevant signaling pathways. In this study we have evaluated the role of these miRNAs (miR146a, miR125a , miR155 and miR23b) on lupus phenotypes in in vivo system by using genetically modified mice (lupus relevant microRNAs knockout and transgenic mice) and systemic delivery of chemically modified miRNA mimic or inhibitor approach. We have examined if genetic alteration or *in vivo* intervention of expression of these miRNAs can modulate lupus phenotypes and pathways. We further have validated the targets and linked cell signaling pathways regulated by these miRNAs *in vivo* system and investigate novel cellular and molecular mechanisms responsible for miRNA mediated immune-regulation. We used genetically modified mice, bone marrow chimeric mice and systems biology analysis approach to elucidate the specific immune cell type(s) or resident cells of target tissues that lupus relevant miRNAs act on, as well as defined the signaling pathways and molecular regulatory networks regulated by these miRNAs *in vivo*. Our study provides novel insights into the mechanism of miRNAs involved in the development of systemic autoimmune diseases, and also could promote the development of novel therapeutic approach for lupus in the future.

P3.29

Defective removal of ribonucleotides from DNA promotes systemic lupus erythematosus

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Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease in which environmental exposures like virus infection and UV-irradiation trigger activation of the innate and adaptive immune system in genetically predisposed individuals. Heterozygous mutations of the 3` repair exonuclease 1 (TREX1) are associated with SLE. Biallelic mutations in TREX1 and the three subunits of rib-

onuclease H2 (RNASEH2A-C) cause Aicardi-Goutières syndrome, an inflammatory encephalopathy with clinical overlap to SLE. We therefore investigated the role of RNase H2 in SLE pathogenesis. RNase H2 is responsible for the removal of misincorporated ribonucleotides from DNA and is indispensable for genome integrity. We demonstrated a genetic association for rare RNase H2 sequence variants with SLE. RNase H2-deficient fibroblasts of AGS and SLE patients accumulated ribonucleotides in genomic DNA resulting in chronic low level DNA damage, constitutive p53 phosphorylation and senescence. Patient fibroblasts proliferated slower than fibroblasts from healthy individuals and showed impairment of cell cycle progression. In addition, patient fibroblasts exhibited constitutive up-regulation of interferon-stimulated genes and an enhanced type I interferon response to the nucleic acid poly(I:C) and UV-irradiation. UV-irradiation induced enhanced cyclobutane pyrimidine dimer formation in ribonucleotide-containing DNA. This suggests that innate immune activation may be caused by immune recognition of DNA metabolites of DNA damage repair and may also explain photosensitivity in SLE patients with RNase H2 mutation. In summary, our findings implicate RNase H2 in the pathogenesis of SLE, and suggest a role of DNA damage-associated pathways in the initiation of autoimmunity.

P3.30

Immune cells in urine as biomarkers in SLE

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The immunopathological events in the kidneys of lupus nephritis (LN) patients are poorly understood due in part to the difficulty in acquiring serial biopsies and the inherent limitations in their analysis. To identify a means to circumvent these problems, we investigated whether immune cells of kidney origin are present in patient urine and whether they correlate with kidney pathology. Flow cytometry analysis was performed on peripheral blood and urine cells of 69 SLE patients, of whom 41 were LN patients. Approximately 60% of non-LN patients had urine lymphocytes; T cells were always present and predominantly $CD8^+$, and B cells were either absent or a mixture of naïve and memory cells. In contrast, >90% of LN patients had urine lymphocytes. In half, the B and T cells resembled those in non-LN patient urine; however, in the remaining patients, the B cells were exclusively Ig-secreting plasmablasts or plasma cells (PB/PCs), and the T cells were predominantly $CD4^+$. In addition, pDCs and IFN frequently accompanied PB/PCs. The majority of patients with urine PB/PCs presented with proliferative nephritis and a significant loss of kidney function, which in some cases progressed to end stage renal disease (ESRD). Thus, urine can provide access to cells that likely represent kidney resident immune cell populations in SLE, and that we suggest can serve as biomarkers to identify patients at risk for developing LN and progressing to ESRD.

P3.31

IFNλ, known to be highly expressed in cutaneous lupus erythematosus, acts on dermal fibroblasts

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Interferon lambda (IFNλ) has been shown to be the dominant epidermal IFN in cutaneous lupus conditions. IFNλ is produced by, and acts on, keratinocytes. Fibroblasts were previously considered to be unresponsive to this type III IFN.
We here report novel findings revealing cell type-specific differences in IFNλ signalling and function in skin resident cells. In dermal fibroblasts IFNλ induces the expression of MxA, a potent antiviral factor, but not other interferon signature genes as it does in primary keratinocytes. In contrast to keratinocytes, fibroblasts fail to phosphorylate STAT1 in response to IFNλ, but instead demonstrate activation of MAPK. Accordingly, inhibition of MAPK activation (p38 and p42/44) blocked the expression of MxA protein. In keratinocytes the inhibition of the MAPK failed to alter MxA protein expression. Functionally, unlike type I IFN, IFNλ does not inhibit proliferation in fibroblasts, which is however seen in keratinocytes. Moreover, in fibroblasts, IFNλ upregulates the expression of TGFβ1-induced collagens.
Taken together, our findings identify primary human dermal fibroblasts as responder cells to IFNλ. Our study shows cutaneous cell type-specific innate IFN signalling and suggests that IFNλ could contribute to cutaneous lupus erythematosus specific inflammation even in the dermal compartment.

P3.32

Increased Interferon activity is associated with progression from Early Incomplete Lupus Erythematosus to SLE

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Objectives. To compare expression of Interferon Stimulated Genes (ISGs) in patients with Early Incomplete Lupus Erythematosus (E-ILE) with (i) patients who have progressed to established SLE and (ii) those who remain as ILE.
Methods. SLE was defined by ACR/SLICC 2012 criteria (n=97). E-ILE was defined by presence of ANA and 1-2 ACR/SLICC clinical criteria with <12 months symptom duration (n=17). ILE was defined as for E-ILE but >12 months duration (n=9). ISGs were measured using TaqMan qPCR. Relative expression of *BST2, CASP1, IFI16, IFI27, IFI44, IFI44L, IFI6, SERPING1, SIGLEC1, SP100, IFIT1 and ISG15* were ln-transformed and expressed as standard deviations from the mean of 20 healthy controls. Overall IFN signature score was derived by adding these values. Kruskal-Wallis and Bonferroni-corrected Mann-Whitney U tests were used.
Results. We found between-group differences (p<0.05) for most ISGs.
Expression was highest for SLE and lowest in ILE. E-ILE had intermediate level of expression. However these three groups did not differ on *IFIT1* (p=0.479) or *ISG15* (p=0.121). There was a significant difference in interferon signature score between groups (p=0.031). Median (IQR) score was 14.5 (1.1, 24.4) for E-ILE. It was higher in SLE 21.8 (4.1, 31.0) and lower in ILE 3.1 (15.7, -5.7).
Conclusion. We found an intermediate level of IFN expression in early incomplete SLE. This was higher after SLE progression, but lower in persistently incomplete disease. IFN expression at onset of symptoms may predict progression, or IFN response may worsen after the first year. Longitudinal analysis will investigate these explanations further.

P3.33

The levels of n-3 and n-6 poliunsaturated fatty acids in patients with systemic lupus erythematosus and their association with serological and clinical characteristics

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Background. Systemic lupus erythematosus (SLE) is an autoimmune systemic inflammatory disease.
N-6 polyunsaturated fatty acids (PUFA) can increase the formation of pro-inflammatory cytokines while N-3 polyunsaturated fatty acids can suppress inflammatory response.
Objective. Our objective was to assess the serum levels of n-6 and n-3 PUFA in patients with SLE and to look for their associations with different features of the disease such as disease duration, disease activity, serological profile, pattern of organ involvement and treatment.
Patients and Methods. The study group consisted of 30 SLE patients (29 female) and 20 controls. In all the subjects the levels of the following fatty acids: n-6 - linoleic acid (LA) and arachidonic acid (ARA) and n-3 - alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were analyzed with use of gas-liquid chromatography coupled with mass spectrometry.
Results. The serum levels of LA and ALA were significantly higher in SLE patients than in controls. The level of LA correlated with the titer of ANA and the dosage of glicocorticosteroids. The levels of ARA, EPA and DHA were inversely correlated with the level of anti-dsDNA antibodies. Analyzing various organ involvement we observed the association between the skin involvement and the level of EPA. The level of LA was significantly higher in patients with detectable antiphospholipid antibodies. Patients not treated with immunosuppressive drugs had significantly higher concentrations of LA, ARA and EPA.
Conclusion. The levels of PUFA are correlated with serological activity of SLE and can play a role in disease pathogenesis.

P3.34

Complement C3 does not contribute to the lupus-like disease elicited by topical treatment with Imiquimod

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Epicutaneous application of a Toll-like receptor 7 (TLR7) agonist, Imiquimod, has recently been shown to induce a lupus-like systemic autoimmune disease. In this murine model of inducible lupus, topical treatment with Imiquimod elicited more potent systemic effects than the intraperitoneal administration indicating that activation of the TLR7-signalling in the skin plays a key role. The complement system is known to have an important role in the pathogenesis of lupus and in the regulation of inflammation. We herein investigated whether lack of C3 could affect the imiquimod-induced lupus-like syndrome. BALB/c wild-type (WT) and C3-deficient (BALB/c.C3$^{-/-}$) mice were treated with topical application of 5% Imiquimod cream (Aldara™) for 11 weeks. Autoantibody production was measured by ELISA and kidney histology was scored by a trained histopathologist. Surprisingly we hardly detected any autoantibodies until almost the end of the experiment. After 11 weeks of treatment both experimental groups showed low titres of anti-snRNP (WT 29.75±11.33, n=5 *vs* C3$^{-/-}$ 97.28±41.53, n=5, p=0.1553), anti-ssDNA (WT 9.252±3.367, n=5, *vs* C3$^{-/-}$ 20.70±12.03, n=5, p=0.386) and anti-chromatin (WT 12.59±7.001, n=5, *vs* C3$^{-/-}$ 16.72±12.60, n=5, p=0.781) antibodies. In addition, no difference was found in glomerulonephritis severity. A mild splenomegaly was observed in both groups and flow cytometry analysis showed a similar decrease in the number of marginal zone B cells. Collectively, these data suggest that C3 does not influence the onset of autoimmunity in the imiquimod-induced lupus model. The study of the involvement of other complement components is currently in progress.

P3.35

Autoimmune Diseases And Systemic Lupus Erythematosa: Fortuitous Association Or Continuum?

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Introduction. Systemic Lupus Eythematosa (SLE) is recognized associated with various autoimmune diseases AID (thyroiditis, Gougerot- Sogreen 'GS'...);
Aim. To review main auto-immunes diseases observed in SLE
Patients and Methods. Retrospective study of SLE cohort observed in internal medicine (single center) from January 1994 to December 2014. AIDS are diagnosed referring to international criteria data. We haven't consider as AID manifestations those constitute criteria diagnosis of SLE (hemolytic anemia, antiphospholipid syndrome 'APLS', thrombopenia …).
Results. Cohort of 214 patients with female distribution, 49 patients have 1 or more auto-immunes diseases (22%) identified as GS disease (11), Hashimoto thyroiditis (9) more cases observed than Basedow disease (2); systemic sclerosis (5), celiac disease (7), Shmid syndrome (2), diabetes (4), pancreatitis (2), hepatitis more than lupus hepatitis referring to biological markers (7), psoriasis (2), vitiligo (2), alopecia (1), rheumatoid arthritis (4), pancreatitis (2) and Crohn's disease (1). AID are diagnosed by biological tests and constitute subclinal diseases in 21 (42%) and were diagnosed long time before SLE (20%); The prognosis is compromised by the liver disease (cirrhosis) in 11% and treatment is specifically for each organ damage
Conclusion. As reported in the international literature data AID are common in SLE. These manifestations constitute in many times a factor of prognosis The AID's treatment is sometimes specifically referring of the organ damage (liver, thyroid) and constitute in some circumstances therapeutically difficulties management (psoriasis). The frequency of this AID justify the screening in long term in SLE following up.

P3.36

Promoter methylation of genes in the innate immune system and microRNA 146a expression in systemic lupus erythematosus: Potential new therapeutic targets

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Systemic lupus erythematous is a multifactorial autoimmune disease that affects women at a higher incidence than men. In addition, women of specific ethnic groups have even higher incidence. Pathogenesis of lupus remains unknown; however, emerging data are beginning to show that aberrant epigenetic mechanisms may play a central role in its onset and progression. This study demonstrated specific gene promoter methylation profiles, using DNA methylation PCR arrays. Two genes, FoxP3, a member of the forkhead family of transcription factors, and ELANE showed significant modulation in methylation profiles, compared to age-matched healthy controls. FoxP3 promoter methylation was significantly increased and this corresponded to a decreased level of expression at the RNA level. Increased methylation of this gene suggests inactivation of Foxp3 through hypermethylation. FoxP3 is an essential transcription factor for regulatory T-cells (Tregs), which are considered the guardians of peripheral tolerance. Decreased expression of Foxp3 gene has been noted in other autoimmune diseases, such as rheumatoid arthritis. The ELANE gene promoter showed a decrease in percent (%) methylation, indicating activation of that gene (hypomethylation). This gene codes for a protein called neutrophil elastase and is known to play a role in inflammation. Using expression profiler arrays and real-time PCR, three other genes showed significantly expression, IL-18 (p<0.013), TNFSF13B (BlyS) (p<0.017) and FASLG (p<0.026). These studies suggest that certain signal pathways may be regulated by epigenetic mechanisms, which may play an important role in lupus onset and progression.

P3.37

Abdominal lesions revealing a systemic disease

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Background. Abdominal manifestations revealing systemic diseases (SD) are difficult to diagnose and often presents as dramatic emergencies with a poor prognosis. Frequencies are based on the underlying entity (antiphospholipids syndrome 'APLS') and diseases (polyarteritis nodosa 'PN', Behcet's disease 'BD', SLE…). Clinical polymorphism is tied to lesion localization and involved mechanisms (acute thrombosis, aneurysm rupture, mesenteric infarct, autoimmune pancreatitis, bacterial overgrowth….).
Patients and Methods. Retrospective study of Internal Medicine recruitment.
Results. 7 females and 2 males and with a mean age of 39 (17-69). We observed venous thrombosis (3), hepatic artery aneurysms (1), fatty liver disease (2), pancreatitis (1), intestinal pseudo-obstruction (1), cholangitis (1) and a mesenteric ischemia (1) in SLE (4), primary APLS (3), Wegener disease (1), and BD (1). Other related lesions were pulmonary artery aneurysm on (1), nephropathy (2) and pulmonary embolism (2). Treatment was based on the underlying condition (anticoagulants, immunosuppressants, steroids, statins, antiobiotics, synthetic antimalarial drugs…). Surgery was required in 4 cases and confirmed the diagnosis of vasculitis in 3 cases. Fatal outcome in 2 cases was caused directly by an abdominal lesion (1) or an pulmonary embolism (1). They were 2 recurring thrombotic events at other sites and concomitant appearance of other diseases' signs (aphtosis bipolar, nephropathy, nasal ulceration, polyarthritis, vespertilio...) as well as immunological elements (APL, ANCA, and anti-nuclear antibodies…).
Conclusion. Abdominal complications constitute diagnosis or prognosis criteria of many SD. It is caused by several mechanisms which necessary must be recognized so targeted treatment may be proposed.

P3.38

Stochastic sensing determination of serum and salivary interleukin-6 in low disease activity systemic lupus erythematosus patients

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Background. Interleukin-6 (IL-6) is one of the main cytokines of the immune pathology, systemic lupus erythematosus (SLE) included.
Objectives. Stochastic sensing assessment of serum and salivary IL-6 in low activity disease SLE patients and non-SLE controls.
Methods. Patients with low disease activity (SLAM score less than 6 points) and non-SLE controls were prospectively included.
Serum and salivary IL-6 were assessed using two stochastic sensors based on metal nanocomposites-graphene pastes. The mean of these determinations was used in all analysis. A concomitant ELISA analysis was performed for the serum IL-6.
Results. 10 SLE patients [90% of feminine sex; mean(SD) age 45.7 (7.4) years; med(inf;sup) age at SLE diagnosis 37 (19;49) years, disease duration 12 (0.8-19) years, SLAM score 2.4 (0;5) points] and 6 non-SLE controls [83.3% of feminine sex, mean (SD) age 44.3 (8.2) years].
Stochastic sensors and ELISA found similar serum IL-6 levels (p<0.001; r=0.997) in both cases and controls. Also, the serum and salivary IL-6 levels assessed by stochastic sensing proved to be correlated (p<0.001; r=0.951).
The serum and salivary IL-6 levels were found to be significant higher in SLE patients than in controls [med(inf;sup) 2.5(0.2-4.7) vs 0.7 (0.4-1.2) pg/mL, p=0.016 respectively 2.7 (1.7-5.3) vs 1.1 (0.5-1.7) pg/mL, p<0.001].
Both IL-6 levels were inversely correlated with the SLE onset age (p=0.035; r=-0.668, respectively p=0.017; r=-0.727). On the contrary, no correlation was found for disease duration or age at inclusion (p>0.05).
Conclusions. The serum and salivary IL-6 levels are correlated and rest significant higher in SLE patients even in low active disease, especially when young age of onset.

P3.39

Looks may be deceiving: autoimmunity versus clinical presentation in systemic lupus erythematosus

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Systemic Lupus Erythematosus (SLE) is known for its multifaceted clinical features and immunological syndrome. Certain autoantibodies have been linked to specific clinical aspects of the disease. However, the diversity of possible associations makes for the uniqueness of each case of SLE.
Objective. Our aim was to analyze clinical and immunological changes in SLE patients and to identify correlations between the two categories.
Methods. We included 54 consecutive patients diagnosed with SLE hospitalized in the rheumatology department of the Clinical Rehabilitation Hospital in Iasi. Venous blood samples were drawn to measure total ANA titers as well as anti-DNAds, anti-Sm ,anti- U1RNP, anti-SSA, anti-SSB and anti-nucleosome/chromatin antibodies. Clinical presentation, biochemical tests and urinalysis were extracted from patients' charts. Disease activity was assessed using the systemic Lupus Erythematosus Disease Activity Index (SLEDAI).
Results. ANA were found in 97% of patients. Prevalence of specific ANA subcategories was as follows: anti-DNAds 30,1%, anti-Sm 26%, anti-U1RNP 16%, anti-SSA 30,3%, anti-SSB 39,4%, anti-nucleosome 33,8%. Significant association (p≤0,02) was found between anti U1RNP and Raynaud's phenomenon, arthritis and leucopenia; anti-SSA, anti-SSB associated with xerostomia and anti-SSB with pericarditis. The association between anti-DNA ds, anti-Sm and anti-nucleosome antibodies were highly correlated with renal symptoms. More than 70% of our patients had SLEDAI ≥ 5.
Conclusion. Previously reported associations of antibodies with SLE clinical features were confirmed by our results. Moreover, our result suggest that anti-nucleosome antibodies could be a useful tool in the diagnosis and assessment of disease activity in SLE patients.

P04 Treatment

P4.01

5-year organ damage and safety in patients with serologically-active SLE treated with belimumab plus standard care

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Objective. Examine long-term damage and safety of belimumab plus standard care (SoC) in patients with serologically-active SLE.
Methods. Pooled interim analysis (GSK201223) from two open-label continuation trials following the BLISS trials. Patients received belimumab plus SoC every 4 weeks. SLICC Damage Index (SDI) was assessed every 48 weeks. The serologically-active population was defined as having both anti-dsDNA and low C3/C4 complement.
Results. 493 patients comprised the serologically-active population (baseline): 469 (95.1%) female, mean (SD) age 35.4 (10.5) years, disease duration 6.8 (6.27) years. Mean (SD) SELENA-SLEDAI was 9.4 (3.94), SDI was 0.6 (1.01).
At Years 5–6 (n=194), 166 (85.6%) had no change from baseline SDI (11.3% had +1, 3.1% had +2). Mean (SD) change in SDI was +0.18 (0.455). Among patients with no baseline damage, 106/123 (86.2%) had no change (12.2% had +1, 1.6% had +2), mean (SD) change in SDI was +0.15 (0.406). Among patients with baseline damage, 60/71 (84.5%) had no change (9.9% had +1, 5.6% had +2), mean change (SD) in SDI was +0.21 (0.532).
Overall, 210 (43%) patients reported drug-related AEs, infections/infestations 140 (28%) and gastrointestinal disorders 67 (14%) were most common. 54 (11%) had herpes zoster; 15 (3%) patients had opportunistic infections; 4 (0.8%) were serious. 6 deaths occurred.
Conclusion. Serologically-active SLE patients treated with belimumab plus SoC for 5 years had low organ damage accrual and clinically manageable AEs. Damage accrual was similar in patients with and without baseline organ damage. Belimumab plus SoC may attenuate future damage.
Funded by GlaxoSmithKline and HGS.

P4.02

Assessing satisfaction with treatment options and medical care in Systemic Lupus Erythematosus (SLE): Development of the Lupus Satisfaction Questionnaire (LSQ)

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The LSQ was developed from concept elicitation (CE) interviews (n=14, from four US rheumatology practices); eight SLE patients had taken belimumab within the past six months, six were biologic treatment naïve. Concepts most frequently mentioned by the first six patients were included in the draft LSQ. When available, wording provided by patients shaped the draft items. During the remaining eight interviews, the same CE questions were asked, and the draft LSQ was cognitively debriefed (CD) to evaluate its content, clarity, and relevance. Patients reported their treatment was effective; 100% (7/7) taking belimumab; 85% (11/13) taking steroids; 69% (9/13) taking hydroxychloroquine. Most patients found the frequency of their treatment acceptable (>75%), were happy with how treatment decisions are made (93%), and were satisfied with the relationship with their nurse (89%) or doctor (79%). 93% reported pills were easy to take (versus 50% for IV treatments, and 100% for injections). Patients also reported being highly satisfied with time spent with health care professionals (HCPs), ease of getting an appointment, and HCP responsiveness. Patients were not satisfied with short- and long-term treatment side effects, traveling to receive treatment, chronic need for medication and limited number of treatment options. Cognitive debriefing revealed the draft LSQ was comprehensive, clear, and relevant. The final LSQ contains 39 items including effectiveness of treatment (4 items), side effects (2), treatment administration (frequency and route) (15), interactions/relationships with HCPs (11), satisfaction with health insurance (3), and overall satisfaction (4). The LSQ's measurement properties will be evaluated in future studies.

P4.03

Belimumab 24-month treatment outcomes in patients with systemic lupus erythematosus (SLE) with high disease activity: Results from the OBSErve real-world study

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OBSErve (117295), a medical chart review study conducted in clinical practices, examined outcomes of patients with SLE following ≥8 belimumab infusions.
Rheumatologists (n=92) extracted patient data for 6 months prior to belimumab (index date), and every 6 months for 24 months. Primary outcome was physician-assessed clinical response to therapy, relative to the previous timepoint. This post hoc analysis examined patients with high disease activity (HDA). Safety was not assessed.
Of 501 patients, 277 completed 24 months; of these, at index, 153 had high anti-dsDNA and low C3/C4, 60 of 85 had SELENA-SLEDAI >10, and 190 received corticosteroids >7.5 mg/day (Table). Improvements in clinical response (≥50%) were observed by 6 months in all HDA subgroups (48.3–53.6%) with continued improvements at 12 (28.8–50.0%), 18 (32.7–36.7%) and 24 months (26.8–30.0%), consistent with the overall 24-month completers. At index, >98.0% of patients with HDA had moderate/severe disease; by 24 months, this reduced to ≤32.0% (all subgroups). From index to 24 months, corticosteroid dose and SELENA-SLEDAI decreased markedly (Table), and proportions of patients with renal dysfunction (laboratory-confirmed), abnormally low white blood cells, haemoglobin and platelets decreased.
In the real-world setting, belimumab therapy provided improvements in clinical response at 6 months that continued through 24 months in the HDA subgroups and overall population. Disease severity, SELENA-SLEDAI, corticosteroid use, and laboratory values also improved.
Study funding: GSK.

Table. Patient outcomes based on 24-month completer HDA groups.

	24-month completer population (n=277)		High anti-dsDNA and low C3/C4 (n=153)[a]		SELENA-SLEDAI >10 (n=60)[a,b]		Corticosteroids >7.5 mg/day (n=190)[a]	
	Index	24 months	Index	24 months	Index	24 months	Index	24 months
Disease Severity, % Moderate or Severe	98.2	27.1	99.3	32.0	100.0	30.0	98.9	28.4
Mean (SD) Corticosteroids Dose (mg/day)	18.0 (12.18)	2.9 (3.36)	18.1 (11.11)	3.1 (3.13)	20.6 (13.81)	3.1 (3.51)	19.9 (11.96)	3.0 (3.42)
Mean (SD) SELENA-SLEDAI Score[c]	12.5 (2.97)	4.4 (3.06)	13.4 (2.55)	4.0 (2.87)	13.8 (1.94)	4.5 (3.23)	12.9 (2.81)	4.5 (3.14)

[a]At index date; patients may be included in multiple subgroups; [b]Of 85 patients with available scores; [c]In patients with scores at index and 24 months.

P4.04

Adherence to treatment - Patient to patient panel outcomes

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Poor adherence to treatment is a significant problem in lupus, with multi-factorial causes, some of which patients will not easily talk with Doctors. To capture insights and make appropriate recommendations, Lupus Europe brought together 10 European Lupus patients (8 female, 2 male), representing diverse Lupus types and origins. Through 2 days interactive group sessions, guided by facilitators with lupus themselves, a working definition of treatment and main factors for poor adherence were identified.
Key findings:
- Patients view treatment much broader than only medical: "Any product or activity that aims at improving the person with lupus' quality of life". Deeply understanding each part of their treatment, being able to raise questions, and feeling ownership for the treatment emerged as the 3 key pillars of adherence.
- Patients plea to doctors is to (a) adhere to internationally recognized standards of care, or refer patients to specialists if they only have few lupus patients; (b) over-explain the importance of each treatment element to create commitment and avoid counter-productive internet searches; (c) acknowledge hearing symptoms described (even if judged irrelevant) to build trust; (d) create a treatment dialog where "YOUR prescriptions become OUR treatment plan".
- These messages and more are summarized in a letter to the medical community. The panelists also created a letter to fellows living with lupus, advising how to tame their lupus, including concrete recommendations on medical follow-up, adherence, reliability of information, and a message of hope and support. Those letters are available for doctors and through national patient organisations.

P4.05

Management of primary and secondary non-responders to B cell depletion therapy in systemic lupus erythematosus: Results from the first 100 patients at a single centre

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Objectives. To evaluate the outcome of repeat cycles of rituximab in SLE responders and non-responders.
Methods. We conducted an observational study of 100 SLE patients treated with rituximab in a single centre (total follow-up: 429 patient-years). Each cycle of rituximab consisted of 2x1000mg infusions repeated on clinical relapse. Patients who demonstrated features of HACA were retreated either with rituximab desensitising regimen or 2x1000mg ocrelizumab. Response was defined as improvement to ≤1 persistent BILAG B and no A/B flare.
Results. 88 patients had complete data (81 female, median age: 39 (range 20-80)). Median time-to-retreatment for cycles 1-3 was 53, 60 and 58 weeks respectively. In cycle 1 (C1), there were 12/88 (14%) primary non-responders. Of these, 5 were retreated at 6 months but none responded. Of the 76/88 (86%) primary responders, 63 were retreated on relapse. Of these, 54 continued to respond (median(IQR) time-to-C1-relapse: 54 (37-93) weeks) while 9 were secondary non-responders (median(IQR) time-to-C1-relapse: 62(47-95) weeks). Of the secondary non-responders (8 were due to HACA), 3/9 were retreated with ocrelizumab, which resulted in complete peripheral B cell depletion and response in 3/3; while 1 patient was retreated using rituximab desensitising regimen but still experienced HACA.
Conclusions. Although initial responses were good, duration of response may not necessarily be predictive to response in a subsequent cycle. Retreatment of C1 non-responders did not appear to be effective in SLE, in contrast to rheumatoid arthritis. Humanised anti-CD-20 antibodies induce depletion in rituximab-resistant patients and may be more effective than rituximab in SLE.

P4.06

Late-onset neutropenia following rituximab treatment in patients with systemic lupus erythematosus

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Background. The incidence and clinical consequences of rituximab-mediated late-onset neutropenia (LON) have been studied in various diseases, but data from Systemic Lupus Erythematosus (SLE) are limited. We studied the prevalence, consequences and predisposing factors for LON following rituximab in SLE.
Methods. Ninety-two patients from the Karolinska SLE cohort treated with rituximab, with or without cyclophosphamide, were enrolled. LON was defined as an unexplained neutrophil count <1,500 cells/μL, corresponding to a neutropenia of grade II–IV according to the National Cancer Institute Common Toxicity Criteria, occurring four weeks or later following rituximab. Four patients with neutropenia during treatment were excluded from this analysis.
Results. Of 88 patients analysed, 28 developed LON (13 grade II, 7 grade III, 8 grade IV; median time after treatment: 222 days). Ten patients presented with fever (3 infections: Staphylococcus aureus sepsis, Pseudomonas aeruginosa sepsis, Streptococcus fasciitis); 18 were asymptomatic. The infections resolved with antibiotics. Eight patients were retreated with rituximab after LON; three developed LON following these subsequent cycles. There was no association between neutropenia grade and severity of complications.
No predictors for LON were identified among dosages of rituximab, prednisone or cyclophosphamide (concurrent/cumulative), preceding neutropenia, sex, age, and disease duration.
Conclusions. SLE patients had a higher prevalence of rituximab-mediated LON (32%) than patients with lymphoma (3–27%) and rheumatoid arthritis (3%). Although this phenomenon is typically self-limiting, our results demonstrate that it is a common complication in SLE patients and underscore the importance of monitoring these patients for neutrophil counts, fever and infections.

P4.07

Long-term safety of rituximab in systemic lupus erythematosus: Repeat cycles are associated with low rates of hypogammaglobulinaemia

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Objectives. To evaluate immunoglobulin levels, serious adverse events and serious infections during rituximab treatment.
Methods. We conducted an observational study of SLE patients treated with at least 2 cycles of rituximab in a single centre between September 2004 and September 2015 (total follow-up: 367 patient-years). Each cycle consisted of 2x1000mg infusions repeated on clinical relapse. IgG levels were measured at baseline and 6 months after each cycle. Severe adverse events were those resulting in hospitalisation which lasted >24 hours, flares requiring intravenous therapy, malignancies or death.
Results. 69 patients (64 female) with a median age of 37 years (range 20-81) were studied. Median time-to-retreatment for cycles 1-4 were 53, 60, 58 and 51 weeks respectively. There were 118 serious adverse events: 3 deaths (2 x multiorgan failure and 1 x pneumonia), one thymoma and 114 hospital admissions (median duration 6 days) were recorded in 45 patients. Of these, 24 were flares requiring parenteral immunosuppressant and 24 were serious infection (6.5/100 patient-years), mostly chest infection. 2 developed low IgG with therapy (Table 1). Low IgM, IgA or IgG was not associated with serious infection; all p>0.05.
Conclusions. Repeat cycles of rituximab are safe and did not result in progressive reduction in IgG in patients with normal immunoglobulins at baseline. Serious infection rates were low. This is important to tailor therapy to patients who have relapsing disease.

Table I. Immunoglobulin levels at baseline and 6 months after each cycle of rituximab.

Timepoint	No. of patient treated	Mean (SD) value IgG (Normal range: 6.0-16.0 g/L)	P value (vs previous cycle)	Total patients with low IgG	Patients with new low IgG since previous cycle
Baseline	69	14.25 (6.42)	N/A	2/62 (3%)	0 (0%)
Cycle 1 6 months	69	11.85 (4.57)	0.005	2/52 (4%)	1 (1%)
Cycle 2 6 months	64	11.27 (5.47)	0.361	1/43 (2%)	1 (2%)
Cycle 3 6 months	44	9.66 (4.04)	0.482	2/19 (11%)	0 (0%)
Cycle 4 6 months	25	8.76 (2.56)	0.13	1/11 (9%)	0 (0%)

P4.08

PPARγ agonists in the prevention and treatment of murine systemic lupus erythematosus

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Peroxisome proliferator-activated receptor-γ (PPARγ) agonists have many immunomodulatory effects, and are used clinically to treat diabetes. We have previously shown that PPARγ agonists rosiglitazone and pioglitazone are beneficial when used early in prevention of lupus and lupus-related atherosclerosis. For our studies, we utilized two mouse models: the MRL.lpr mouse which is an established lupus-like model, and the gld.apoE-/- mouse, which is a model of accelerated atherosclerosis and lupus. We demonstrate that marked amelioration of disease is mediated in part by the adipose-derived cytokine adiponectin. We hypothesized that the effect of adiponectin might be mediated through direct engagement of one of the four described specific adiponectin receptors: AdipoR1, AdipoR2, calreticulin and T-cadherin. To identify the relevant adiponectin receptor(s) involved in lupus disease, we used pristane to induce a lupus-like phenotype to AdipoR1-, AdipoR2-, and T-cadherin-deficient mice and compared disease manifestations eight months after injection. Analysis of circulating antinuclear autoantibodies revealed that only the AdipoR2-deficient mice were resistant to the autoantibody increases observed in the AdipoR1-, T-cadherin-, or adiponectin-deficient mice. Similarly, AdipoR2-deficiency conferred protection to renal disease. Our data provide valuable insights into the functions of adiponectin receptors in the context of autoimmunity, while identifying potential novel therapeutic targets in SLE.

P4.09

Aseptic necrosis of femoral head in systemic lupus erythematosus

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Purpose. The adverse effect of corticosteroid such as osteoporosis, peptic ulcer, opportunistic infections, and diabetes mellitus could be well controlled recently along the development of many agents for such complications. Aseptic necrosis of femoral head (ANF), however, has been still remained as unresolved complications of corticosteroid.
ANF raises the severe troubles in quality of life for the patients. We studied the frequency of ANF in our patients with systemic lupus erythematosus (SLE), and whether we could prevent ANF.
Patients and Method. Two hundreds and sixty-eight SLE patients were registered in our Division. One hundred patients (200 femoral heads) were studied the lesions of ANF with magnetic resonance imaging.
For the prevention of ANF, we prescribed warfarin followed with low molecule heparin, alendronate, and atorvastatin for the 51 hospitalized patients treated with high dose of corticosteroid (more than 40 mg/day of prednisolone) including SLE, polymyositis, dermatomyositis, adult onset Still's disease, microscopic polyangitis from April 2009 to November 2011. The frequency of ANF was compared with historical control.
Results. Fifty-six patients with SLE showed ANF, and 40 patients had bilateral ANF. Ninety-six femoral heads had bone necrosis in SLE patients.
The prevention had no effect to protect ANF. While the frequency during the prevention was 21.6% (11 in 51 patients), the control showed 25.0% (13 in 52 patients).
Discussion. As the pathogenesis of ANF was thought as the obstruction of artery, we tried to prevent with anti-coagulant. However, the frequency of ANF was not improved. ANF is still remained as unresolved complications.

P4.10

Subcutaneous immunoglobulin in the treatment of systemic lupus erythematosus - a case report

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Introduction. High-dose intravenous human immunoglobulin (IvIg) has been used in the treatment of several immune-mediated conditions. Side effects are rare but might limit its use. Subcutaneous human immunoglobulin (ScIG) has been used as replacement therapy in primary immunodeficiencies, for which lower doses are needed.
Case report. A 52-year-old-Caucasian-woman has been treated over 10 years with topical immunomodulators, systemic corticosteroids, hydroxychloroquine and azathioprine for systemic lupus erythematosus with exuberant cutaneous involvement. Due to poor disease control, IvIg was started with marked improvement, but important adverse effects led to therapeutic discontinuation and subsequent clinical worsening. ScIg three times weekly was initiated immediately after another IvIg cycle, in order to maintain stable therapeutic levels. An excellent clinical response was observed over 12 months of ScIg treatment. The patient was completely asymptomatic and decided to discontinue ScIg administration. A pronounced worsening occurred and restarting ScIg did not improve the symptoms. Another cycle of IvIg was administered, followed by ScIg three times weekly, with complete remission and clinical stability achieved after 2 months.
Discussion. Subcutaneous administration of human immunoglobulin for immunomodulatory purposes has not been previously reported. It was effective and well tolerated, with a favourable safety profile when compared to IvIg. It can be a valid therapeutic option in case of important side effects from intravenous administration. Additionally, ScIg is a cost-saving option, given that a lower total dose of immunoglobulin is needed to achieve the same therapeutic effect. The administration can be done at home, saving hospital associated-costs and diminishing laboral absenteeism.

P4.11

Hydroxychloroquine Blood Levels in SLE: Clarifying dosing controversies and improving adherence

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Hydroxychloroquine is used for its effect on systemic lupus erythematosus disease activity and long-term benefits. Both can be limited by adherence. This can be assessed using blood levels. Conflicting data exist regarding blood levels and disease activity. There is dosing controversy; rheumatologists recommend weight-based, while ophthalmologists advocate height-based 'ideal body-weight' dosing.
Methods. Patients were prescribed hydroxychloroquine not to exceed 6.5mg/kg (max400mg/day, dialysis: 200mg 3/wk, renal insufficiency: 200mg daily). Levels were measured quarterly (therapeutic range 500-2000 ng/ml). Patients were divided according to baseline level. To assess the impact of measurement and counseling on adherence, we compared the proportion of patients with a level of 500ng/ml or higher based on how many prior assessments they had.
Results. The proportion of patients with therapeutic hydroxychloroquine levels in differed significantly by age, gender and vitamin D level. There was a trend toward lower levels with renal failure. Blood levels were similar regardless of height and ideal body weight. Comparing those with undetectable, sub-therapeutic and therapeutic levels, disease activity decreased (SLEDAI 2.92, 2.36 and 2.20) (p=0.04, for trend). At first, 56% were therapeutic and with repeated measurement this increased to 80% (p=<0.0001).
Conclusion. There was a trend towards higher disease activity with lower hydroxychloroquine levels. We show that weight-based dosing is appropriate and that height did not influence levels. Measurement, counseling and repeated testing can increase adherence.

Characteristics		<15 ng/ml	15-500 ng/ml	500-2000 ng/ml	≥2000 ng/ml	*p*
All (n=686)	88 (13%)	216 (31%)	366 (53%)	16 (2%)		
Gender	Female (n=633)	84 (13%)	206 (33%)	329 (52%)	15 (2%)	0.050
	Male (n=53)	4 (8%)	10 (19%)	38 (71%)	1 (2%)	
Age	≤30 yrs (n=89)	10 (11%)	18 (20%)	59 (66%)	2 (2%)	0.0018
30-44 yrs (n=244)	28 (11%)	98 (40%)	114 (47%)	4 (2%)		
45-59 yrs (n=230)	36 (16%)	75 (33%)	114 (49%)	6 (3%)		
60 + yrs (n=123)	14 (11%)	25 (20%)	80 (65%)	4 (3%)		
BMI	<20 (n=66)	9 (14%)	20 (30%)	34 (52%)	3 (5%)	0.26
20-24.99 (n=203)	25 (12%)	57 (28%)	114 (56%)	7 (3%)		
25-25.99 (n=185)	30 (16%)	55 (30%)	97 (52%)	3 (2%)		
30+ (n=215)	19 (9%)	79 (37%)	114 (53%)	3 (1%)		
SLEDAI	0 (n=267)	27 (10%)	83 (31%)	150 (52%)	7 (3%)	0.38
1-3 (n=217)	32 (15%)	71 (33%)	112 (52%)	2 (1%)		
4+ (n=202)	29 (14%)	62 (31%)	104 (51%)	7 (3%)		
Vitamin D	< 40 ng/ml (n=359)	55 (15%)	125 (35%)	170 (47%)	9 (3%)	0.011
40+ ng/ml (n=321)	33 (10%)	89 (28%)	192 (60%)	7 (2%)		
Creatinine (mg/ml)	<1.4 (n=618)	76 (12%)	195 (32%)	334 (54%)	13 (2%)	0.029
1.4-4.9 (n=15)	5 (33%)	4 (27%)	6 (40%)	0 (0%)		
5.0 + (n=6)	1 (17%)	3 (50%)	1 (17%)	1 (17%)		
Height (inches)	<60 (n=20)	5 (25%)	3 (15%)	11 (55%)	1 (5%)	0.31
60-62.5 (n=221)	22 (10%)	78 (35%)	113 (51%)	8 (4%)		
63-67.9 (n=320)	44 (14%)	97 (30%)	174 (54%)	5 (2%)		
68+ (n=113)	15 (13%)	33 (29%)	63 (56%)	2 (2%)		
Ideal Body Weight	Less than (n=95)	14 (15%)	28 (29%)	50 (53%)	3 (3%)	0.82
Greater than (n=574)	69 (12%)	183 (32%)	309 (54%)	13 (2%)		

P4.12

RING, an investigator-initiated trial aimed at testing the efficacy of rituximab in refractory lupus nephritis: rationale, trial design and call for participation

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Rationale. Lupus nephritis (LN) remains a severe complication of SLE, impacting survival and quality of life. Despite improvement in immunosuppressive regimens, at least 20% of LN patients do not achieve a sufficient level of response after 6 months of treatment. Several studies have demonstrated that an absence of early proteinuria decrease is a poor long-term prognostic factor. The RING trial is designed to test the efficacy of rituximab (RTX) in these refractory LN patients.
Design. 194 biopsy-proven LN patients with persistent proteinuria despite at least 6m of treatment will be randomized. Half of them will receive 5g of RTX (cave not provided as SD) within a 18m period (1g at w0, 2, 24, 48 and 72). Standard of care will be pursued in the others. The primary endpoint is the number of patients achieving complete response at w104. Patients will be recruited by lupologists who already collaborated in two previous European-based investigator-initiated LN trials.
Inclusion criteria. SLE, age ≥15, ISN/RPS Class III, IV or V LN (biopsy within 24m), previous treatment with Euro-Lupus/NIH cyclophosphamide or azathioprine or mycophenolate mofetil, maximum 10 mg prednisolone/day, uP/C ratio ≥1 (mg/mg), contraception, informed consent.
Exclusion criteria. recent or ongoing renal flare, 24-h proteinuria decline >50% over previous 6m, treatment with ≥10 mg prednisolone/d in the last 2 weeks before screening, previous treatment with RTX, previous treatment with other biologics within the last 6m.
Current status. Five countries have obtained regulatory authorization and the first 6 patients have been randomized. More centers are welcome (frederic.houssiau@uclouvain.be).

P4.13

H.P. Acthar gel (Acthar) attenuates disease activity in patients with persistently active Systemic Lupus Erythematosus (SLE) requiring corticosteroids

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This 8 week double-blind randomized placebo-controlled pilot study assessed clinical efficacy of Acthar in patients with persistently active SLE despite moderate dose corticosteroids. Eligibility criteria included hybrid SLEDAI (hSLEDAI) >2 with arthritis &/or skin involvement and BILAG A or B in mucocutaneous &/or musculoskeletal systems despite 7.5-30 mg prednisone daily for ≥4 weeks before screening. 38 subjects were randomized to SC Acthar 80U every other day (Acthar80) or 40U daily (Acthar40), or Placebo. Study medication was maintained for 4 weeks, then tapered to 2x/wk administration of the assigned dose. Change from baseline was assessed for hSLEDAI (wk 2, 4, 6 & 8), BILAG, CLASI, and tender swollen joint count (wk 4 & 8). Baseline hSLEDAI, BILAG and CLASI were similar between groups, though tender swollen joint count was higher in subjects receiving Acthar80 vs Acthar40 or Placebo ($p \leq 0.05$). Acthar led to significant improvement in hSLEDAI and BILAG.

Activity index *change from baseline*	Time	Placebo *LS mean (SE) n=12*	Acthar 40U QD *LS mean (SE) n=13*	Acthar 80U QOD *LS mean (SE) n=13*	Acthar (combined) *LS mean (SE) N=26*
Hybrid SLEDAI	4 wk	-1.2 (0.6)	-1.0 (0.5)	-2.0 (0.6)	-1.5 (0.4)
	6 wk	-1.4 (0.7)	-2.9 (0.7)	-3.5 (0.7)*	-3.2 (0.5)*
			p= 0.129	*p=0.045*	*p=0.04*
	8 wk	-0.8 (0.9)	-3.7 (0.9)*	-3.9 (0.9)*	-3.8 (0.6)*
			p=0.026	*p=0.020*	*p= 0.008*
BILAG 2004	4 wk	-4.7 (1.6)	-5.2 (1.5)	-7.2 (1.6)	-6.1 (1.1)
	8 wk	-1.8 (1.5)	-8.1 (1.4)*	-9.3 (1.6)*	-8.6 (1.0)*
			p=0.005	*p=0.002*	*p=0.001*

Clinical benefit was also demonstrated by improvements in CLASI activity ($p \leq 0.051$ for Acthar40 and combined Acthar vs Placebo at wk 4 & 8) and tender swollen joint count ($p < 0.02$ for Acthar80 vs Placebo at wk 8). There were no significant differences in treatment-emergent adverse events between groups. These controlled data suggest that Acthar reduced disease activity in patients requiring corticosteroids for persistently active SLE, with improvements occuring within 8 wk of treatment initiation.

P4.14

Evaluation Of Use of Belimumab in Clinical Practice SEttings (OBSErve) in Argentina

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Introduction. Studying clinical effectiveness of belimumab treatment in clinical practice of Systemic Lupus Erythematosus(SLE) is relevant in assessing external validity of controlled trials.
Methods. Retrospective chart review in 13 sites, including 40 patients. Primary objective: Change in overall clinical manifestations assessed by a 6-point scale similar to PGA. Secondary objectives: Change in SELENA SLEDAI; Number of flares by mSS Flare index; Steroid dose; Other drugs and evaluation of health economic parameters, all assessed 6 months before and 6 (n: 40) & 12 (n: 30) months after treatment.
Results. Baseline parameters: Age 40±14 yrs; female 90%; SLE duration ≥5 yrs 58%; hypocomplementemia 73%; high anti-dsDNA 60%; steroid dose ≥7.5 mg/day 70% and SELENA SLEDAI >10, 58%. Change in overall manifestations and secondary objectives are shown below:

Overall Change in 6 point scale	Worsened	No Change	Improved <20%	Improved 20-49%	Improved ≥ 50-79%	Improved ≥ 80%
6 months	0%	8%	10%	20%	45%	18%
12 months	3%	10%	10%	10%	23%	43%

	SELENA SLEDAI score (SD)	Number of flares mean/6months (SD)	Steroid dose mg/day (SD)	Steroid Sparing Effect mg/day (SD)	Steroid discontinuation
Baseline	12 (±7)	1,2 (±0,4)	17 (±16)	-	-
6 months	5 (±5)*	0,2 (±0,3)*	7 (±5)*	-11 (±13)*	6%
12 months	5 (±6)*	0,2 (±0,5)*	6 (±8)*	-13 (±17)*	18%

*p<0.001 vs baseline (Wilcoxon).

No significant modifications in other medications or health economic parameters were found.
Conclusions. Two thirds of patients obtained ≥ 50% overall response with relevant reductions in SELENA SLEDAI, number of flares and steroid dose. Results are consistent with controlled trials and support the use of belimumab in clinical practice.
GSK sponsored this study.

P4.15

Long term efficacy and safety of tacrolimus as a maintenance therapy for lupus nephritis

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Background. This study examined the long-term outcomes of tacrolimus for the treatment of lupus nephritis (LN) after changing form azathiprine or mycophenolate mofetil (MMF) due to intolerability.
Methods. We retrospectively reviewed 36 LN patients who received tacrolimus for 39.2 months (ISN/RPS classification IV : n=31, V : n=4, IV + V : n=1). Tacrolimus was used as a maintenance therapy as an alternative to azathiprine (n = 15) or MMF (n = 21) after induction therapy with high-dose glucocorticois and cyclophophamide or MMF in all patients.
Results. After induction therapy, proteinuria (3.4±3.34 gm/24 hr to 1.56±1.78 gm/24), GFR (81.83±28.1 ml/min/1.73m2 to 119.34±32.64), serum C3 (51.64±20.21 mg/dL to 73.34±19.0), C4 (8.54±6.04 mg/dL to 13.8±6.98) and anti-dsDNA antibody (92.45±74.54 IU/mL to 72.78±68.67) were improved. These improvements were maintained by tacrolimus therapy after 39 months with changing from MMF or azathioprine; proteinuria (0.22±0.19), GFR (110.06±36.84), serum C3 (77.27±15.85), C4 (14.88±6.33) and anti-dsDNA antibody (48.87±55.01). One patient developed end-stage renal failure, with 1-, 2- and 3-year renal survival rates of 100 %, 96% and 96%, respectively. Two patients (7.4%) had infections that required hospitalization (urinary track infection, herpes zoster).
Conclusion. The results suggest tacrolimus was shown to have favorable outcome with minimal complications in treating LN, and warrants further investigation to define its role as a long-term maintenance agent.

P4.16

Targeted plasmacytoid dendritic cell (pDC) depletion with an anti-CD123 mAb - a potential novel treatment for Systemic Lupus Erythematosus (SLE)

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Aims. pDCs produce IFNα, a key pathogenic cytokine in SLE. A novel anti-CD123 mAb, CSL362, effects ADCC against CD123-expressing cells and neutralizes IL-3 signaling. This study of SLE and healthy donors evaluates CD123 expression on pDCs and other cells and CSL362's *ex vivo* effect on pDCs, IFNα production and IFNα-inducible gene expression from PBMCs.
Methods. CD123 expression was assessed by quantitative flow cytometry using Quantibrite-PE beads (n=50). Viable pDC percentage after 24hr culture with CSL362, CSL362's Fab portion (which only neutralizes IL-3 signaling), or isotype control (IC) was determined by flow cytometry (n=44). IFNα production after stimulation with TLR9 agonist (CpG), following pre-treatment with CSL362, Fab or IC (n=20), was measured by ELISA. A targeted 'IFN gene score', com-

prising eleven IFNα-inducible genes, was validated by qPCR on whole blood RNA, by comparing the average of the log2 fold-change for the genes between SLE and healthy donors (n=50). This score was also evaluated in PBMCs stimulated with CpG, following CSL362 or IC pre-treatment (n=12).
Results: In peripheral blood, pDCs most highly expressed CD123. CSL362 potently depleted pDCs (15.8±3.1% [mean±SEM], p<0.0001) and inhibited CpG-induced IFNα production (0.8±0.6%, p<0.0001) compared to IC; effects not observed with Fab. The IFN gene score was elevated in SLE (3.0±0.4) compared to healthy (0.4±0.3, p<0.0001) donors. CpG-induced upregulation of the score (4.7±0.7) was reduced by CSL362 pretreatment (1.3±0.6, p=0.001). Conclusions: CSL362 potently decreased pDCs and CpG-induced IFNα production and IFNα-inducible gene expression ex vivo. Cytoreductive therapy with CSL362 may therefore represent a novel treatment strategy in SLE.

P4.17

Multi-state modelling predictions of organ damage in SLE patients treated with belimumab plus standard of care

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Aims. To estimate probability of organ damage accrual in SLE patients treated with belimumab plus SoC over 5 years
Methods. We examined pooled interim data (GSK201223) from two open-label studies that enrolled patients completing the BLISS studies. Patients received belimumab every 4 weeks plus SoC. SLICC Damage Index (SDI) values were assessed every 48 weeks. A Multi-State Model (MSM) was used to model the probability of damage accrual or death in five years. Univariate analysis explored the impact of covariates (including age, race and baseline medications).
Results. 998 patients comprised the modified intent-to-treat population. Baseline SDI scores were: 0 (58.6%), 1 (23.5%), ≥2 (17.6%). 954 patients were eligible for the MSM analysis. The estimated probability of transitioning between SDI states was:

	Probability of Change in SDI Score or Death in 5 years				
Current SDI State	n=954	0	1	≥2	Death
0		0.873	0.103	0.011	0.013
1			0.805	0.184	0.011
≥2				0.987	0.013

The only covariates shown to significantly increase the probability of damage accrual were a medical history of hypertension and baseline age.
Conclusion. In this cohort, SLE patients treated with belimumab plus SoC had a low predicted probability of organ damage accrual or death over 5 years. Patients with pre-existing damage also had a low predicted probability. Hypertension and age were identified as risk factors for organ damage.
Studies funded by GlaxoSmithKline and HGS

P4.18

Treatment with anti-HMGB1 monoclonal antibody does not alleviate lupus nephritis in MRL/lpr mice

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Introduction. High Mobility Group Box 1 (HMGB1) is a nuclear DNA binding protein that acts as an alarmin when secreted. In systemic lupus erythematosus (SLE) serum levels of HMGB1 and anti-HMGB1 are increased. Therefore HMGB1 might represent a potential therapeutic target in SLE. We investigated whether treatment with a monoclonal anti-HMGB1 antibody beneficially affects lupus nephritis development in MRL/lpr mice.
Materials and Methods. Seven week old MRL/lpr mice were injected intraperitoneally twice weekly for 10 weeks with 50 ug monoclonal anti-HMGB1 (2G7, mouse IgG2b) (n=12) or control antibody (n=12). Every two weeks blood was drawn. Urine was collected at 7, 11 and 17 weeks. Mice were sacrificed at 17 weeks and spleens and kidneys were harvested. Kidney pathology was evaluated using the lupus nephritis classification system.
Results. Body and spleen weight, total white blood cell count and differential white blood cell counts were similar between the two groups. Lupus nephritis of mice treated with anti-HMGB1 mAb was classified as class III (n=3) and class IV (n=9), while mice treated with control mAb were classified as class II (n=4), class III (n=1) and class IV (n=5). IgG and C3 deposits in kidneys were similar in mice treated with anti-HMGB1 mAb or control mAb. There were no differences in albuminuria, urine HMGB1 and serum levels of complement C3, anti-dsDNA, IFNα, IL-6, IL-17A, or TNF between the two groups.
Conclusion. In MRL/lpr mice, treatment with a monoclonal anti-HMGB-1 antibody does not affect development of lupus nephritis, disease progression or pro-inflammatory cytokines levels.

P4.19

Long-term preserved renal function in class III or IV lupus nephritis without aggressive immunosuppression

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According to the current guidelines, intravenous cyclophosphamide or mycophenolate mofetil, in combination with corticosteroids, are the standard of care for treating class III/IV lupus nephritis (LN), despite their severe side-effects such as sepsis, avascular bone necrosis, gonadal dysfunction and malignancy. In the guidelines, treatment indications are regardless of clinical parameters such as eGFR, proteinuria, and hematuria at the time of biopsy. Randomized clinical trials on which LN treatment guidelines are based have often excluded patients with mild clinical renal disturbances, *e.g.* eGFR >80 mL/min and/or proteinuria <1-2 g/24h. Moreover, these trials have never subanalysed histologically milder cases of the spectrum of proliferative LN. It is possible that milder therapy regimens would suffice in a hitherto undefined proportion of patients with mild class III/IV LN, although evidence for this hypothesis is lacking. We identified three patients from a historical cohort of patients with class III/IV LN at our hospital who were undertreated for class III/IV LN according to current guidelines, having received only prednisolone and/or hydroxychloroquine in combination with ACE inhibitors for LN. The follow-up ranges from 10 to 24 years without exacerbations of LN, a relatively preserved creatinine clearance of 50-85 mL/min, proteinuria of 1-3 g/24h, and absent erythrocyturia at the time of last follow-up. These observations provide evidence for the existence of a subgroup of patients with class III/IV LN for whom conservative therapy might be justified.

P4.20

A single-site, investigator-initiated, open-label trial of the adrenocorticotropic hormone analog H.P. Acthar® Gel (repository corticotropin injection) among subjects with active systemic lupus erythematosus

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Background. Patients with SLE not adequately controlled with conventional treatments need alternative options. This study evaluated the efficacy of H.P. Acthar® Gel (Acthar Gel) for reducing active lupus disease severity among such patients. A previously published Acthar Gel trial among patients with active SLE found mean SLEDAI-2K scores reduced at Day 28. This post-hoc analysis evaluates SLE Responder Index (SRI) and joint improvements.
Methods. Ten females (mean age=49 yrs, disease duration=7 yrs, SLEDAI-2K=10) self-administered Acthar Gel 1 mL (80 U/mL) for 7-15 days and were assessed weekly for 28 days. Outcome measures included SLEDAI-2K and SRI. Student's t-test compared data obtained at each assessment.
Results. Statistically significant improvements in the primary outcome SLEDAI-2K occurred at all follow-up visits (p<0.05), and 7 patients were SRI responders (Table I). Eight patients had benefits in painful, tender, and swollen joints (Table II). Acthar Gel was well-tolerated, but bilateral edema was present in one patient. No treatment-related serious adverse events occurred.
Conclusions. The primary endpoint of SLEDAI-2K was met, and SRI and joint counts improved.
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Table I. SLEDAI-2K and SRI Responder Scores.

Subject	SLEDAI-2K			SRI Responder
	Day 0	Day 14	Day 28	
1	8	6	6	NO
2	8	2	2	YES
3	8	6	6	NO
4	16	14	12	YES
5	16	12	0	YES
6	8	8	0	YES
7	8	4	6	YES
9	8	2	2	YES
10	8	2	0	YES
12	8	0	6	NO

Table II. Joint Count.

Subject	Painful				Tender				Swollen			
	Day 0	Day 14	Day 28	Change (28 Days)	Day 0	Day 14	Day 28	Change (28 Days)	Day 0	Day 14	Day 28	Change (28 Days)
1	14	9	12	-2	23	14	21	-2	11	5	9	-2
2	7	1	0	-7	20	3	0	-20	9	2	4	-5
3	13	3	1	-12	25	8	8	-17	11	3	4	-7
4	10	14	10	0	18	24	23	5	8	9	13	5
5	6	0	0	-6	20	0	1	-19	8	0	1	-7
6	11	3	0	-11	23	16	2	-21	12	9	1	-11
7	5	0	3	-2	14	1	12	-2	12	1	3	-9
9	10	0	0	-10	22	2	5	-17	14	0	1	-13
10	17	0	0	-17	25	0	0	-25	9	0	0	-9
12	9	0	11	2	23	0	14	-9	12	0	18	6

P4.21

Hydroxychloroquine use in lupus patients during pregnancy is associated with prolonged pregnancy duration in preterm births by over one week

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Objective. to investigate the association between hydroxychloroquine (HCQ) use and pregnancy outcomes and disease activity in a Dutch systemic lupus erythematosus (SLE) population.
Methods. data of all pregnancies occurring in a single center were prospectively gathered between 2000 and 2014. Lupus activity during pregnancy was assessed using the SLE Disease Activity Index (SLEDAI) and pregnancy outcomes were compared between HCQ-users and non-users. Preterm life birth (PTL) was defined <37 weeks of gestation. The association between HCQ-use and occurrence of flares as well as pregnancy outcomes was analyzed using Chi-square test. Difference in duration of pregnancy between HCQ groups was analysed using student's t-test.
Results. sixty-four SLE patients with 113 pregnancies were included (33 in the HCQ-group versus 80 in the non-HCQ-group). The majority of patients were Caucasian. Flares during pregnancy and postpartum did not significantly differ between HCQ-users and non-users. There were no significant differences between the groups in the percentage of term births, abortion rates or miscarriage. There were no congenital anomalies in either group. Within the PTL the use of HCQ was associated with a significantly longer pregnancy duration (36.2 versus 35.0 weeks, p=0.019) and significantly less prednisone use throughout pregnancy (p=0.021).
Conclusion. in our cohort of predominantly Caucasian SLE patients HCQ use was not associated with lower disease activity or reduced frequency of PTL. However, our data strongly suggest that HCQ may prolong the intra-uterine period for preterm births and reduces prednisone therapy, underscoring the beneficial effect of HCQ in lupus pregnancies.

P4.22

Systemic Lupus Erythematous and Progressive Multifocal Leukoencephalopathy: focus on lymphopenia

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Progressive multifocal leukoencephalopathy (PML) caused by reactivation of the polyomavirus JC virus (JCV) occurs in autoimmune disease (AID), most frequently in Systemic Lupus Erythematosus (SLE).
We report an HIV-negative 34 year old female with SLE diagnosed on the basis of photosensitivity, Jaccoud arthropathy, alopecia, fatigue, antinuclear antibody (ANA) and anti-dsDNA. From 2004 she was treated with immunosuppressant therapy (IST) - steroids and azathioprine - during which time total lymphocytes ranged from 600 to 1400/µl. In 2011 she complained of decreased sensation and weakness of the right hand and 3 months later developed nausea, vertigo and gait instability. MRI revealed lesions in the posterior fossa. Bacterial, viral and paraneoplastic screen in blood and CSF were negative, except for CSF JC virus (700 copies/ml). IST was discontinued and after plasmapheresis, cidofovir, mirtazapine, mefloquine and cycles of cytarabine were sequentially added but there was progressive deterioration with a fatal outcome one year after onset. Severe lymphopenia was most likely responsible for JCV reactivation and during treatment $CD4^+$ T cells ranged from 262 to 381/µl. We were unable to understand the lack of hydroxychloroquine therapy.
In the light of recent reports of PML in SLE patients treated with rituximab or belimumab, we highlight that other IST may be implicated. Furthermore, lymphopenia in SLE is often regarded as a manifestation of AID itself. Current recommendations support maintaining lymphocytes over 1000/µl and principally advocate therapy adjustment without proposing supportive therapies. Lymphopenia remains frequently ignored in clinical practice. Instead, it should constitute a major concern in SLE.

P4.23

Lymphocyte depletion, recovery and efficacy in NZBWF1 lupus mice following continuous or intermittent dosing regimen of Venetoclax (ABT-199), a potent and selective BCL-2 Inhibitor

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Proteins in the BCL-2 family are key regulators of apoptosis, or programmed cell death. We report here that continuous daily treatment with 30mpk venetoclax (ABT-199), a selective BCL-2 inhibitor, produces a sustained lymphocyte depletion in peripheral blood that correlates with reduced disease severity in NZBWF1 lupus mice. The time course for lymphocyte depletion and recovery following multiple dosing regimen was investigated. While a single 30mpk dose of venetoclax leads to significant lymphocyte depletion within 24 hours followed by recovery to baseline by day 7, 7 days of continuous dosing is followed by lymphocyte recovery by day 28. To assess efficacy endpoints, venetoclax was administered once daily to NZBWF1 lupus mice by one of three dosing schedules: continuous dosing for 28 weeks (30 mg/kg); dosing on day 1 of a 7 day cycle for 28 cycles (100mg/kg); intermittent dosing on days 1-7 of a 28-day cycle for 7 cycles (30 or 100 mg/kg). Weekly proteinuria and survival endpoints reveal comparable efficacy between the intermittent dosing cycles at 100mpk dose and continuous dosing at 30 mg/kg. Numbers of B and T cells from the first two intermittent cycles showed trends toward partial or complete recovery by day 28 versus sustained depletions in animals with continuous dosing. Therefore we have identified an intermittent dosing schedule for venetoclax that conveys compelling efficacy in NZBWF1 lupus mice without persistent lymphocyte depletion. This dosing regimen may translate into a more favorable benefit-risk profile and hence has been incorporated into a phase 1 trial in SLE patients.

P4.24

Venetoclax (ABT-199), a Potent and Selective BCL-2 Inhibitor, is Efficacious in Mouse Models of Lupus Nephritis and Reduces Human Lymphocyte Lifespan *in vitro*

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Proteins in the BCL-2 family are key regulators of apoptosis, or programmed cell death. We have evaluated the effects of venetoclax (ABT-199), a highly potent and orally available BCL-2 selective inhibitor, in two mouse models of lupus nephritis and in human cells in vitro. In the mouse models (spontaneous and IFN alpha-induced NZBW F1), venetoclax treatment dose-dependently reduced the incidence of severe proteinuria and prolonged survival in both models compared to vehicle controls and attenuated glomerulonephritis, tubular dilatation, immune cell infiltrates and IgG deposition in the kidney. Venetoclax mediated a significant reduction in the numbers of splenic T cells but conferred a preferential reduction in select B cell subsets. Interestingly, venetoclax did not impair the number of $CD138^+$ long-lived plasma cells in the bone marrow, which was consistent with unaltered circulating anti-dsDNA titers in these animals. Venetoclax efficacy also correlated with a dose - dependent reduction of lymphocytes in peripheral blood of NZBWF1 mice. Consistent with these findings, human lymphocytes from both healthy donors and systemic lupus erythematosus (SLE) patients treated with venetoclax in vitro have reduced lifespan. Taken together, these data underscore the essential role of BCL-2 in the pathogenesis of lupus and support further exploration of selective BCL-2 inhibition in autoimmune diseases such as SLE/Lupus Nephritis.

P4.25

Plasma soluble Vascular Adhesion Molecule-1 (sVCAM-1) as an exploratory marker of response to therapy in patients with persistently active Systemic Lupus Erythematosus (SLE)

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Increased soluble vascular cell adhesion molecule-1 (sVCAM-1) has been described in vascular inflammatory diseases such as atherosclerosis, and prior reports suggest that sVCAM-1 may correlate with overall, CNS, and renal disease activity in systemic lupus erythematosus (SLE). We therefore evaluated sVCAM-1 as an exploratory endpoint for efficacy in an 8 week double-blind randomized placebo-controlled pilot study of H.P. Acthar gel (repository corticotropin injection) in patients with persistently active SLE. 38 subjects with persistently active SLE including arthritis &/or skin involvement despite 7.5-30 mg prednisone daily for ≥4 weeks before screening were randomized to receive SC Acthar 80U every other day (Acthar80) or 40U daily (Acthar40), or Placebo. Study medication dosing was maintained for 4 weeks, then tapered to 2x/wk administration of the assigned dose. Plasma levels of sVCAM-1 were measured at randomization, and at weeks 4 and 8 of the study. In order to determine whether sVCAM-1 might accurately predict response to therapy, we evaluated the relationship between sVCAM-1 and disease activity measures, including hybrid SLEDAI (hSLEDAI), total BILAG score, CLASI activity index, and tender swollen joint count, and circulating anti-ds-DNA antibodies. Significant correlations were identified between sVCAM-1 levels and anti-dsDNA antibodies ($r=0.54$, $p<0.0001$) as well as disease activity as assessed by hSLEDAI ($r=0.34$, $p=0.0005$) and total BILAG ($r=0.24$, $p=0.0147$) scores, but not by CLASI activity ($p=0.20$) or tender & swollen joint count ($p=0.43$). These data suggest that sVCAM-1 may be a useful non-invasive marker of response to therapy in patients with persistently active SLE.

P4.26

Ultrasoluble curcumin/turmeric significantly reduces lymphadenopathy and proteinuria in MRL-lpr/lpr mice, but only curcumin increases survival

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Commercial curcumin (CU), derived from food spice turmeric, has been widely studied as a potential therapeutic for a variety of oncological and inflammatory conditions. Lack of solubility/bioavailability has hindered CU's therapeutic efficacy in human diseases. We have solubilized CU with heat/pressure in water, obtaining upto 36-fold increase in solubility compared to CU solubilized at room temperature. We hypothesized that ultrasoluble curcumin/ultrasoluble turmeric will ameliorate lupus like disease in MRL-lpr/lpr mice. Eighteen MRL-MpJ and 18 MRL-MpJ MRL-lpr/lpr mice (6-week-old females) were used. Six mice of each strain received autoclaved water, ultrasoluble CU or ultrasoluble turmeric in the water bottle. Ultrasoluble curcumin/turmeric ameliorates lupus in MRL-lpr/lpr mice, by significantly reducing lymphoproliferation, proteinuria, lesions and autoantibodies. CU-treated mice enjoyed a 20% survival advantage over control mice. However, turmeric-treated animals lived an average of 16 days shorter than control mice due to complications unrelated to lupus-like illness. CU or turmeric-treatment inhibited lymphadenopathy significantly compared to control mice ($p=0.03$ and $p=0.02$ respectively) by induction of apoptosis. Average lymph node weights were 248±1147, 99±330 and 49±67 mg respectively for control, CU and turmeric-treated mice. TUNEL assay showed that lymphocytes in lymph nodes of turmeric and CU treated mice underwent apoptosis. Salivary gland histopathology studies show significantly reduced cellular infiltration in the turmeric-treated MRL-lpr/lpr mice, compared to control mice, while a trend towards reduced kidney damage was observed in CU and turmeric-treated mice. These studies show that ultrasoluble curcumin/turmeric could prove useful as a therapeutic intervention in SLE.

P4.27

Variations of BOLD: Can hydroxychloroquine be temporarily stopped during clinical trials in SLE?

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Background. We previously reported that hydroxychloroquine (HCQ) interferes with critical immunologic targets of biologics, including BLyS. Many lupus trials have begun limiting background treatments and the BOLD study safely withdrew all immunosuppressants (IS), however the impact of also holding HCQ remains unknown.
Methods. 74 SLE patients withdrawing IS were evaluated, 41 from the BOLD study, including 10 who stopped HCQ. All BOLD patients received temporary intramuscular steroids to lower initial disease activity. 33 others completed two medication washout visits preparing for an interventional trial (ABC). Like BOLD, background IS were stopped at Visit 1 (V1). Unlike BOLD, HCQ was stopped in all 26 patients taking it, and intramuscular steroid treatment was not mandated, elected by fewer of these patients and at much lower doses (see table).
Results. Clinical improvement by the second visit (V2) was negligible in ABC but significant in BOLD. Withdrawing HCQ had little impact on early disease activity in either study. In the BOLD study, HCQ withdrawal had no effect on time to flare or severity of flare once steroid effects waned (table).
Conclusions. When aggressive steroids are given at baseline with initial achievement of a low disease target (the BOLD design), HCQ withdrawal does not seem to exacerbate later disease flares. Early results from a study using less steroids suggest feasibility of safe and interpretable trials in non-organ threatening SLE.

	Baseline prn Steroid (ABC)		Baseline Treat to Low Disease Target (BOLD)		
Initial Response	Not on HCQ (n=7)	Stopped HCQ (n=26)	Not on HCQ (n=11)	Stopped HQ (n=10)	Continued HCQ (n=20)
% given im steroid	43	62	90	100	100
Mean depomedrol	133 mg	132 mg	298 mg	448 mg	352 mg
Mean V1/V2 SLEDAI[1]	6.0/6.7 (ns)	7.3/7.2 (ns)	7.5/3.4	8.4/4.0	8.6/4.7
			p=0.037	**p<0.001**	**p<0.001**
Mean V1/V2 BILAG[1]	10.7/11.8 (ns)	11.0/11.2 (ns)	14.2/3.4	15.3/8.4	15.3/2.5
			p<0.001	**p<0.001**	**p<0.001**
Mean V1/V2 PGA[1]	1.6/1.5 (ns)	1.6/1.6 (ns)	2.0/0.9	1.8/0.7	1.9/0.9
			p<0.001	**p<0.001**	**p<0001**
% SFI flare at V1/V2[2]	71/29 (ns)	46/38 (ns)	82/9	90/0	45/5
			p=0.002	**p<0.001**	**p=0.008**
Steroid Washout					
Mean V1/FV[3] SLEDAI[1]		7.4/6.5 (ns)	8.4/8.2 (ns)	8.6/8.0 (ns)	
Mean V1/FV BILAG[1]		14.1/15.4 (ns)	15.3/15.1 (ns)	15.2/14.5 (ns)	
Mean V1/FV PGA[1]		2.0/2.0 (ns)	1.8/1.6 (ns)	1.9/1.9 (ns)	
Highest V1/FV		27%	0	20%	
BILAG:		9%	20%	10%	
A/A		0	30%	5%	
B/A		64%	50%	65%	
A/B					
B/B					
Median Time to Flare		56 days (30.1-81.8)	56 days (12.6-79.4)	53 days (16.4-89.5)	

[1]T test or Rank Sum as needed; [2]Fishers Exact Test; [3]FV: Flare Visit; [4]Log Rank Test.

P4.28

Short term effect of Belimumab on endothelial progenitor cells in patients with Systemic Lupus Erythematosus

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Background. Impairment of endothelial progenitor cells (EPCs) is associated with atherosclerosis. EPCs are reduced and impaired in Systemic Lupus Erythematosus (SLE) patients, partially accounting for endothelial dysfunction. In mice, the inhibition of B Lymphocyte Stimulator (BLyS) seems to reduce the atherosclerotic plaque.
Objective. To assess the effect of Belimumab on EPC number in SLE patients.
Methods. Consecutive SLE patients due to start Belimumab and healthy controls were enrolled.
SLE disease activity was evaluated by SLEDAI 2K at baseline and after 4 and 12 weeks. EPCs were evaluated by flow cytometry and defined as percentage of CD34/KDR double-positive peripheral blood mononuclear cells.
Data were expressed as mean±standard deviation and T-test was performed. A p value <0.05 was considered significant.
Results. We enrolled 7 female patients (mean age 45.6±11.2 yrs, mean disease duration 17.8±10.8 yrs) with active disease (mean SLEDAI 8.4±2.6). Mean baseline EPCs number was significantly lower in patients *vs* controls (0.072+0.004 vs 0.025 + 0.02, p=0.01).). At week 4, the mean number of EPC increased significantly (p=0.025 vs baseline; p=n.s. vs controls); at week 12 no difference *vs* baseline nor week 4 was observed. No correlation between SLEDAI and EPCs was detected.
Conclusion. This pilot study is the first to suggest a short-term effect of BLM on EPC number in SLE patients. Mouse models established a role for B cells in atherosclerosis. Anti-BLyS could act by selectively depleting the pro-atherogenic B2 cells subpopulation or, indirectly, by modulating pro-inflammatory cytokines and Th17 cells, involved in the atherosclerotic process.

P4.29

Decreased disease activity and corticosteroid usage and improved quality of life during belimumab treatment in patients with systemic lupus erythematosus - a prospective real-life observational study

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Background. Belimumab is the first biologic approved to treat Systemic Lupus Erythematosus (SLE). We investigated the effects of belimumab in patients with active SLE despite standard-of-care therapy.
Methods. Fifty-one belimumab-treated patients from Karolinska, Skåne, and Linköping University Hospitals were enrolled and followed longitudinally. Disease activity was assessed using SLE Disease Activity Index 2000 (SLEDAI-2K) and Physician's Global Assessment (PGA). Patients reported pain, fatigue and well-being levels using Visual Analogue Scales, and functional status using the Health Assessment Questionnaire (HAQ).
Belimumab was mainly chosen for musculoskeletal (n=24), mucocutaneous (n=23), hematological (n=9), renal (n=5), respiratory (n=4), and neurological (n=3) manifestations.
Results. Significant decreases over time were observed for SLEDAI-2K (median baseline score: 7; range: 2–24; p<0.001), PGA (p<0.001) and prednisolone dosages (mean baseline dose: 11.36 mg/day; p<0.001), corresponding to a decrease of 4.9 mg/day over a year. C4 levels increased significantly (p=0.006). We observed significant improvements in well-being (p<0.001), pain (p<0.001) and fatigue (p=0.018), but no significant changes in HAQ.
Reasons for discontinuation included inadequate/uncertain effect (n=7), flare (n=5: increased proteinuria; arthritis, headache; rash, alopecia; lupus nephritis WHO class III; CNS-lupus), adverse events (n=3: acute myeloid leukemia; ground glass opacity in computed tomography scan of the lungs, pulmonary arterial hypertension; insomnia, arrhythmia), allergic reactions (n=2) and pregnancy plans (n=2).
Conclusions. In this real-life observational study, belimumab treatment decreased disease activity, reduced corticosteroid usage and improved the patients' quality of life in terms of pain, fatigue and well-being over time, but had no significant effects on their functional status.

P4.30

IFNα kinoid induces neutralizing anti-IFNα antibodies that decrease the expression of IFN-induced and B cell activation associated transcripts: analysis of extended follow-up data from the IFN-K phase I/II study

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Introduction. Interferon α Kinoid (IFN-K) is a therapeutic vaccine composed of IFNα2b coupled to a carrier protein. We previously reported that IFN-K induced a polyclonal anti-IFNα antibody (Ab) response, capable of neutralizing all IFNα subtypes, and down-regulating the IFN gene signature in whole blood RNA samples from patients included in a phase I/II placebo-controlled trial.
Objective. We analyzed extended follow-up data obtained from 6 patients included in the phase I/II trial, in terms of persistence of neutralizing anti-IFNα Abs, gene expression profiling, clinical safety and disease activity.
Results. Longitudinal measurements of serum anti-IFNα neutralizing activity, compared to changes in global gene expression profiles in whole blood RNA samples revealed a significant correlation (r=-0.47, p=0.004) between decreased IFN scores, and presence of neutralizing anti-IFNα Ab.
In addition, long-term follow-up data unmasked a correlation between neutralizing anti-IFNα Ab titers and decreased expression of genes involved in B cell activation.
Two out of the 6 patients kept long-term high titers serum neutralizing anti-IFNα Abs, now up to day 1,430. None of them developed a BILAG A flare, while 2 out of the 4 other patients did. None of the patients experienced serious adverse events due to viral infections during the extended follow-up period.
Conclusion. IFN-K induces polyclonal anti-IFNα neutralizing Abs that display disease-modifying properties. Long-term persistence of anti-IFNα neutralizing antibodies in two patients who received IFN-K at 120 µg or 240 µg is safe and is associated with low disease activity.

P4.31

Effect of mofetil mycophenolate induction therapy in renal survival in patients with proliferative lupus nephritis

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Introduction. Proliferative Lupus Nephritis (PLN) is a common complication of lupus. Its incidence varies from 27.9% to 49.0%. Classical induction therapy is cyclophosphamide (CYC) and mofetil mycophenolate (MMF), although severe LN, using the CYC is preferred. In addition to race and histopathological class, the serum creatinine, percentage of crescents and chronicity index are predictors of poor prognosis.
Objectives. Primary end point is to determine renal survival (time since renal biopsy to dialysis dependent ESRD) in both groups. The secondary outcome is to determine renal survival in severe LN and remission rate in both groups.
Methods. The study type cohort of 100 patients with PLN where 6-month induction therapy with MMF (2-3 g/day) vs IV CYC (0.5 to 1 g/m2) in monthly pulses are compared. Follow-up time was 60 months. There was no significant difference between the initial clinical variables in both groups. The cumulative survival rates at 1, 3 and 5 years were 98.9%, 98.9% and 67.2%.
There was no significant difference in global renal survival in both groups (p=0.199). In severe LN (serum creatinine >5.5 mg/dl or dialysis support at the beginning) there was no significant difference in renal survival (p=0.548). There was no significant difference in partial remission (OR=0.30 (0.02-5.21)), complete remission (OR=0.51 (0.03-10.11)) or both (OR=2.41 (0.39-14.77) p=0.341).
Conclusion. Mofetil Mycophenolate is as effective as IVCYC in inducing remission in PLN. Renal Survival in MMF group shows that can be used as induction PLN severe as well as IVCYC.

P4.32

CCL20 as a biomarker of disease activity and cardiovascular risk in SLE

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Background. Systemic inflammation in Systemic Lupus Erythematosus(SLE) is associated with an increased risk of cardiovascular disease. Improved disease control is associated with improvement in measures of endothelial dysfunction such as brachial artery flow mediated dilatation(FMD) as well as a reduction in circulating endothelial microparticles(EMPs). We aimed to investigate the effect of improved disease activity on a panel of inflammatory and cardiovascular biomarkers in SLE and establish their relationship with measures of endothelial dysfunction.
Methods. 20 patients with active SLE were assessed at baseline and at 4 months following alteration of treatment. Disease activity, FMD and EMPs were assessed at both timepoints. Serum was stored from both visits and sent for proteomic analysis using Proseek multiplex array.
Results. Disease activity improved significantly over time as did both measures of endothelial dysfunction. The improvement in disease control was associated with altered expression of the proteins identified in Table 1. When the relationship between the identified proteins and markers of endothelial dysfunction was assessed FMD demonstrated correlation with IL-10 (r=-0.32), EGF (r=-0.33) and CCL20 (r=0.37). CCL20 also demonstrated an inverse correlation with absolute EMP levels (r=-0.36, p=0.29).
Conclusion. CCL20 warrants further investigation as a potential marker of disease activity and cardiovascular risk in SLE.

Table I. Proteins altered following improvement in disease activity.

Upreg ulated Protein Expression	Down-regulated Protein Expression
Leptin (LEP)	Brain Derived Neurotrophic Factor (BDNF)
Matrix metalloproteinase 3 (MMP3)	Sulfotransferase 1A1 (ST1A1)
CCL20	IL-10
	Epidermal Growth Factor (EGF)
	CUB domain containing protein 1 (CDCP1)
	Tumour Necrosis Factor Receptor Superfamily 9 (TNFRSF9)

P4.33

Belimumab treatment in the real life: report on a small series of patients with systemic lupus erythematous

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Objective. to report our experience with Belimumab in patients affected by systemic lupus erythematosus (SLE).
Methods. we retrospectively reviewed the clinical records of those patients with SLE treated with Belimumab followed in our Lupus Clinic.
Results. a total of 11 patients (10 F) were treated. Mean age (SD) was 41.4 (12.5) years, mean disease duration 9 (5.8) years, mean tratment duration 20.9 (15.1) months. All patients had active disease before treatment, all were anti-dsDNA positive and had reduced levels of complement. Disease activity score (ECLAM) improved from a mean (SD) of 4.5 (2.1) to 2.4 (2.2) after six months. Steroid treatment was tapered from a mean (SD) of 8.9 (4.3) to 4.6 (3.7) mg prednisone equivalent after six months of Belimumab therapy. Three patients experienced adverse events, in a case leading to treatment interruption, because mitral valve substitution was planned. Eight patients are still under treatment, 3 suspended for various reasons (see Table I).
Discussion. in this small series of lupus patients taken from the real life, treatment with Belimumab appeared to be efficacious in reducing disease activity and steroid dosage, and relatively safe.

Table I. Clinical characteristics and response to Belimumab treatment in 11 patients with active SLE

ID	Clinical involvement	Belimumab dose	Change in disease activity score (ECLAM)	Adverse events	Reason for interruption
VR	Articular, hematological	670 mg	2	no	-
CS	Mucocutaneous, articular, renal, hematological	400 mg	3.5	no	-
BB	Articular, hematological	800 mg	2	Maculopapular rash	-
CL	Mucocutaneous, articular, hematological	600 mg	1.5	no	-
RP	Mucocutaneous, articular, hematological	780 mg	2.5	Atrial flutter	Planning heart valve substitution
ZG	Mucocutaneous, articular, hematological	600 mg	3	no	No
PK	Mucocutaneous, articular, hematological	620 mg	3.5	no	Planning pregnancy
MP	Mucocutaneous, articular	580 mg	1.5	No	Clinical remission
TN	Mucocutaneous, articular, renal, hematological	720 mg	3	Herpes Zoster	-
DGE	Articular, hematological	600 mg	2	no	-
BB	Articular, Hematological	560 mg	1.5	no	-

P4.34

Belimumab in systemic lupus erythematosus after inadequate response to a cocktail of active therapies

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Systemic lupus erythematosus (SLE) is characterized by variable clinical course. Nowadays, there are new drugs with a novel mechanism of action which may be indicated for the treatment of patients with SLE. The aim is to describe the case of a patient with SLE in which the initiation of belimumab was programmed.
The case of a 54 year old female patient with SLE and renal involvement is described. At the age of 54 the patient developed arthralgias, chest pain, morning stiffness, Raynaud's phenomenon, dry mouth and eyes and photosensitivity. On a CT scan pleuritic fluid and lymphadenopathy of the chest and neck were observed and proteinuria was found. A renal biopsy showed membranoproliferative glomerulonephritis with focal and segmental glomerulosclerosis. Pulse methylprednisolone was administered followed by prednisolone orally. A year later she presented with proteinuria and mycophenolate mofetil was administered. The patient entered a phase of remission of the disease. Subsequently she presented with diffuse arthralgias and myalgias. Hydroxychloroquine, azathioprine and prednisolone were administered. Complement levels decreased. As the patient has SLE, an inadequate response to a regimen of active drugs and is now in a relatively stable condition, the initiation of belimumab was programmed.
Belimumab is a synthetic monoclonal antibody which inhibits B-cell activating factor (BAFF) indicated for the prevention and treatment of flares in SLE. As, until very recently there was a paucity of medications for the treatment of SLE, belimumab is a long awaited addition in the armamentarium of rheumatologists for the treatment of systemic lupus erythematosus.

P4.35

Treatment with a selective histone deacetylase 6 inhibitor decreases lupus nephritis in NZB/W mice

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To date, there are 17 histone deacetylase (HDAC) enzymes, divided into 4 classes, which alter protein function by removing acetyl groups from lysine residues. Prior studies report that non-selective HDAC inhibitors decrease disease in various lupus mouse models. Selective HDAC-6 inhibition acts on cytosolic proteins to decrease B cell proliferation and differentiation by inhibiting α-tubulin function. Since B cells play a critical role in the initiation and propagation of systemic lupus erythematosus, we hypothesized that a selective HDAC-6 inhibitor (HDAC6i) will alleviate disease in a mouse model. Intraperitoneal injections of HDAC6i (0.3 mg/kg, 1 mg/kg, or 3 mg/kg), vehicle control, or dexamethasone were administered to 21-week-old, female NZB/W mice, 5 days a week, for 13 weeks. Disease was evaluated by body weight, proteinuria, serum levels of anti-dsDNA antibody, cytokines and immunoglobulins, and post mortem evaluation of nephritis and B cell populations in the bone marrow and spleen. Treatment with HDAC6i decreased glomerular scores, spleen weights, and urine protein scores when compared to vehicle-treated mice. No differences in B cell development and differentiation in the bone marrow, and B cell activation in the spleen were noted. We conclude that HDAC-6 inhibitors are effective at decreasing lupus nephritis and disease in NZB/W mice, however further studies are warranted to investigate the underlying mechanism, particularly in regards to B cell pathophysiology.

P4.36

Human embryonic stem cell-derived hemangio-mesenchymal cells (HMCs) prevent lupus nephritis progression and extend lifespan in lupus-prone NZB x NZW F1 mice

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Cell-based therapies, such as adult tissue-derived mesenchymal stromal cells (MSCs) are showing promise in small clinical trials for systemic lupus erythematosus (SLE). However, the inability to manufacture large scale quantities from a single donor without compromising functionality limits their utility while the use of multiple donors leads to variability in MSC quality. Hemangio-mesenchymal cells (HMCs), which have immunomodulatory properties similar to MSCs but are derived from a virtually inextinguishable human embryonic stem cell (hESC) source, can circumvent issues regarding scalability and consistent quality. Here, we show that HMCs have therapeutic utility in SLE; they extend the survival of lupus-prone NZB x NZW F1 (also referred to as BWF1) mice by preventing progression of their otherwise fatal lupus nephritis (LN). HMC treatment led to statistically significant reductions in proteinuria and serum creatinine. They preserved renal architecture and prevented interstitial inflammation and protein cast formation. HMC treatment led to significant reductions in the circulating levels of tumor necrosis alpha (TNF-α) and interleukin 6 (IL-6), two inflammatory cytokines implicated in SLE progression. Mechanistically, *in vitro* data support these findings as co-culture of HMCs with lipopolysaccharaide (LPS)-stimulated BWF1 lymphocytes decreased the secretion of TNF-α and IL-6 into the culture supernatant. Moreover, co-culture of HMCs enhanced the percentage of regulatory T cells in the BWF1 lymphocyte pool. Collectively, these results suggest that HMC immunomodulatory capabilities are therapeutically useful and represent an important step in the development of a commercially scalable and efficacious cell-based treatment for SLE/LN.

P4.37

Clinically Meaningful Change Estimates for Generic Patient Reported Tools Used in SLE against various disease activity endpoints

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Objectives. Disease specific minimally important differences (MID) estimates for Patient reported outcome (PRO) tools used in intervention trials help power studies, interpret, understand and apply results for physicians, patients, payers and policy-makers. PROs are increasingly used for drug approval. In SLE, we lack MID estimates for PRO tools. Herein, we analyzed data for MCID estimates for generic PROs (SF-36 and FACIT-Fatigue) in SLE.
Methods. Longitudinal data from Belimumab clinical trials (867 SLE patients) were analyzed against disease activity-DA (SELENA-SLEDAI-SS, BILAG) anchors. Established DA MCID and composite end-points (SFI, SRI) from SLE trials were tested, using mixed-model analysis for first 4 visits, 28 days apart. For SFI and SRI, we used 6,069 observations from 7 visits, censoring SRI at first visit meeting the criteria.
Results. 867 SLE patients (95% women) with mean (SD) age 35.5 (11.1) yrs participated. Median (IQR) SS, BILAG were 10.0 (4.0) and 17 (11.0). Both PROs were responsive to DA improvements, but not consistently responsive to DA worsening. MCID estimates against DA are in Table I. (BILAG-organ not shown).
Conclusions. SF-36 and FACIT-Fatigue MID estimates against DA anchors are presented. Data do not conclusively support their ability to respond to DA worsening. Analyzing aggregated trials data, studies using both generic and disease specific PRO tools are indicated.

Table I. (Mean (p value)) for MID for PRO and DA in SLE.

Anchor PGA	Improving: Decrease of ≤-0.3; N =658	Stable: Δ PGA -0.3 to 0.3; N =1717	Worsening: Increase PGA ≥+0.3; N=220
PF	4.01 (<0.0001)	1.50 (<0.0001)	-1.75 (0.04)
RP	5.75 (<0.0001)	1.89 (<0.0001)	-1.22 (0.25)
BP	7.28 (<0.0001)	2.25 (<0.0001)	-3.12 (0.01)
GH	5.02 (<0.0001)	1.56 (<0.0001)	-2.25 (0.0039)
VT	5.99 (<0.0001)	1.51 (<0.0001)	-1.91 (0.03)
SF	5.19 (<0.0001)	1.58 (<0.0001)	-3.83 (0.0008)
RE	4.74 (<0.0001)	1.43 (<0.0001)	-1.78 (0.11)
MH	3.93 (<0.0001)	1.34 (<0.0001)	-1.21 (0.15)
MCS	2.33 (<0.0001)	0.69 (<0.0001)	-0.97 (0.03)
PCS	2.29 (<0.0001)	0.71 (<0.0001)	-0.80 (0.02)
FACIT-FT	2.84 (<0.0001)	0.69 (<0.0001)	-1.29 (0.0022)
Anchor SS	Improving: decrease SS ≤-7.0; N=1022	Stable: Δ SS -7.0 to 8.0; N=2521	Worsening: increase SS ≥+8.0; N=25
PF	3.82 (0.01)	1.73 (<0.0001)	-0.18 (0.94)
RP	5.29 (0.004)	2.46 (<0.001)	-3.3 (0.29)
BP	9.74 (<0.0001)	2.75 (<0.0001)	-2.42 (0.49)
GH	8.04 (<0.0001)	1.82 (<0.0001)	-0.17 (0.94)
VT	7.56 (<0.0001)	2.10 (<0.0001)	-3.82 (0.14)
SF	3.37 (0.08)	1.94 (<0.0001)	-4.72 (0.17)
RE	6.60 (0.0004)	1.73 (<0.0001)	3.58 (0.28)
MH	4.58 (0.001)	1.64 (<0.0001)	-1.87 (0.46)
MCS	2.71 (0.0005)	0.87 (<0.0001)	-0.32 (0.82)
PCS	2.62 (<0.0001)	0.89 (<0.0001)	-0.86 (0.39)
FACIT-FT	3.19 (<0.0001)	0.97 (<0.0001)	-1.03 (0.41)
Anchor BILAG	Improving: decrease BILAG<-7; N=1647	Stable: Δ BILAG-7 to +8; N=1644	Worsening: increase BILAG >+8; n=177
PF	3.10 (<0.0001)	1.46 (<0.0001)	-0.77 (0.44)
RP	4.37 (<0.0001)	1.92 (<0.0001)	-0.18 (0.88)
BP	7.60 (<0.0001)	1.56 (<0.0001)	-4.72 (0.0003)
GH	4.29 (<0.0001)	1.22 (<0.0001)	-0.46 (0.60)
VT	5.29 (<0.0001)	1.21 (0.004)	-1.37 (0.16)
SF	4.86 (<0.0001)	1.08 (0.004)	-2.87 (0.03)
RE	3.54 (<0.0001)	1.58 (<0.0001)	-1.95 (0.11)
MH	4.00 (<0.0001)	1.04 (0.0002)	-1.93 (0.04)
MCS	2.11 (<0.0001)	0.59 (<0.0001)	-1.16 (0.02)
PCS	1.93 (<0.0001)	0.63 (<0.0001)	-0.54 (0.16)
FACIT-FT	2.58 (<0.0001)	0.62 (<0.0001)	-1.97 (<0.0001)
Anchor SFI	Have Resolved; N=358	Same; N=1810	New Flare; N=535
PF	3.93 (<0.0001)	1.71 (<0.0001)	0.15 (0.83)
RP	4.87 (<0.0001)	2.46 (<0.0001)	0.54 (0.54)
BP	8.84 (<0.0001)	2.76 (<0.0001)	-1.64 (0.09)
GH	4.40 (<0.0001)	1.80 (<0.0001)	0.98 (0.13)
VT	6.2 (<0.0001)	1.98 (<0.0001)	-0.28 (0.70)
SF	4.71 (<0.0001)	2.02 (<0.0001)	-1.18 (0.21)
RE	3.79 (<0.0001)	1.94 (<0.0001)	0.36 (0.70)
MH	5.30 (<0.0001)	1.60 (<0.0001)	-1.15 (0.10)
MCS	2.47 (<0.0001)	0.24 (<0.0001)	-0.34 (0.36)
PCS	2.12 (<0.0001)	0.88 (<0.0001)	0.15 (0.58)
FACIT-FT	2.87 (<0.0001)	0.96 (<0.0001)	-0.40 (0.25)
Anchor SRI	SRI4	SRI6	SRI8
PF	6.43 (<0.0001)	8.35 (<0.0001)	4.23 (<0.0001)
RP	8.35 (<0.0001)	8.35 (<0.0001)	10.66 (<0.0001)
BP	11.68 (<0.0001)	11.68 (<0.0001)	12.67 (<0.0001)
GH	6.96 (<0.0001)	6.96 (<0.0001)	8.16 (<0.0001)
VT	7.85 (<0.0001)	7.85 (<0.0001)	9.98 (<0.0001)
SF	7.78 (<0.0001)	7.78 (<0.0001)	7.97 (<0.0001)
RE	6.49 (<0.0001)	6.49 (<0.0001)	9.22 (<0.0001)
MH	6.48 (<0.0001)	6.48 (<0.0001)	7.71 (<0.0001)
MCS	3.43 (<0.0001)	3.44 (<0.0001)	4.20 (<0.0001)
PCS	3.41 (<0.0001)	3.41 (<0.0001)	4.39 (<0.0001)

P05 Epidemiology and clinical research

P5.01

Analysis of cardiovascular events (CVE) in a large nationwide cohort of patients with systemic lupus erythematosu: RELESSER Registry

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Objectives. To estimate the frequency of cardiovascular events (CVE) occurred after diagnosis in a large Spanish cohort of patients with systemic lupus erythematosus (SLE) and to investigate the main risk factors for atherosclerosis.
Patients. RELESSER is a nationwide multicenter registry of SLE. This is a cross-sectional study. Demographic and clinical variables, presence of traditional risk factors and CVE were collected. A CVE was either a myocardial infarction, angina, stroke and/or peripheral artery disease. Multiple logistic regression analysis was performed to investigate possible risk factors for atherosclerosis.
Results. From 2011 to 2012, 3,658 SLE patients were enrolled. Of this, 374(10.9%) patients suffered at least a CVE. In 269 (7.4%) patients the CVE occurred after SLE diagnosis (86,2% women, median [IQR] of age 54.9 [43.2-66.1], and SLE duration of 212.0 [120.8 - 289.0]). The main characteristics of these patients are shown in the Table I. Strokes (5.7%) were the most frequent CVE, followed by ischemic heart disease(3.8%), and peripheral artery disease (2.2%). Multivariate analysis identified age (HR [95% CI]=1.03 [1.02-1.04]), hypertension (1.71 [1.20-2.44]), smoking (1.48 [1.06-2.07]), diabetes (2.2 [1.32-3.74]), dyslipidemia (2.18 [1.54-3.09]), neurolupus (2.42 [1.56 - 3.75]), valvulopathy (2.44 [1.34-4.26]), serositis (1.54 [1.09-2.18]), antiphospholipid antibodies (1.57 [1.13 - 2.17]), low complement (1.81 [1.12-2.93]), and azathioprine (1.47 [1.04-2.07]) as risk factors of CV events.
Conclusion. We have confirmed that SLE patients suffer a high prevalence of premature CV disease. Both traditional and nontraditional risk factors contribute to this higher prevalence.

Table I. Main characteristics of the 269 patients of RELESSER Registry who suffered at least one CV.

Variables	Patients con CVE
Sex: Female, n (%)	232 (86.2)
Ethnicity: Caucasian, n (%)	256 (97.3)
Age at first CV event, mean (SD) years	48.6 (17.1)
Age at diagnosis, median (IQR) years	37.3 (25.3 - 49.3)
Delay in diagnosis, median (IQR), months	9.3 (2.0 - 36.5)
Hypertension, n (%)	151 (56.6)
Dyslipidemia, n (%)	159 (60.2)
Smoking: ever, n (%)	121 (47.5)
Diabetes mellitus, n (%)	42 (15.8)
SELENA-SLEDAI, median (IQR)	2.0 (0.0-4.0)
SLICC/ACR-DI, median (IQR)	3.0 (2.0-5.0)
Serositis, ever, n (%)	97 (36.2)
Renal disorder, ever, n (%)	119 (45.2)
Neurological disorder, ever, n (%)	53 (20.0)
Valvular disease (SLICC), n (%)	57 (21.5)
Anti-dsDNA, n (%)	208 (78.8)
Low complement, n (%)	216 (83.7)
Antiphospholipid antibody positive, whatever, n (%)	137 (53.7)
Antimalarial drugs, ever, n (%)	195 (75.6)
High dose of glucocorticoids (>30 mg/day), ever, n (%)	108 (44.4)
Azathioprine: ever, n (%)	124 (47.7)
Mycophenolate Mofetil/Mycophenolic acid: ever, n (%)	58 (22.2)
Cyclophosphamide: ever, n (%)	86 (33.2)
Rituximab, n (%)	26 (9.9)

P5.02

Immunosuppressant treatment patterns in lupus nephritis: a retrospective US claims database analysis

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Background. US-based treatment guidelines recommend six months of immunosuppressant therapy before continuing or switching regimen for class III/IV lupus nephritis (LN) patients; yet, published data are limited in real-world settings. We analyzed a US commercial/Medicaid claims database to describe its utilization pattern in LN patients.
Methods. LN patients initiating cyclophosphamide or mycophenalate mofetil (MMF) 2010-2013 were included. We evaluated utilization of cyclophosphamide, MMF, rituximab, azathioprine, and calcineurin inhibitors, and described discontinuation, switch, and add-on patterns during 1-6 months and 7-12 months post-initiation.
Results. Final sample included 1,567 LN patients initiating cyclophosphamide (16.1%) or MMF (83.9%). As per guidelines, 1,262 patients (80.5%) received treatment beyond six months, of whom 83.7% remained on the same initial medication throughout. In these patients, 78.9% continued on index medication during 7-12 months, while 10.1% discontinued shortly after, and 11.0% added on or switched therapy. Of the 305 patients who discontinued within 6 months, 92.8% were on the same initial medication while the rest added on or switched. Discontinuation rate was higher in cyclophosphamide than MMF initiators (30.2% versus 17.4%). Overall, 2.7% of patients started dialysis or received kidney transplantation within one year of treatment initiation; the rate was highest among those who discontinued within 6 months (6.6%).
Conclusion. One out of five LN patients discontinued therapy within 6 months and some required switching or additional therapy early on. Future research to understand factors such as lack of efficacy or tolerability/safety issues driving the unmet needs of immunosuppressant therapy is warranted.

P5.03

Influence of clinical and immunological activity in pregnancies of women with systemic lupus erythematosus

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Background. In our center we observed in preliminar studies that within pregnant SLE patients, Anti-Ro Ab carriers suffered less abortions than non-carriers.
Objectives. It comes to test whether this results are statistically significant and if there is an association with other variables such as previous abortion and disease activity, described in the literature.
Methods. Population of 105 SLE pregnant women, atended in our Hospital pregnancy and Lupus Unit. Anti-Ro/La Ab and antiphospholipidic Ab analysis in the 105 patients mentioned. Also analysis of the SLE activity through Lupus Activity Index in pregnancy (LAIP) and Systemic Lupus Erythematosus Disease Activity Index in pregnancy (SLPDAI) tools applied to 88 prospective pregnancies, and the influence of previous abortions.
Results. 32 pregnancies with a history of previous abortion, resulting in 78.13% abortions and 21.87% births.
56 pregnancies with no prior history of abortion, resulting in 5.35 % abortions and 94.64 % births ($p<0.0001$). 44 pregnancies Anti-Ro carriers, had 22.72% abortions and 77.27% births; and of 61 pregnancies non-carriers, causes 42.62% abortions and 53.38% births; OR:0.396, CI:0166-0944; $p<0.05$.
Other valued Ab presence, has not been significant, neither disease activity.
Conclusions. Previous abortions presence is the most negative influence on pregnancy outcome. Anti-Ro Ab presence is a protective factor of pregnancy. Disease activity does not affect pregnancy outcome, although the observed trend is to increase the abortion risk, enhancing SLPDAI value; we believe this result is determined by selecting pregnancy time in terms of disease activity.

P5.04

Analysis of cerebrospinal fluid anti-NR1 glutamate receptor antibodies in neuropsychiatric systemic lupus erythematosus

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Background/Purpose. We previously demonstrated that serum autoantibodies against N-methyl-D-aspartate receptor subunit1 (NR1) is elevated in neuropsychiatric systemic lupus erythematosus (NPSLE). However, the role of anti-NR1 in the pathogenesis of NPSLE still remains unclear. The present study therefore explored the levels and fine epitopes of anti-NR1 in cerebrospinal fluid (CSF) and serum in SLE.
Methods. Paired serum and CSF specimens were obtained from 113 patients with NPSLE, 20 patients with various rheumatic diseases other than SLE (non-SLERD). Sera were also obtained from 76 healthy individuals. Anti-NR1 were measured by ELISA, using the N-terminal 100-amino-acid peptide of murine NR1 (mNR1), as well as 4 different preparations of 25-amino-acid synthetic peptides within the N-terminal 100-amino-acid sequence of human NR1.
Results. Sera from NPSLE patients bound more efficiently to the amino-acid sequences of positions 19-44(NR1-A) or positions 57-81(NR1-C) than those of positions 37-62(NR1-B) or positions 75-100(NR1-D). Serum anti-mNR1, anti-NR1-A and anti-NR1-C were significantly elevated in NPSLE compared with non-SLERD, although there was no significant difference between diffuse and focal NPSLE. There was no significant difference in CSF anti-mNR1 between diffuse and focal NPSLE, although CSF anti-mNR1 was significantly elevated in NPSLE compared with non-SLERD. Of note, both CSF anti-NR1-A and anti-NR1-C were significantly elevated in diffuse NPSLE compared with focal NPSLE, while the difference was less remarkable for CSF anti-NR1-A.
Conclusion. The results indicate that CSF antibodies to NR1 were elevated in NPSLE. More importantly, the data demonstrate that CSF anti-NR1-C play a pivotal role in the pathogenesis of diffuse NPSLE.

P5.05

Damage and mortality in Systemic Lupus Erythematosus: Cluster analysis of patients from SLE Registry from the Spanish Society for Rheumatology (RELESSER)

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Background. Damage in SLE is associated with mortality. Not every damage manifestation is associated in the same way.
Objectives. To evaluate damage accrual patterns and mortality in a large sample of SLE patients.
Methods. After K-means cluster analysis, 3 different clusters with similar damage accrual were identified. Mortality was analysed with Kaplan-Meier log-rank test and Cox regression.
Results. 3,656 patients from 45 Spanish Rheumatology Units were studied. In Cluster1 patients had mild or no damage. In Cluster2 all had musculoskeletal damage but no cardiovascular and in Cluster3 all had cardiovascular damage. There were statistically significant (SS) differences (p<0.001) in: prevalence of damage in each SDI system, average SDI score, number of systems damaged and mortality rate. Cluster3 patients were older and had more males, being SS between the 3 clusters for both variables. Comparing survival curves:log-rank test showed SS differences(for triple and double comparisons). Survival rate at 10-20-30 years after SLE diagnosis, was lower in Cluster2 and Cluster3 compared to Cluster1 (p=0.068 when Cluster2 is compared to Cluster 1 at 10 years, p<0.01 for the rest). Between Cluster2 and Cluster3, there were no significant differences in survival at 10 years. It was significantly lower in Cluster3 at 20&30 years (p=0.025 for both). Cox regression showed a mortality hazard ratio of Cluster2 and Cluster3 that was 1.9 and 3.5 higher than Cluster1 respectively (SS).
Conclusions. SLE patients can be divided into homogeneous groups based on damage accrual, having different mortality rates.

Detailed data

	Total (n= 3656)	Cluster 1 n= 2949 (80.66%)	Cluster 2 n=415 (11.35%)	Cluster 3 n= 292 (7.99%)	*p*-value
Damage: Ocular	311 (8.5%)	171 (5.8%)	76 (18.3%)	64 (21.9%)	< 0.001
Damage: Neuropsychiatric	221 (6.0%)	123 (4.2%)	47 (11.3%)	51 (17.5%)	< 0.001
Damage: Renal	225 (6.1%)	132 (4.5%)	36 (8.7%)	57 (19.5%)	< 0.001
Damage: Pulmonary	132 (3.6%)	58 (2.0%)	33 (8.0%)	41 (14.0%)	< 0.001
Damage: Cardiovascular	292 (7.9%)	0	0	292 (100%)	< 0.001
Damage: Peripheral Vascular	163 (4.5%)	88 (3.0%)	37 (8.9%)	38 (13.0%)	< 0.001
Damage: Gastrointestinal	71 (1.9%)	44 (1.5%)	15 (3.6%)	12 (4.1%)	< 0.001
Damage: Musculoskeletal	504 (13.7%)	0	415 (100%)	89 (30.5%)	< 0.001
Damage: Skin	124 (3.4%)	56 (1.9%)	35 (8.4%)	33 (11.3%)	< 0.001
Damage: Diabetes	88 (2.4%)	56 (1.9%)	12 (2.9%)	20 (6.8%)	< 0.001
Damage: Malignancy	170 (4.6)	114 (3.9%)	38 (9.2%)	18 (6.2%)	< 0.001
Damage: Premature gonadal failure	92 (2.5)	48 (1.6%)	28 (6.7%)	16 (5.5%)	< 0.001
Deaths	207 (5.6%)	102 (3.7%)	45 (10.8%)	60 (20.5%)	< 0.001
Number of patients with damage	1391 (38.0%)	684 (23.2%)	415 (100%)	292 (100%)	< 0.001
Mean number of domains damaged	0.6 (±1.1)	0.30 (±0.62)	1.86 (±1.05)	2.50 (±1.38)	< 0.001
SLICC	1.1 (±1.6)	0.68 (±1.11)	2.60 (±1.78)	3.82 (±2.4)	< 0.001
Age at SLE diagnosis	35.1 (±14.6)	34.43(±14.07)	36.68(±15.75)	40.26(±15.6)	< 0.001
Gender:					
Male	9.7%	257 (8.7%)	40 (9.7%)	56 (19.2%)	< 0.001
Female	90.3%	2686 (91.3%)	374 (90.3%)	236 (80.8%)	
Race: Caucasian	93.2%	2644 (92.4%)	384 (95.8%)	279 (96.9%)	0.0746
Race: Afroamerican	0.2%	8 (0.3%)	0	0	
Race: Latinoamerican	5.2%	163 (5.7%)	14 (3.5%)	8 (2.8%)	
Race: Asian/Oriental	0.6%	20 (0.7%)	1 (0.2%)	0	
Race: Other	0.8%	26 (0.9%)	2 (0.5%)	1 (0.3%)	
SLE duration (months)		30.23 (±51.30)	35.27 (±62.80)	32.76 (±59.64)	< 0.001
Follow-up time (months)		109.93 (±81.29)	167.12 (±98.95)	154.9(±100.17)	0.6420

P5.06

Increased Low Density Lipoprotein Particle Numbers in High Versus Low SLE Activity, A Potential Mechanism for Enhanced Cardiovascular Risk

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Systemic lupus erythematosus (SLE) associates with cardiovascular (CV) disease. Lipoprotein subclasses have shown higher very low density lipoprotein and lower high density lipoprotein in SLE. Little is known about how these change with disease activity. The NMR LipoProfile test® also contains a glycoprotein signal termed GlycA, an inflammatory marker. We evaluated patients during high and low disease activity to determine how lipoproteins and GlycA change.
Methods. Patients were identified as part of the Hopkins Lupus Cohort and were included if they had at least one visit with SLEDAI of 4+ (high disease activity) and one visit with SLEDAI<3 (low disease activity). Lipoprotein particle and GlycA levels were compared between high activity and no/low disease activity visits. Further analysis compared consecutive visits to evaluate acute changes in lipoprotein parameters
Results. 33 patients met inclusion criteria. The total low-density lipoprotein particle number (LDL-P) and small LDL-P levels were higher with disease activity as was VLDL size. In those with no disease activity, followed by a flare there were changes demonstrated in triglycerides and LDL particles. GlycA was unchanged with disease activity.
Conclusion. We demonstrate adverse changes in lipoprotein profiles with lupus disease activity. This gives insight into one mechanism by which disease activity influences atherosclerosis. GlycA was unchanged, but higher than reported controls, which may make it useful in stratification of CV risk in SLE.

Marker	Mean (SD) during visits with SLEDAI 4+	Mean (SD) during visits with SLEDAI <=3	Mean (SD) Difference	*p*-value
Total very low density lipoprotein & Chylomicron	50.5 (28.0)	53.1 (21.2)	-2.6 (30.1)	0.63
Large very low density lipoprotein	3.3 (2.2)	3.0 (1.9)	0.3 (1.5)	0.30
Medium very low density lipoprotein	13.3 (8.7)	12.3 (8.6)	1.0 (7.3)	0.44
Small very low density lipoprotein	33.9 (23.0)	37.8 (18.9)	-3.8 (26.5)	0.41
Total very low density lipoprotein	1047.8 (317.7)	976.6 (309.8)	71.2 (145.9)	0.0085
Intermediate density lipoprotein	223.9 (81.4)	239.4(103.4)	-15.4 (89.1)	0.33
Large low density lipoprotein	369.2 (276.9)	365.7 (221.1)	3.4 (175.7)	0.91
Small low density lipoprotein	454.7 (266.4)	371.5 (229.5)	83.2 (156.5)	0.0045
Total high density lipoprotein	31.2 (9.2)	31.7 (7.2)	-0.5 (5.8)	0.60
Large high density lipoprotein	9.0 (4.3)	9.7 (4.5)	-0.7 (2.7)	0.15
Medium high density lipoprotein	10.1 (5.0)	11.2 (4.1)	-1.0 (5.1)	0.26
Small high density lipoprotein	12.1 (6.2)	10.9 (5.6)	1.2 (5.6)	0.23
Very low density lipoprotein size	48.3 (6.1)	46.2 (6.4)	2.1 (6.4)	0.075
Low density lipoprotein size	21.1 (0.8)	21.2 (0.6)	-0.1 (0.7)	0.42
High density lipoprotein size	9.8 (0.6)	9.8 (0.6)	-0.02 (0.3)	0.71
Triglycerides	109.5 (35.4)	108.3 (32.1)	1.2 (27.2)	0.79
High density lipoprotein	56.5 (20.4)	59.0 (18.4)	-2.5 (10.8)	0.20
GlycA	486.2 (81.6)	469.7 (82.4)	16.5 (82.4)	0.26

P5.07

Symptoms of attention deficit hyperactivity disorder in patients with systemic lupus erythematosus

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Objectives. This study aims to examine whether SLE patients have more features of adult attention deficit hyperactivity disorder (ADHD) and their relation to anxiety and depressive symptoms.
Methods. Symptoms and clinically significant items of the inattention and hyperactivity/impulsivity domains of ADHD were examined in Part A and Part B by the screening instrument of ADHD Self-Reported Scale (ASRS) respectively. Anxiety and depressive symptoms were measured by HADS-A and HADS-D respectively.
Results. There were no differences in symptom scores of inattention and hyperactivity/impulsivity between inactive SLE patients (n=117) and age- and sex-matched controls (n=64). However, SLE patients had more clinically significant items in the inattention domain compared with controls (p=0.006), particularly among those who had previous cerebral involvement (p=0.004). Patients who had psychiatric diseases had more clinically significant items of the hyperactivity/impulsivity domain (p=0.006). Possible ADHD was found in 7.7% of SLE and 6.3% of healthy subjects (p=1.00) by the screening tool. Patients with higher inattention symptom scores were more likely to be unemployed but not for duration of education and smoking habit. Anxiety and depressive symptoms correlated with ADHD symptoms.
HADS-A was independent predictive factor for clinically significant symptoms of inattention (p<0.001) and hyperactivity/impulsivity (p=0.04) by logistic regression.
Conclusions. Inactive SLE patients, particularly those who had previous cerebral lupus, had more clinically significant symptoms of inattention but not hyperactivity/impulsivity reflecting underlying cognitive impairment. Anxiety and depressive symptoms were common confounders for ADHD-like symptoms.

P5.08

Systemic lupus erythematosus patients with past neuropsychiatric involvement is associated with cognitive impairment: a longitudinal study

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Background. Studies on cognitive impairment in patients with past history of neuropsychiatric lupus (NPSLE) were often confounded by psychiatric and other disease related factors.
Objectives. This study aims to evaluate cognitive function in NPSLE patients in relation to psychiatric factors longitudinally in comparison to matched controls.
Methods. NPSLE patients and matched disease and healthy controls were examined by full neurocognitive tests that covered 8 cognitive domains at 2 timepoints 12 months apart. Depressive and anxiety symptoms were measured by HADS.
Results. 18 NPSLE and 18 patients with systemic lupus erythematosus (SLE) who had no previous cerebral involvement (non-NPSLE) matched to age, sex and disease duration, and 16 age- and sex- matched healthy subjects were recruited.
NPSLE patients consistently reported more cognitive symptoms and anxiety symptoms than non-NPSLE patients over both time-points. NPSLE patients had significantly worse simple and complex attention, memory, reasoning and visuospatial processing compared to non-NPSLE patients, among which memory and simple attention remained significantly impaired after adjustment to confounders. Anxiety and depressive symptoms were found to have an effect on raw scores but not demographically adjusted T score of neurocognitive tests. Unlike non-NPSLE subjects, NPSLE patients also failed to demonstrate practice effect upon re-evaluation over 12 months. Both NPSLE and non-NPSLE patients had worse memory than healthy subjects, with deficiency in more memory tests for NPSLE patients.
Conclusions. NPSLE patients had significantly worse and persistently impaired cognitive functions involving memory, visuospatial processing and complex attention and impaired learning compared to non-NPSLE patients over 12-month reassessment.
Disclosure

P5.09

Quality of life in SLE of various disease durations and in correlation to disease burden. A cross sectional study

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Background. Despite improved possibility to treat organ involvement in SLE, the quality of life (QoL) is still impaired.
Objective. The aim of this study was to evaluate QoL in patients with (SLE) in relation to disease duration, disease activity and organ damage.
Method. Patients with SLE (n=163), ≥4 ACR-criteria and median disease duration (DD) 9 years (range 0.1-42), from northern Sweden completed the Short Form (SF)-36 health survey. Disease activity was assessed using SLEDAI, and organ damage by SLICC/ACR-DI. The SF-36 health survey consists of eight domains; Physical Function (PF), Role Physical (RP), Role Emotional (RE), Social Function (SF), Bodily Pain (BP), Mental Health (MH), Vitality (VT), Global Health (GH) but is also summarized into two overriding dimensions: physical (PCS)- and mental (MCS) component summary.
Results. Lower PF, RP, GH, VT, SF, RE and PCS was associated with significantly higher SLICC/ACR-DI (p<0.02) and remained significant adjusted for SLEDAI and DD except for RE. Higher SLEDAI also adjusted for DD was significantly associated with lower RP, SF, RE and MCS (p<0.05). Patients with longer DD scored significantly lower PF, GH, SF, and PCS (p<0.05) compared with < 15 years DD, while patients <1 year DD scored significant lower in RE and MCS (p<0.05) compared with ≥1 year DD.
Conclusion. In patients with SLE, greater disease burden *i.e.* SLICC/ACR-DI as well as SLEDAI was associated with lower QoL. Mental components were lower in newly diagnosed patients, whilst physical components were impaired with longer DD.

P5.10

The Effect of Geography on the Efficacy of Sifalimumab, an Anti-Interferon-Alpha Monoclonal Antibody, in Moderate to Severe Systemic Lupus Erythematosus

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Geographical differences were assessed as potential confounders of efficacy of sifalimumab in a Phase IIb, randomized, double-blind, placebo-controlled study of adults with moderate to severe systemic lupus erythematosus (SLE). Patients received monthly intravenous sifalimumab (200, 600, or 1200 mg) or placebo. The study employed a pre-specified stratification factor based on geographic region: Region 1: high expected standard of care (SOC) response (Central America, South America, Eastern Europe, Asia); Region 2: low expected SOC response (North America, Western Europe, South Africa). Of the 431 patients randomized and dosed, 68.7% were from Region 1 and 31.3% from Region 2. More patients who received sifalimumab met the primary efficacy endpoint, the SLE responder

index, at Week 52: placebo, 45.4%; 200 mg, 58.3%; 600 mg, 56.5%; 1200 mg, 59.8%) with greater response rates observed in Region 1 than in Region 2 (Table). This distinction was not attributable to differences in baseline SLEDAI-2K, physician global assessment, or BILAG-2004 scores which were similar in both regions. Differences in several demographic and clinical characteristics were seen between patients in Region 1 vs Region 2 (Table). Response to treatment with sifalimumab showed a greater distinction in the primary endpoint in patients who received sifalimumab vs placebo in Region 2 compared with Region 1. This may, in part, be reflective of regional populations with different baseline characteristics or differences in SOC.

	Region 1	Region 2
SLE Responder Index, %		
Placebo	54.1	26.5
Sifalimumab 200 mg	60.0	54.5
Sifalimumab 600 mg	62.2	44.1
Sifalimumab 1200 mg	65.8	47.1
Mean demographic data, %		
Age, years	38.0	42.5
Weight, kg	64.7	72.8
Disease duration, months[a]	80.1	138.4
SLICC/ACR damage index	0.5	1.1
On-study treatment use, %		
Antimalarials	70.9	78.5
Azathioprine	30.4	15.6
Methotrexate	11.8	21.5
Mycophenolate	3.7	22.2
Corticosteroids	92.9	68.9
Average dosage, mg	11.7	9.3

aMedian values.

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P5.11

Geographic Differences in Demographics, Clinical Characteristics, and Standard of Care in Multinational Studies of Patients with Moderate to Severe SLE

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Most randomized controlled trials (RCTs) include stratification factors to assure a balanced allocation of subgroups that might respond differently to therapeutic interventions. Despite such stratification, geographic differences can be confounders in efficacy analyses. We compared demographic data, baseline clinical characteristics, and standard of care (SOC) across geographic regions of two worldwide Phase IIb RCTs with the fully human, IgG_1 κ monoclonal antibodies sifalimumab and anifrolumab in patients with moderate to severe systemic lupus erythematosus (SLE). This *post-hoc* analysis compared combined baseline data from the studies between pre-specified geographic regions with an expected high placebo plus SOC response (Region 1 [R1]: Central America, South America, Eastern Europe, Asia) and low placebo plus SOC response (Region 2 [R2]: North America, Western Europe, South Africa). Patients with active lupus nephritis or severe neuropsychiatric SLE were excluded. Of the 736 randomized and dosed patients, 68.9% were from R1, and 31.1% were from R2. There were no clinically meaningful differences between regions in mean SLEDAI 2K, BILAG-2004 composite, or physician global assessment scores. However, differences were seen in several demographic characteristics and on-study treatment use (Table). These differences may impact the analysis of the treatment response with SOC and/or investigational drug. Therefore, an imbalance in patients from regions with expected high or low SOC response should be considered in the design and statistical considerations in SLE RCTs.

	Region 1	Region 2
Mean demographic data		
Age, years	38.0	43.0
Body mass index, kg/m^2	25.2	28.1
Disease duration, months	81.8	131.2
SLICC/ACR damage index	0.5	1.1
Double-stranded DNA antibodies, %	85.0	67.3
Hypocomplementemia, %		
C3	44.8	33.6
C4	29.0	18.3
On-study treatment use, %		
Azathioprine	28.8	12.2
Mycophenolate	5.1	21.0
Corticosteroids	94.1	65.1
≥10 mg/day	66.9	36.7

Acknowledgements. Funded: MedImmune

P5.12

Hydroxychloroquine level variability and predictors in patients with connective tissue diseases

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Purpose. Hydroxychloroquine (HCQ) dose adjustment in patients with impaired renal function has been suggested to prevent toxicity. However, there is scant evidence to support this practice. We measured HCQ blood levels in patients with a diagnosis of connective tissue disease (CTD) and normal versus impaired renal function (GFR ≤60 ml/min) to assess the impact of renal impairment on HCQ clearance.
Methods. CTD patients on HCQ at a steady state dose of up to 6.5 mg/kg daily were eligible. Whole blood random HCQ levels were checked on patients with normal and impaired renal function. Patients on dialysis were excluded. Univariate analyses were performed on additional variables to evaluate other possible confounders on HCQ levels.
Results. There were no statistically significant differences in HCQ levels between the impaired renal function cohort (n=11, GFR range 21-59 ml/min; median GFR 45 ml/min, mean [HCQ] 1052.7 ng/ml ± 653.2) and patients with GFR >60 ml/min (n=25, range 62-120 ml/min; mean [HCQ] 1010.4 ng/ml ± 491.5; p=0.7310). There was no association between age, concomitant use of proton-pump inhibitors or prednisone, ethnicity, body mass index or duration of HCQ therapy and HCQ level.
Conclusion. There is wide inter-patient variability in HCQ blood levels. The influence of impaired renal function on HCQ metabolism and toxicity remains elusive. While there is growing interest in utilizing HCQ levels to guide therapy and prevent toxicity, additional studies in larger patient populations are required to establish clinical utility.

P5.13

PRECISESADS: Towards a Reclassification of the Systemic Autoimmune Diseases Through a -OMICS Approach

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PRECISESADS is a project funded by the Innovative Medicines Initiative of the European Union that has as aim to use several omics measurements to reclassify the systemic autoimmune diseases independently of the clinical diagnoses. The project will combine transcriptomics, epigenomics, metabolomics, genomics, cytokine production, autoantibodies and flow cytometry measurements. The data will be integrated with state-of-the-art bioinformatics approaches to define new clusters of patients that overlap across diseases. The diseases to be analyzed are SLE, RA, systemic sclerosis, Sjögren´s syndrome, antiphospholipid syndrome, mixed connective tissue disease and patients with disease manifestations without fulfilling criteria (undifferentiated). The two cohorts are: a cross-sectional of 2000 patients and 600 controls, and an inception cohort to be followed longitudinally (baseline, year 1 and year 2) of 200 patients. The major clusters of patients will be identified in the cross-sectional cohort, and the inception will be used to see how newly diagnosed patients with little or no treatment match to the clusters and how treatment modifies the clusters. The project started on February 1st, 2014 and will continue until the end of January of 2019. The challenges and recent successes will be described in the presentation. The members of the project will be also mentioned in the presentation. *The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n°115565, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.*

P5.14

Cardiovascular disorders in a multi- ethnic cohort of patients with Systemic Lupus Erythematosus from Berkshire, United Kingdom

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Background. South-Asian populations exhibits premature atherosclerosis, but there is limited data regarding cardiovascular disorders (CVD), in South-Asian lupus patients.
Objectives. The study aimed (1) to compare the prevalence of CVD and traditional risk factors for CVD between lupus patients of different ethnicities, (2) to estimate the use of corticosteroids and Hydroxychloroquine in lupus patients with and without CVD.
Methods. This is a retrospective study of 82 lupus patients undergoing regular clinical reviews from 2013 to 2015 at Wexham Park Hospital, a large district hospital in Southern England. The patients were categorised into four ethnic groups Caucasians, South-Asians, Blacks and Others. Demographic and clinical data were obtained from chart reviews.
Results. Prevalence of CVD in lupus patients in our cohort appeared to be higher in South-Asians than Caucasians, Blacks or Others, but the differences were not statistically significant (8.3% vs.6.8%, 0%, 0%). All Caucasians lupus patients with CVD were women older than 55 years and men older than 45 years. In contrast, 50% of South-Asians lupus patients with CVD were below the above age limits. Hypertension was not associated with CVD burden in any ethnic group. We observed a tendency toward higher corticosteroids use (60% vs. 44%, p=0.65) and lower Hydroxychloroquine use (40% vs. 77%, p=0.10) in CVD than non-CVD patients.
Conclusion. CVD burden is not statistically different in Caucasian and South-Asians lupus patients. In our cohort South-Asians lupus CVD patients were younger, but further studies might clarify if this reflects just a higher CVD burden in South-Asian populations.

P5.15

Peripheral nervous system involvement in SLE evaluated in a single centre over a fourteen-year study period

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Objectives. To assess the prevalence and clinical features of PNS involvement in a large cohort of Systemic Lupus Erythematosus (SLE) patients.
Methods. SLE patients consecutively observed at our tertiary referral centre over a period of 14 years (from 1999 to 2013) were selected. PNS manifestations were ascertained according to the 1999 American College of Rheumatology case definitions. An additional case definition was carried out by using our attribution algorithm for allocating NP events (derived from a recent Italian multicenter study). Demographic, clinical and laboratory data were assessed. Patients with PNS manifestations were compared with a control group of SLE patients without PNS involvement.
Results. In a cohort of 804 SLE patients the overall prevalence of PNS involvement was 7.2% (58 of 804 patients), with 65.5% of the events attributable to SLE (38 of 58). The peripheral polyneuropathy was the most common manifestation (27 patients, 3.3%), followed by cranial neuropathy (2.2%), single and multiple mononeuritis (1, 7%), myasthenia (0.4%) and plexopathy (1 case).
The average age of SLE onset was significantly higher in patients with PNS manifestation than in controls (mean ± SD; 45.3±16.3 vs 38.2±14.5; p=0.002). Patients with PNS involvement had an higher damage index (SDI) than controls (mean ± SD, 1.5±1.8 vs 1.0±1.1; p=0.011).
Conclusion. In our patients PNS involvement is an uncommon, but not a so rare complication of SLE. A careful neurological evaluation for this manifestation should be included especially in patients with later onset.

P5.16

Damage accrual in a group of systemic lupus erythematosus (SLE) patients deceased during a 10-year period

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Background. Permanent organ damage is associated with a higher mortality risk in patients with systemic lupus erythematosus (SLE).
Objective. Comparison of damage accrual in SLE patients deceased early and late during the disease course.
Patients/Methods. Assessment of damage accrual (by means of the SLICC/ACR damage index) in SLE patients deceased during the 2002-2011 period in a single center. SLE patients with at least four ACR classification criteria for SLE and at least one visit to our center within three years before death were included. The χ^2 test and Fisher exact test, as well as the t-test and Mann-Whitney U test were used to evaluate differences between categorical and continuous variables, respectively. The study was approved by the local ethics committee.
Results. We identified 90 deceased SLE patients (68 females and 22 males). 21 patients deceased within five years following diagnosis (early death group, EDG) and 69 thereafter (late death group, LDG). Damage accrual at the time of death was higher in the LDG compared to the EDG (5.59±3.15 versus 2.62±2.18, t=4.0315, p=0.0001), as well as the frequency of malignancy and musculoskeletal damage (24/69 versus 1/21, χ^2=7.962, p=0.005 and 48/69 versus 5/21, χ^2=13.923, p=0.0002, respectively). Conversely, damage accrual after one year following diagnosis was higher in the EDG compared to the LDG (2.12±1.62 versus 0.99±1.37, U=838.5, p=0.006).
Conclusion. Although damage accrual is more pronounced in patients deceased after a longer disease course, higher early damage seems to be a feature of SLE patients deceased within five years following diagnosis.

P5.17

Circulating levels of iC3b and C3 levels correlate with SLEDAI-2K Responder Index-50 (S2K RI-50) disease activity scores – the CASTLE (Complement Activation Signatures in Systemic Lupus Erythematosus (SLE)) study

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Background. A major unmet need in SLE is a biomarker that tracks with disease activity. Low serum C3 and C4 levels reflect complement activation, but can be elevated during the acute phase response. iC3b levels, proteolytically derived from C3b, increase with complement activation. The iC3b/C3 ratio reflects both complement consumption and production.
Objectives. To correlate disease activity by S2K RI-50 with iC3b/C3 ratios, anti-dsDNA Abs, ESR, CRP, C4, ethnicity, and prednisone dose.
Methods. 6 adult SLE patients were enrolled from the Washington University SLE Clinic. C3 and C4 were measured by nephelometry; iC3b using the Kypha COMPACT™ test. Linear models analysis was used to generate predictive models of S2K RI-50 scores.
Results. iC3b, C3, C4, iC3b/C3 ratio, dsDNA, and ESR each correlated with concurrent S2K RI-50 scores (Table I). Linear models analysis yielded a model where iC3b, C3, ESR, and prednisone dose highly predicted S2K RI-50 scores (Table I). Adding ethnicity further improved the model, while removing iC3b significantly reduced the model's predictive ability.
Conclusions. S2K RI-50 scores correlated with iC3b levels, and iC3b/C3 ratios further strengthened this relationship. Linear models analyses confirmed the predictive value of iC3b to S2K RI-50 scores. These data warrant further investigation of iC3b/C3 as a potential biomarker for disease activity in SLE.

Table I.

	R^2 value	*p* value
iC3b	0.1549	<0.001
C3	0.2011	<0.001
C4	0.1455	<0.001
dsDNA	0.153	<0.001
ESR	0.058	<0.038
CRP	0.017	<0.26
iC3b/C3	0.2447	<0.001
Model (iC3b, C3, ESR, prednisone dose)	0.4359	<0.001

P5.18

Cumulative incidence, associated factors and clinical impact of severe infections in a cohort of over 3,500 patients with Systemic Lupus Erythematosus

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Objectives. To estimate the cumulative incidence of severe infection (Sinf) and investigate associated factors and clinical impact in a large Systemic Lupus Erythematosus (SLE) cohort.
Methods. All patients in the Spanish Rheumatology Society Lupus Registry (RELESSER) were retrospectively investigated for Sinfs. Patients with and without infections were compared in terms of damage, comorbidities and clinical characteristics using bivariate analysis and Cox regression to compare survival rates until first infection.
Results. 3,658 SLE patients were included: 90% female, median age 32.9 years. The mean follow-up (months) was 120.2 (±87.6). A total of 705 (19.3%) patients suffered ≥1 Sinf. Total Sinfs recorded was 1,227. Incidence rate: 29.2 (95% CI: 27.6 - 30.9) infections per 1,000 patients-year. Survival until second infection was lower than that until first infection (p<0.000). Although respiratory infections were the most common localization (35.5%), bloodstream infections were the most frequent cause of mortality by infection (42.0%). In the Cox regression, the following were associated with infection: age at diagnosis (HR 1.016; 95% CI:1.009-1.023) Latin-American ethnicity (HR 2.151; 95% CI:1.539-3.005) corticosteroids (HR 1.271; 95% CI: 1.034-1.561) immunosuppressors (HR 1.348; 95% CI:1.079-1.684), hospitalization by SLE (HR 2.567; 95% CI:1.905-3.459), Katz severity index (HR 1.160; 95% CI:1.105-1.217), SLICC damage index (HR 1.069; 95% CI:1.031-1.108) and smoking (HR1.332; 95% CI:1.121-1.583). Duration of antimalarial use (months) was protective (HR 0.998; 95% CI: 0.997-0.999).
Conclusions. Severe infection constitutes a predictor of SLE severity, is more common in Latin-Americans and is associated with age, previous infection and smoking. Antimalarials exerted a time-dependent protective effect.

P5.19

Is Age of Lupus Onset a Predictor of Renal Disease Severity?

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Objective. The purpose of our study is to investigate the association between age of systemic lupus erythematosus (SLE) disease onset and outcomes of renal disease.
Methods. We collected data from SLE patients who are enrolled in our longitudinal SLE Database study within our institution. Data included but are not limited to demographics, SLE criteria, past medical history, historical and current medications, and organ damage. Patients were grouped into childhood-onset (cSLE) or adult-onset (aSLE).
Results. The study population consisted primarily of African American (77%) females (91%). The mean age of SLE onset was 30.6 years (sd = 14.0). There was a significant association between medication use and age groups; where a larger percentage of cSLE patients were prescribed cyclophosphamide or mycophenolate mofetil than aSLE patients. The cSLE group had a significantly higher prevalence of renal disease and time-to-onset of renal involvement is significantly less in cSLE (see Table). Age at SLE onset was significantly associated with time to onset of renal disorder (HR_{Age}=0.766, $\chi_{(1)}$=20.7, p<0.001). No significant difference was detected between cSLE and aSLE in renal damage outcomes such as GFR, chronic proteinuria, or end-stage renal disease.
Conclusions. Our findings suggest that SLE-associated renal disease is more prevalent in cSLE and that a younger age of SLE onset is associated with increased risk of developing renal disease.

Table

	Total N = 535	aSLE N = 432	cSLE N = 103	*p*
Renal Disorder				
5 Years	137 (38.9)	95 (34.2)	42 (56.8)	< 0.001
10 Years	204 (66.9)	149 (62.3)	55 (83.3)	0.001
20 Years	236 (89.4)	177 (87.6)	59 (95.2)	0.092
Dialysis				
5 Years	21 (15.3)	16 (16.0)	5 (13.5)	0.720
10 Years	37 (37.4)	28 (38.9)	9 (33.3)	0.610
20 Years	51 (71.8)	37 (69.8)	14 (77.8)	0.516
Low GFR				
5 Years	20 (15.8)	17 (17.5)	3 (10.0)	0.323
10 Years	32 (38.5)	25 (41.0)	7 (31.8)	0.449
20 Years	37 (69.8)	29 (69.1)	8 (72.7)	0.813
Proteinuria				
5 Years	21 (15.4)	18 (18.0)	3 (8.3)	0.169
10 Years	28 (32.6)	22 (35.5)	6 (25.0)	0.352
20 Years	31 (62.0)	25 (62.5)	6 (60.0)	0.884
ESRD				
5 Years	15 (10.5)	12 (11.2)	3 (8.3)	0.626
10 Years	32 (33.0)	25 (35.2)	7 (27.0)	0.442
20 Years	41 (66.1)	32 (66.7)	9 (64.3)	0.869

P5.20

An Australian story: patient perceptions of SLE flare activity, symptoms, triggers and management.

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Living with SLE commonly involves a daily symptom background with various day-to-day life, goals and activity impacts. Symptoms are managed to prevent organ damage and achieve acceptable levels of patient tolerance, however, exacerbation periods (flares) still occur. Reported illness impacts vary between patients and clinicians and are influenced by illness severity; flare predictability, frequency and intensity; symptom characteristics; available supports and importantly patient resilience and self-management capacity. To further understand lupus' health impacts we explored flare symptoms, triggers and management with a focus on the patient lived experience.
Mixed methods were used to retrospectively explore patient-perceived flare in 101 female Australian SLE patients using a novel flare definition focussed on patient-perspectives.
Our population were similar to other Caucasian populations, with average annual flare frequency of 6.8 discrete flares and 29.9 self-reported flare days. Frequently published flare triggers of UV radiation, infection and stress were confirmed, with new triggers of temperature & weather changes; work and household chemicals, identified. Symptoms were consistent with other populations, however the Australian population reported joint and muscle pain (73.3%) more frequently than fatigue. Additional symptoms of gastrointestinal issues (13.9%) and shortness of breath (9.9%).
Most flares were self-managed with patients making considered management choices without medical input. Medical support barriers included availability and past experiences reflecting incongruence between clinician and patient views of symptom impact and ultimately flare occurrence highlighting the need for improvements in patient/clinician interactions. Overall the results indicated that SLE symptom exacerbations can be influenced by everyday behaviours and lifestyle choices.

P5.21

Cognitive and emotional processing in systemic lupus erythematosus: An fMRI study

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Background. Cognitive dysfunction and mood disorders are common aspects of Systemic Lupus Erythematosus (SLE). They are now being investigated using functional magnetic resonance imaging (fMRI). The few studies undertaken in this area have suggested that patients with SLE employ compensatory brain mechanisms to maintain adequate cognitive function.
Objectives. This study aims to explore functional brain differences between SLE participants and healthy controls during cognitive and emotional processing.
Methods. 11 SLE participants who met ACR criteria and 9 healthy controls undertook a working memory task (n-back) and a facial emotional recognition task (FERT) during fMRI. The n-back task had three levels (0-, 1- and 2-back) with the 2-back level being the most difficult. The FERT displayed faces expressing different emotions: happiness, sadness, fear and neutral. Both tasks were analysed using region of interest (ROI) analysis in SPM12.
Results. Participants were well matched on key variables. During the n-back task, 2- vs 0-back condition, SLE participants had an increased BOLD response in the middle frontal gyrus (MFG) (p=0.04). SLE participants also had an increased BOLD response in the amygdala when processing sadness vs neutral (p=0.01) during the FERT.
Conclusions. The increased BOLD response in frontal regions during the n-back may indicate that SLE participants utilise compensatory mechanisms to maintain adequate cognitive function. SLE participants also had an increased response in emotional processing areas when viewing sad faces. Research with depressed patients has shown this to be a potential biomarker for depression, which may be of importance for SLE participants.

P5.22

Elevated Level of Plasma Coagulation Factor XIII Correlates To Atherosclerosis In Lupus Patients

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Background. Atherosclerosis and cardiovascular disease are serious comorbidities in patients with systemic lupus erythematosus (SLE), but the causes for the increased risk are not fully understood. Coagulation factor XIII (FXIII), which is a transglutaminase, is positioned at the final step of the coagulation pathway. FXIII forms crosslinks between fibrins, and strengthens the overall clot. It has also been reported that in monocytes, intracellular FXIII crosslinks Type 1 Angiotensin receptor dimer which accelerates atherosclerosis. Since FXIII abnormalities cannot be detected by routine screening coagulation tests such as prothrombin time and activated partial thromboplastin time, this marker has not been previously examined for an association with atherosclerosis in SLE.
Methods. We examined plasma levels of FXIII activity (FXIIIa) in 44 SLE patients who had previously participated in our longitudinal Biomarkers of Atherosclerosis in SLE study. B-mode and Doppler scanning of carotid arteries was performed at baseline and at 24- 36 months. FXIIIa levels were measured in the blood samples using ELISA (Technoclone).
Results. 52% of SLE subjects had elevated FXIIIa (reference range 69-143%). FXIIIa was significantly correlated with carotid internal media thickness at follow-up (r=0.37, p=0.03). FXIIIa levels were numerically higher in SLE patients with plaque at follow-up, although this did not reach statistical significance.
Conclusions. Although further confirmatory testing is underway, FXIIIa may be a good marker for atherosclerosis in SLE, and can be checked by routine blood collection.

P5.23

RAPID3 and Physician Global Correlate Well with SELENA-SLEDAI in Systemic Lupus Erythematosus Patients

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Aim. Compare SELENA-SLEDAI (SS) to instruments frequently implemented in the regular office setting.
Design. Consecutive SLE patients were evaluated. Physician compiled measures included: SS, SLICC/ACR Damage Index (SDI), physician global, RAPID3, medication score (MEDS):
1 point: hydroxychloroquine, methotrexate, azathioprine, prednisone <10 mg/day.
2 points: cyclosporine, dapsone, and non-nephritis mycophenolate mofetil (MMF), prednisone 10-20 mg/day.
3 points: MMF for maintenance nephritis.
4 points: MMF for induction nephritis, cyclophosphamide; prednisone >20 mg/day, or biologics.
Patient reported measures included: MDHAQ, pain, patient global.
Results. 99 validated SLE patients were enrolled. SELENA-SLEDAI correlated best with physician global but also with patient global, MEDS, and RAPID3. Combining the RAPID3 with MEDS improves the correlation over RAPID3 alone.
Conclusion. Validated SLE measures used successfully in clinical trials can be impractical in practice settings. Either RAPID3 alone or RAPID3+MEDS is an easy and quick assessment that can be readily incorporated into almost any rheumatology practice, particularly if they are already collecting the RAPID3 for other rheumatic conditions. Those with severe SLICC Damage Index scores did not correlate with the RAPID3 in our study. Study funding-GSK

P5.23 Table I. Correlation of SS with simple measures.

	Individual Measures						Combined Measures			
	MEDS	MDGlobal	MDHAQ	PtPain	PtGlobal	RAPID3	MEDS_ MDglobal	RAPID3_ MEDS	RAPID3_ MDglobal	RAPID3_ MEDS_ MDglobal
Spearman Coefficient (R)	0.2395	0.6596	0.1709	0.1472	0.329	0.2561	0.4351	0.3224	0.2908	0.3521
p-value	0.0169	<.0001	0.0908	0.1458	0.0009	0.0105	<.0001	0.0011	0.0035	0.0004

Table II. Correlation of SS with simple measures by SDI.

SDI Group	Correlation	Meds	MDGlobal	MDHAQ	PtPain	PtGlobal	RAPID3	Meds+ MD Global	RAPID3+ Meds	RAPID3+ MD Global	RAPID3+ Meds+MD Global
None (0)	Spearman Coefficient (R)	0.1394	0.7525	0.2091	0.2842	0.5053	0.4458	0.3919	0.4989	0.4935	0.5454
(n=42)	p-value	0.3786	<.0001	0.1839	0.0682	0.0006	0.0031	0.0103	0.0008	0.0009	0.0002
Mild (1-2)	Spearman Coefficient (R)	0.26	0.4402	0.2948	0.2611	0.4254	0.3486	0.3857	0.3985	0.3514	0.4026
(n=36)	p-value	0.1257	0.0072	0.0809	0.1241	0.0097	0.0372	0.0202	0.0161	0.0356	0.0149
Severe (>=3)	Spearman Coefficient (R)	0.4106	0.7745	-0.0422	-0.2381	-0.2025	-0.2598	0.5599	-0.0666	-0.2384	-0.0362
(n=21)	p-value	0.0644	<.0001	0.8558	0.2987	0.3786	0.2555	0.0083	0.7743	0.298	0.876

P5.24

Population-based analysis of hospitalizations in Sardinia, a West-European region, reveals major changes in hospital utilization for patients with Systemic Lupus Erythematosus over the period 2001-2012

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Objective. To evaluate hospital admissions in SLE patients through a retrospective population-based study analyzing hospitalization data during 2001-2012 in Sardinia, an Italian region with universal Health System coverage.
Methods. Data on the hospital discharge records with the ICD-9-CM code for SLE (710.0) were obtained from the Department of Health and Hygiene and analysed mostly focusing on primary and non-primary diagnosis and Diagnosis Related Group (DRG) code. The two-tailed Cochran-Armitage test for trend was applied. In order to estimate SLE prevalence, administrative data and medical records from the third level Rheumatology Center at University clinic of Cagliari were assembled.
Results. This study included 6,222 hospitalizations in 1,675 patients (87% women);. Hospitalizations with SLE as primary diagnosis were 3,782 (58.0%) and significantly decreased during study period. The annual number of renal, hematologic and neuropsychiatric disorders as non-primary diagnosis associated with SLE remained constant; however, their percentage raised (p<0.0001) because of a declined number of admissions for SLE without associated diagnosis and without complications (DRG code 241). Hospitalizations with SLE as non-primary diagnosis showed a significant upward trend in number and percentage of cerebrovascular accident (p=0.0004), acute coronary syndrome (p=0.0004) and chronic renal failure (p=0.0003), but not infections, as underlying primary diagnosis.
After correction for hospitalization (93.8%) and survival (91.1%) rates, the 2001-2012 SLE prevalence in Sardinia was estimated to be 99.3 per 100,000 inhabitants.
Conclusions. While overall hospitalizations for SLE patients declined, those for cerebrovascular accident, acute coronary syndrome and chronic renal failure as underlying primary diagnosis increased during the study period.

P5.25

Twenty-year brain magnetic resonance imaging follow-up study in Systemic Lupus Erythematosus: factors associated with accrual of damage and central nervous system involvement

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Objective. To evaluate the long-term progression of cerebral MRI abnormalities in patients with longstanding SLE.
Methods. Thirty patients (age 53.5±11.3) underwent brain MRI at baseline (b-MRI) and after 19.4±3.7 years of follow-up (fu-MRI). Two neuroradiologists visually analyzed the MRIs comparing: 1) white matter hyperintensities (WMHI), 2) cerebral volume, 3) parenchymal defects; these outcomes were also built in a modified MRI scoring system (mMSS) to estimate the cumulative parenchymal damage.
The independent risk factors for accrual of MRI brain damage, as well as the association between MRI abnormalities and the development of new neuropsychiatric (NP) manifestations classified according to 1999 ACR case definition were also analyzed.
Results. Twenty-three patients (76.7%) showed worsening of mMSS; 19 (63.3%) had increased number and volume of WMHIs, 8 (26.7%) had significant cerebral volume loss, 6 (20%) showed new ischemic parenchymal lesions. Only 6 patients had normal MRI. Antimalarial agents (p=0.006; OR 0.08) were protective against worsening of WMHIs. Higher cumulative dose of corticosteroids (p=0.026; OR 8.8) and dyslipidemia (p=0.044; OR 10.1) were associated with increased mMSS and cerebral volume loss, respectively. Higher mMSS score at baseline was independently associated with worsening of WMHIs (p=0.001; OR 5.7) and development of new NP events (p=0.019; OR 2.0); higher load of deep WMHIs at b-MRI (p=0.018; OR 2.0) was independently associated with stroke risk.
Conclusion. This study shows that MRI brain damage in SLE patients progresses independently from NP involvement as effect of potentially modifiable risk factors and it is associated with increased risk of new NP events.

P5.26

Association between atherosclerosis and cardiovascular disease in SLE patients

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Objective. Patients with systemic lupus erythematosus (SLE) are at increased risk of clinical significant cardiovascular disease (CVD). The aim of this study was to investigate the association between three measures of atherosclerosis and a history of CVD.
Methods. In a cross-sectional study of a Danish predominantly population-based SLE cohort the patients were screened for measures of atherosclerosis (coronary artery calcification (CAC) by means of cardiac CT, carotid intima-media thickness (IMT) and plaque demonstrated by ultrasound of carotid arteries, and ankle-brachial index (ABI) measured as blood pressure in arm and ankle). Patients with a history of CVD were compared to those without CVD.
Results. Of 125 SLE patients, 21 had a history of CVD. Both CAC and IMT/plaque showed a strong association to CVD (OR 4.16 and 2.95, p=0.004 vs. p=0.03, respectively). However ABI did not. Nephropathy, renal involvement ever, disease duration and SLICC were associated with CVD, whereas age and smoking were not (Table I).

Table. Comparison of SLE patients with and without CVD.

	Mean/median or frequency			Logistic regression		
	No CVD (n=104)	CVD (n=21)	*p* value	OR	95% CI	*p* value
Age (years)	49.2±14.0	55.1±48.0	0.08	1.03	0.99, 1.07	0.09
Female	93 (89%)	19 (90%)	1.00	1.12	0.23, 5.48	0.89
Caucasian	101 (97%)	21 (100%)	1.00	NA	NA	NA
BMI (kg/m^2)	25.2±5.9	25.5±4.9	0.84	1.01	0.93, 1.09	0.84
Smoking ever	65 (63%)	14 (67%)	0.80	1.2	0.45, 3.23	0.72
Family history of CVD	27 (26%)	6 (29%)	0.79	1.14	0.40, 3.24	0.81
Hypertension	61 (59%)	18 (86%)	0.02	4.23	1.17, 15.26	0.03
Hypercholesterolemia	54 (64%)	16 (76%)	0.05	2.96	1.01, 8.68	0.05
Nephropathy	3 (3%)	5 (24%)	0.003	10.52	2.29, 48.37	0.002
Renal involvement ever	26 (25%)	10 (48%)	0.06	2.73	1.04, 7.16	0.04
Antiphospholipid antibodies	52 (50%)	14 (67%)	0.23	1.96	0.73, 5.26	0.18
Disease duration, (years)	11.3±8.4	17.9±11.2	0.003	1.07	1.02, 1.13	0.005
SDI	1 (0-9)	3 (1-11)	<0.001	1.50	1.19, 1.91	0.001
Coronary atherosclerosis	25 (24%)	12 (57%)	0.01	4.16	1.55, 13.33	0.004
Carotid atherosclerosis	28 (27%)	11 (52%)	0.04	2.95	1.13, 7.69	0.03
Lower-extremity atherosclerosis	12 (12%)	5 (24%)	0.14	2.68	0.82, 8.77	0.10

Coronary atherosclerosis: Agatston>99U. Carotid atherosclerosis: carotid IMT>1.00 mm or plaque. Lower-extremity atherosclerosis: ABI<0.90 or >1.4. Nephropathy: s-creatinine>120. SDI: systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.
Conclusion. In SLE patients, the presence of CVD is significantly associated with CAC and carotid IMT and plaque, but not with ABI or important traditional risk factors as age or smoking.

P5.27

Effect of supervised physical exercise in adipokines in patients with systemic lupus erythematosus

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Background. adipose tissue is recognized as a proinflammatory organ involved in endothelial injury and atherosclerosis. Cardiovascular disease is an important cause of morbidity and mortality in SLE patients and disturbances in adipokynes levels has been described in these patients. Chemerin was described as an adipokine involved in macrophage infiltration into adipose tissue contributing to the development of inflammation and insulin resistance.
Objectives. to evaluate the effect of supervised physical exercise (SPE) on adiponectin, resistin, chemerin, linpocalin-2, retinol biding-protein-4 (RBP4) and plasminogen activator factor-1 (PAI-1) in SLE patients. Methods: prospective, controlled, nonrandomized study. SLE women were allocated in exercise group (EG) or control group (CG) according their availability to participate in the SPE 3X/week for 16 weeks. Adiponectin, resistin, lipocalin-2 and PAI-1 were assessed by LUMINEX-xMAP, and chemerin and RBP-4 by ELISA (Merck Millipore) at baseline (T0) and after 16 weeks (T16).

Results. Thirty-four SLE patients were evaluated (mean age 33.4±7.7years). Eighteen patients were allocated in the EG and 16 in the CG. Both groups were comparable and homogeneous regarding demographic variables, cardiovascular risk factors, adipokines and BMI at baseline. At T16 we observed a decrease in chemerin in the exercise group (44.9±12.8 vs 36.3±11.9, p=0.005), without significant changes in the control group. No significant differences occurred in BMI and other adipokines, comparing T16 and T0 in both groups
Conclusion. this is the first study demonstrating that physical exercise reduce chemerin in SLE patients and this can be useful tool to reduce risk of premature atherosclerosis in these patients.

P5.28

A signal of improvement in lupus disease activity at 3 months predicts further valid improvement at 6 months

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Objective. To determine if a signal of improvement in disease activity at 3 months predicts further improvement at 6 months.
Methods. Consecutive active lupus patients seen between 2012-2014 were screened and included if they had: At least 1of these systems active (vascular, renal, musculoskeletal, serosal or skin) and 2) started or increased glucocorticoids and/or immunosuppressants.
Outcome measures: SLEDAI-2K and SLEDAI-2K Responder Index 50 (S2K RI-50).
A signal of improvement by SLEDAI-2K or 52K RI-50 is defined as any decrease in SLEDAI-2K or S2K RI-50 scores at 3 months respectively.
Study endpoints at 6 months: Improved [SLEDAI-2K (baseline- last visit) decreased by ≥4) and not improved (SLEDAI-2K decreased <4).
Patients with SLEDAI-2K signal at 3 months were identified and those who did not have a SLEDAI-2K signal were evaluated for 52K RI-50 signal. Patients with signals were reevaluated at 6 months to determine if they had further improvement.
Results. 87 patients (SLEDAI-2K at baseline 8.9±5.1) were studied. 62% had a SLEDAI-2K signal at 3 months. Of the 33 patients who did not have a SLEDAI-2K signal, a S2K RI-50 signal was identified in 33%.
In patients with SLEDAI-2K signal at 3 months, 57% improved at 6 months. In patients with 52K RI-50 signal at 3 months, 54% improved at 6 months.
Conclusion. A signal of improvement at 3 months predicts further improvement in disease activity at 6 months. 52K RI-50 signal at 3 months, which is not discerned by SLEDAI-2K, predicts improvement in half of the patients at 6 months.

P5.29

Incidence and factors associated with the presence of cardiac alterations in patients with systemic lupus erythematosus - data from a Inception cohort

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In Systemic Lupus Erythematosus (SLE) heart involvement occur with a high prevalence; the incidence and time of presentation have not been assessed, and-dition associated factors have been reported inconsistently. The aim of the study was to evaluate the incidence and predictors of cardiac involvement in patients with SLE.
Method. inception Cohort Study. Pericarditis, valvular disease, myocardial and pulmonary arterial hypertension (PAH) in patients with SLE were evaluated by transthoracic echocardiogram to joining the cohort and follow-up. The incidence rate was calculated and the factors associated with their presence were evaluated.
Results. A total 80 patients were evaluated, a time tracking of 937 patient-years, 49 (61.2%) cardiac disorders were detected, with an incidence rate of 52.2 / 1000 (95% CI 39.5-69.1) patient-years. Twenty six events (53%) occurred during the first year of disease progression. Affectation the pericardium was found in 20 (25%), valve 24 (30%), myocardial 13 (16%) and PAH in 14 (17%). The positivity for anti-RNP, FR, C3 low and high ESR were significantly associated with the presence of cardiac events (p<0.05). The only predictor of cardiac disease was the presence of positive rheumatoid factor (HR 2.8, 95% CI 1.4-5.7, p=0.004).
Conclusion. Cardiac manifestations occur with high incidence in the early course of the disease and are associated with positivity for anti-RNP, FR and C3 low. The presence of positive rheumatoid factor is a predictor of cardiac involvement in patients with SLE.

P5.30

Vitamin D and bone mineral densities in female patients with systemic lupus erythematosus

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Introduction. Vitamin D deficiency, previously reported in SLE, is an important risk factor for low bone mineral density (BMD).
Methods. We studied 324 female SLE patients and 289 age matched population controls. Demographic and clinical data, levels of 25-hydroxy vitamin D (25(OH)D) were tabulated. BMD in lumbar spine, total hip and femoral neck were assessed by dual x-ray absorptiometry. Osteoporosis was defined as T-score less than -2.5 S.D. and osteopenia as T-score less than -1S.D. in at least one measured location. p<0.05 was considered significant.
Results. Mean age was 46.6±15.1 in patients and 47.4±14.7 years in controls, 49% vs 42% were postmenopausal. 25(OH)D levels were equal in vitamin D-non-supplemented patients (N=153) and controls (N=275). Supplemented patients had higher levels (p=0,001). 25(OH)D insufficiency (25-50 nmol/L) was present in 26.4% of SLE patients and 31.6% of controls while 0.6% and 1% were 25(OH)D deficient (<25 nmol/L), respectively. Osteopenia was present in 59.8% and osteoporosis in 18.2% of SLE patients. Of premenopausal females 6.9% had lower BMD that expected in minimum one location.
Conclusions. Low 25(OH)D levels were unexpectedly equally common in SLE patients and controls. BMD was associated with menopausal status, BMI, smoking, disease duration and SLICC but not with 25(OH)D levels.

Univariate analysis with standardized beta coefficients of variables related to BMD in SLE patients. Only statistically significant variables are shown.

	BMD lumbar spine		BMD total hip		BMD femoral neck	
	Pre-menopausal	Post-menopausal	Pre-menopausal	Post-menopausal	Pre-menopausal	Post-menopausal
Age (yrs.)	0.15*	-0.17*	ns	-0.31***	ns	-0.37***
BMI (kg/m^2)	0.26**	0.19*	0.29**	0.29**	0.19*	0.27**
Disease duration (yrs.)	ns	ns	-0.17*	-0.18*	-0.24**	-0.22**
Years since menopause	-	-0.17*	-	-0.19*	-	-0.21*
SLICC/ACR excluding osteoporosis item	ns	-18*	ns	-0.16*	ns	ns
Bisphosphonate treatment (y/n)	-0.16*	ns	-0.17*	-0.17*	ns	-0.21**
Corticosteroid treatment duration (months)	-0.28**	ns	-0.30**	ns	-0.38***	ns
Smoking ever (y/n)	ns	ns	ns	-0.21**	ns	-0.24**
25(OH)D (nmol/L)	ns	ns	ns	ns	ns	ns

*p<0.05,; **p<0.01; ***p<0.001. ns, not significant. BMD: bone mineral density; BMI: body mass index; SLICC/ACR: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; 25(OH)D, 25-hydroxy vitamin D.

Multivariate analysis with standardized beta coefficients of variables related to BMD in SLE patients. Only statistically significant variables are shown.

	BMD lumbar spine		BMD total hip		BMD femoral neck	
	Pre-menopausal	Post-menopausal	Pre-menopausal	Post-menopausal	Pre-menopausal	Post-menopausal
Age (yrs.)	ns	ns	ns	-0.30*	ns	-0.25*
BMI (kg/m^2)	0.24**	0.19*	0.30**	0.31***	0.20*	0.27**
Disease duration (yrs.)	ni	ni	ns	ns	-0.19*	-0.16*
SLICC/ACR excluding osteoporosis item	ni	-0.18*	ni	ns	ni	ni
Smoking ever (y/n)	ni	ni	ni	-0.24**	ni	-0.29**
R^2	0.08	0.09	0.13	0.24	0.09	0.23

*p<0.05; **p<0.01; ***p<0.001. ns, not significant ni, not included in model BMD, bone mineral density; BMI, body mass index; SLICC/ACR, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; 25(OH)D, 25-hydroxy vitamin D.

P5.31

Plasma myeloperoxidase levels are inversely associated with future piHDL formation in women with SLE

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Background. SLE patients have increased atherosclerosis that is not adequately explained. We previously discovered that pro-inflammatory HDL (piHDL) associate with the presence and progression of carotid plaque in SLE. Although HDL function is stable over months, it is unknown whether piHDL is stable over years, and it is also unknown what features predict future HDL function in SLE. Myeloperoxidase (MPO) is an enzyme that has been implicated in oxidation, inflammation, and the generation of piHDL *in vitro*. To determine whether plasma MPO levels might predict future piHDL, we measured HDL function and MPO levels at baseline and at 24-36 month follow-up in a longitudinal cohort of SLE patients.
Methods. 187 female SLE subjects were studied. Plasma MPO was measured at baseline using ELISA, and HDL function was measured at baseline and follow-up as previously described (Arthritis Rheum 2006 PMID 16868975).
Results. 68% of patients with baseline piHDL and 28% with normal HDL function had piHDL at follow-up. Baseline MPO levels were inversely correlated with HDL function at follow-up (r=-0.31, p<0.0001) but not at baseline. 71% of patients in the lowest 50% of baseline MPO had piHDL at follow-up, compared to 31% in the highest 50% (p<0.0001). Using logistic regression to control for traditional cardiac risk and SLE factors and medications, only baseline piHDL (OR 7.1 p<0.001) and MPO levels in the lowest 50% (OR 7.0, p<0.001) predicted piHDL at follow-up.
Conclusions. In conclusion, plasma MPO levels are significantly and independently inversely associated with future piHDL in patients with SLE.

P5.32

Risk factors for osteoporosis and fragility fractures in premenopausal women with Systemic Lupus Erythematosus

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Systemic Lupus Erythematosus (SLE) is associated with osteoporosis (OP) and fragility fractures (FFx). In this work we analyzed the prevalence of OP and FFx in pre-menopausal SLE female patients and the risk factors (RF) associated with their occurrence.
We retrospectively collected epidemiological and clinical data, together with bone mineral density (BMD) values and therapies of patients. Reduced BMD and OP were defined according to the World Health Organization. Only FFx occurred after the onset of SLE and unrelated to trauma were registered. With univariate and multivariate analysis we studied the associations of OP and FFx with possible RF.
From an initial cohort of 186 SLE patients, men and post-menopausal women were excluded. The remaining 114 women (mean age 39.1±8.6 years, mean disease duration 13.4±8 years) were analyzed. Forty-one (36%) had a reduced BMD and 18 (15.8%) had OP; 6 (5.3%) of them had at least one FFx. Univariate analysis showed a correlation between OP and age, GC, chronic renal failure (CRF), therapy with antiepileptic drugs (AED) and with anticoagulants (AC) (p<0.04) and between FFx and age, total amount of GC, AEDs and AC (p<0.03). At the multivariate analysis AEDs remained an independent predictor for OP (p<0.05), while AC showed a tendency to predict FFx occurrence (p 0.07).
More than one third of premenopausal women with SLE showed a reduced BMD; almost half of these had developed OP and about 15% of them had already experienced one or more FFx. Together with traditional RF, AEDs or AC could predispose to them.

P5.33

Plasma cytokines and chemokines profile in patients with Systemic Lupus Erythematosus: its potential use as biomarkers of kidney damage

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Introduction. Systemic lupus erythematosus(SLE) is an autoimmune disease in which the innate and adaptive response plays a significant roll, mainly mediated by cytokines. Lupus nephritis -LN-is the most severe complication associated with SLE.
Objective. To identify differential expression of cytokines profiles and circulating chemokines in plasma of SLE patients with different degrees of renal compromise compared to SLE patients without LN, from a reference center in the Colombian Caribbean region.
Methods. This was a case-control study. Plasma samples from 10 patients with NL class-II 10 patients with NL class-III, and 30 patients with NL class-IV were analyzed. As a control plasma from 30 SLE patients without nephritis were used. Plasma samples were analyzed using the Luminex technology of 38 analytes (EGF, Eotaxin, FGF-2, Flt-3 ligand, Fractalkine, G-CSF, GM-CSF, GRO, IFN-α2, IFN -γ, IL-10, IL-12 (p40), IL -12(p70), IL-13, IL-15, IL-17, IL-1Rα, IL-1α, IL-1β, IL-2, IL -3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IP-10, MCP-1, MCP-3, MDC (CCL22), MIP-1α, MIP-1β, TGF-α, TNF-α, TNF-β, VEGF, sCD40L, RIL-2Ra) using MILLIPLEX®-MAP-Human Cytokine/Chemokine-Magnetic-Bead-Panel-Premixed 39 Plex.
Results. Significant differences(p<0.05) was found between concentrations of cytokines EGF, G-CSF, GM-CSF, GRO, IFN, IL4, IL8, IP10, MCP, MDC, MIP.1a, sIL2Ra,TNFb when SLE-patients with LN vs SLE-patients without LN were compared.
Conclusion. These preliminary data suggest that there are differences in the LN plasma patients level of some chemokines and proinflamatory cytokines. Results support the hypothesis that circulating levels in plasma samples of these molecules may be considered, in future, as a damage biomarkers in LN of SLE patients.

P5.34

Prognosis, Survival and Renal Function in Patients with Lupus Nephritis

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Introduction. Lupus nephritis is the most common glomerulonephritis in the Colombian Caribbean region, despite there is less published information about its evolution and clínico-pathotogical aspects
Objective. To evaluate prognosis, survival and renal function of patients with LN residing in the Colombian Caribbean region controlled between 2008-2014.
Methodology. 229 patient study with LN corroborated by histology according to the International Society of Nephrology Clasification /Renal Pathology Society (ISN/ RPS. 2003) treated with induction and maintenance therapy and with a systemized following of at least 2 years. The pharmacological treatments included prednisolone, azathioprine, and Cyclophosphamide mycophenolate mofetil in isolation or combined and the clinical laboratory and histopathology variables were correlated as predictive value of therapeutic response. To achieve this as methodology a non-parametric descriptive statistics ANOVA (k-w) was used and canonical correspondence analysis
Results. 229 patients in total of 34±12 of age, which 88% women, whose evolution were controlled during 24±6 months. The most common form of clinical presentation was nephrotic syndrome and asymptomatic hematuria-proteinuria (68.07%) the type III and IV of LN (84,23%) were associated with patients under 25 of age and a negative response to treatment. The estimated glomerular filtration rate measured by MDRD4 showed a significant improvement at 24 weeks with regard the baseline figure of 74,36
Conclusion. The early detection and reference of NL patients allows an early approach and therapy. Which will prevent chronic kidney disease.

P5.35

Joint involvement in patients affected by Systemic Lupus erythematosus: application of the Swollen to Tender joint count Ratio

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Background. Joint involvement is a frequent manifestation in Systemic Lupus Erythematosus (SLE) patients. To date, no specific indices to evaluate this manifestation are available. The application of the Disease Activity Score 28 (DAS28) was proposed, demonstrating a moderate/high disease activity in 50% of patients with a joint involvement not defined by SLEDAI-2K. In the present study, we used the swollen to tender joint count ratio (STR) in a SLE cohort.
Methods. We enrolled 100 SLE patients (F/M 95/5, mean±SD age 46.3±10.6 years, mean±SD disease duration 147.1±103.8 months), with joint symptoms (≥1 tender joint). Disease activity was assessed by SLEDAI-2K. We assessed the swollen and tender joint count (0-28); the STR was calculated. According with the STR values, SLE patients have been grouped into three disease activity categories: low (STR <0.5), moderate (≤0.5 STR ≤1.0), high (STR >1.0). The DAS28-ESR was also calculated.
Results. The median STR value was 0.03 (IQR 0.6). According with the STR values, 70 patients had low disease activity, 23 moderate and 7 high. A positive correlation between the STR and DAS28-ESR (p=0.001; r=0.33) and between STR and ESR (p=0.01; r=0.25) was observed. Considering the 66 patients without joint involvement defined by SLEDAI-2K, 9% showed a moderate activity, while 29.4% of the remaining patients with joint involvement identified by the SLEDAI-2K had a low STR.
Conclusions. We used for the first time the STR index to evaluate joint involvement in SLE patients, demonstrating its higher sensitivity than SLEDAI-2K.

P5.36

Long-term outcomes and predictors of mortality in systemic lupus erythematosus (SLE) associated pulmonary arterial hypertension (PAH)

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Objectives. This study aimed to describe the long-term outcomes and predictors of mortality in SLE-PAH patients in a single-center.
Methods. A prospective cohort of SLE-PAH patients was established and followed from 2006 to 2014, in Peking Union Medical College Hospital. All enrolled SLE patients were diagnosed with PAH by right heart catheterization (RHC). Clinical and laboratory data were recorded as well as long-term outcomes including PAH-related death, and treat-to-target. Survival and independent outcomes predictors were analyzed.
Results. A total of 104 RHC-confirmed SLE-PAH patients were enrolled. RHC revealed mPAP was (46.9±11.4) mmHg, CI was (2.7±0.8) L/(min×m2). 46.2% were in WHO functional class I/II. All received glucocorticoids and immunosuppressants. 64.4% were treated with PAH-targeted medications. The patients were followed up for 18.6 months (1.8-90.7), during which 14 (13.5%) patients died, and 51 (49.0%) patients got treat-to-target achievement. The overall survival rates as 1 and 3 years were 93.0%, 78.0%, respectively. The right atrial pressure elevation (>5mmHg) was the only independent risk factor of PAH-related death (HR 7.767, p=0.017). Hypocomplementemia (HR 4.692, p=0.007), Early diagnosed PAH by RHC (<6months) (HR 4.859, p=0.007), and CI≥2.5 L/min/m2 (HR 4.290, p=0.013) were independent predictive factors for treat-to-target achievement.
Conclusions. This study described the long-term outcome in a cohort of patients with SLE-PAH Those PAH patients with active SLE and reserved heart function might be in good prognosis.

P5.37

Influence of Socioeconomic Factors on Phenotype and Disease Activity Degree in Chinese Patients with Systemic Lupus Erythematosus

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Objective. To estimate influences of socioeconomic factors on phenotype and disease activity index in patients registered in the Chinese SLE Treatment and Research group (CSTAR).
Methods. A prospective cohort study of 2104 patients with SLE was conducted by the CSTAR registry. The interaction between socioeconomic factors and disease characteristics was examined. Socioeconomic factors incorporated were Average Monthly Income per capital, occupation, education, marital status and residential regions, while disease characteristics were analyzed by factors of disease phenotype, disease activity degree, etc. Multivariable logistic regression models were applied to eliminate confounding effects.
Results. Increased risks of oral ulceration were found in patients in manual vocations (OR1.59, p<0.05), while patients with lower levels of education were associated with decreased risks (OR 0.64, p<0.05). Reduced risks of serositis were seen in northern SLE patients (OR 0.57, p<0.05), and added risks of photosensitivity in mid-western patients (OR 1.40, p<0.05).
As for the influences on disease activity, independent risk factors were also demonstrated, includinglow income, manual vocations and residing in mid-western China (OR1.54, OR 1.45 and OR 1.53, respectively, p<0.05).
Conclusions. Phenotype pattern varied among patients registered in CSTAR database in different socioeconomic status. Low income, manual vocations, and residing in mid-western China appeared to predictors for higher disease activity degree, which may contribute to the development of SLE, and need to be managed actively.

P5.38

Lymphopenia through out Systemic Lupus Erythematosus (SLE) evolution: impact on activity, organ system involvement and damage

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Objective. To analise lymphopenia and lymphocyte variation through the evolution of SLE and its relation with organ system involvement, immunological profile, disease activity, organ damage, infection and neoplasia
Methods. Retrospective study of 38 patients charts and blood tests from diagnosis til end 2014. Only patients with frequent visits and followup in our center since diagnosis were included. Sociodemographic characteristics, cumulative SLE manifestation, SELENA-SLEDAI, lymphocytes and hemoglobin count, SLICC damage index, drugs dose, infection and neoplasia were collected. Data were analysed in SPPS 22.
Results. 36 female (18:1), mean age at diagnosis 31,3 yo, mean followup time 12,3 years, 89,5% had mucocutaneous involvement, 89,5% articular, 31,6% renal, 13,2% NPSLE, 52,6% haematological, 100% ANA positive. Lymphopenia <1000/mcL was present at diagnosis in 42,4%, in the first year 48,6% and ever through followup 57,9%. Increase of >500/mcL occured in the first two years in 50% and in the first five in 94,7%. Lymphopenia at diagnosis correlated with more active disease during the first 5 years, positive anti-Sm and anti-RNP. Lowest lymphocytes in the first year correlated with anemia, positive anti-dsDNA, low complement. Increase in lymphocytes during the first five years correlated with increased hemoglobin, low complement, anti-dsDNA, positive anti-ribossome P, Coombs' and activity. No correlation was found with damage accrual, infection or neoplasia.
Conclusion. lymphopenia at diagnosis and lymphocytes increase (even with lymphopenia) were markers of disease activity but not related to damage accrual.

P5.39

Anemia through out Systemic Lupus Erythematosus evolution: impact on activity, organ system involvement and damage

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Objective. To analise anemia and haemoglobin variation in SLE and its relation with organ system involvement, immunological profile, disease activity, organ damage, infection and neoplasia.
Methods. Retrospective study of 38 patients charts and blood tests from diagnosis til end 2014. Only patients with frequent visits and followup in our center since diagnosis were included. Sociodemographic characteristics, cumulative SLE manifestation, SELENA-SLEDAI, lymphocytes and hemoglobin count, SLICC damage index, drugs dose, infection and neoplasia were collected. Data were analysed in SPPS 22.
Results. 36 female (18:1), mean age at diagnosis 31,3 years, mean followup time 12,3 years, 89,5% had mucocutaneous involvement, 89,5% articular, 31,6% renal, 13,2% NPSLE, 52,6% haematological, 100% ANA positive. Anemia <10,9g/dL was present at diagnosis in 32,4%, in the first year 35,1% and ever through followup 44,7%. Increase of >1,01g/dL occured in the first two years in 66,7% and in the first five in 74,3%. Anemia at diagnosis correlated with more active disease during the first 5 years, positive anti-dsDNA, Coombs' test and low complement. Lowest haemoglobin in the first year correlated with lymphopenia, positive anti-dsDNA and anti-Ro, Coombs' test and low complement. Increase in haemoglobin during the first five years correlated with low complement, anti-dsDNA, Coombs' test, renal involvement, infection and activity. Lowest haemoglobin during the time of followup correlated with time to damage. No correlation was found with neoplasia.
Conclusion. anemia at diagnosis and haemoglobin increase were markers of disease activity and correlated with infection, time to damage, but not with the ocurrence of damage.

P5.40

Breastfeeding Practice in Patients with Systemic Lupus Erythematosus

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Introduction. Breastfeeding has been shown to improve the wellbeing of a mother and her infant, but it is unknown how breastfeeding is pursued in systemic lupus erythematosus (lupus) patients. We sought to determine the rate of breastfeeding and the factors influencing this rate among women with lupus and a recent pregnancy. Further, we reassessed the current data available about the safety of common lupus medications in breastfed infants.
Methods. Data was collected prospectively from patients enrolled in Duke Autoimmunity in Pregnancy Registry who fulfilled the 2012 SLICC criteria and for whom post-partum breastfeeding status was known. During and following pregnancy, physician assessments of SLE activity, medications, breastfeeding plans and practice were collected. The safety of medications in breastfed infants was assessed through a comprehensive review of LactMed, a national database.
Results. A total of 51 pregnancies in 84 women with SLE were included in the study. Half of the lupus patients (n=25) practiced breastfeeding. The rate of breastfeeding was not significantly affected by socioeconomic factors. In contrast, lupus disease activity, pregnancy outcome (preterm birth) and intention to breastfeed early in pregnancy were significantly associated with breastfeeding practice in lupus patients. In reviewing LactMed, the majority of lupus medications appears to have minimal transfer into breast milk and is likely compatible with breastfeeding.
Conclusion. A significant portion of lupus patients practiced breastfeeding and most desire to breastfeed. Hydroxychloroquine, azathioprine, methotrexate, prednisone, and likely rituximab and belimumab have limited transfer into breast milk and should not be considered a contraindication to breastfeeding.

P5.41

Depression as a risk factor for severe damage in systemic lupus erythematosus patients

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Objective. to determine the factors associated with Systemic Lupus International Collaborating Clinics Damage Index (SDI) in SLE patients by linear regression analysis.
Methods. 180 SLE patients were enrolled in this study. All of them met the full ACR revised criteria for SLE classification. The organ damage was assessed by the SDI. Mental disorders (MD) were diagnosed in accordance with the ICD-10 criteria in semi-structured interview by psychiatrist. Psychiatric scales were used: Hospital Anxiety and Depression Scale (HADS), Per-ceived Stress Scale (PSS-10) and projective psychological methods for affectivity (anxious, melancholic or apathetic) types. MDs were diagnosed in 78,8% of SLE patients. Chronic depression - dysthymia and recurrent depressive disorder prevailed (25,6% and 14,4% accordingly). Dual-energy X-ray absorptiometry was used for osteoporosis detection.
Results. 86 (47,8%) of SLE patients had SDI ≥2 points. The patients with SDI ≥2 were older (37,5±1,35 vs. 32,03±1,23 years, p=0,003), were frequently female (90,7% vs. 80,9%, p=0,046). In a linear regression model the SLE duration (β=0,321), duration of cyclophosphamide treat-ment (β=0,150), presence of arterial hypertension (β=0,190), high body mass index (β=0,083) and osteoporosis (β=0,085), as well as depressive disorders diagnosis, HADS-D (β=0,207) and perceived stress severity (PSS) (β=0,07), melancholic or apathetic affectivity type (β=0,127) were independently associated with severe SDI in SLE patients (area under the ROC curve=0,873).
Conclusion. Chronic depression, perceived psychosocial stress, definite psychological type (melancholic or apathetic affectivity) along with SLE duration, cyclophosphamide treatment, ar-terial hypertension, high body mass index and osteoporosis are the leading factors of severe SDI in SLE patients

P5.42

Lupus cystitis in Korean patients with systemic lupus erythematosus: risk factors and clinical outcomes

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This study was performed to investigate the clinical characteristics and risk factors of lupus cystitis. We retrospectively reviewed 1064 patients at Seoul St. Mary's Hospital in Seoul, Korea from 1998 to 2013. Lupus cystitis was defined as unexplained ureteritis and/or cystitis as detected by imaging studies, cystoscopy, or bladder histopathology without urinary microorganisms or stones. Twenty-four patients had lupus cystitis. Three-fourths of patients with lupus cystitis had concurrent lupus mesenteric vasculitis (LMV). The initial symptoms were gastrointestinal in nature for most patients (79.2%). High-dose methylprednisolone was initially administered to most patients (91.7%). Two patients died of urinary tract infections. Sixty-five age, sex-matched SLE patients SLE who were admitted with other manifestations were included as the control group. Patients with lupus cystitis showed a lower C3 level (p=0.031), higher SLE Disease Activity Index score (p=0.006), and higher ESR (p=0.05) upon admission; more frequently had a history of LMV prior to admission (p<0.001); and less frequently had a history of neuropsychiatric lupus (p=0.031) than did patients with SLE but without lupus cystitis. The occurrence of lupus cystitis was associated with a history of LMV (OR, 21.794; 95% CI, 4.061-116.963). The median follow-up period was 3.4 years, and the cumulative 1-year mortality rate was 20%. Complications developed in 33.3% of patients with lupus cystitis and were related to survival (p=0.021). Our results suggest that the possibility of lupus cystitis should be considered when a patient with SLE and history of LMV presents with gastrointestinal symptoms or lower urinary tract symptoms.

P5.43

Systemic Lupus Erythematosus in Spanish males (RELESSER)

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Background. To describe the demographic, clinical and immunological manifestations in male patients with Systemic Lupus Erythematosus(SLE) Methods: Patients diagnosed of SLE. RELESSER database: Spanish Society of Rheumatology were included. Design: multicenter retrospective cross-sectional study.
Results. A total of 3658 patients were included: 353 men (9.7%) and 3298 women (90.2%). Average onset of symptoms of 37±17 and 32±14 years of age respectively. Male/female ratio was 1/9. Age of onset of symptoms and age at diagnosis was higher in men than in women (p<0.0001). Diagnosis in males was sooner than in females (p=0.04). Males have more cardiovascular comorbidities (p<0.001). Table I Clinical manifestation. During follow-up 208 patients died: 30(9.3%) male and 178(5.9%) women (p=0.02). On multivariate analysis, the only statistically significant variable was age. It was seen that patients over 50 year-old had a higher mortality than those under 50 year-old, regardless of gender, delay in diagnosis, risk factors and clinical features OR: 5.32 (CI: 3.61 to 7.84) p<0.001.
Conclusion. Patients with SLE older than 50 years old are at increased risk of mortality. In male patients with SLE: the age at diagnosis and the onset of symptoms is higher than in women. The diagnostic delay is lower in men than in women. Men have more cardiovascular comorbidities, especially those over 50 years-old and also more serositis, renal and cardiovascular involvement than women.

Clinical Manifestation	Missing N	Male (N:353) N(%)	Women (N:3298) N(%)	Value of *p*
Systemic Manifestations				
- Weight loss	68	48 (13,7%)	309 (9,5%)	0,01
- Lymphadenopathy	74	49 (14%)	320 (9,9%)	0,02
- Splenomegaly	108	19 (5,5%)	99 (3,1%)	0,02
Cutaneous Manifestations				
- Exanthema	62	190 (54,3%)	2180 (67,1%)	<0,0001
- Alopecia	86	54 (15,8%)	1229 (38%)	<0,0001
Osteoarticular Manifestations				
- Erosive arthritis	60	20 (5,8%)	342 (10,5%)	0,01
- Avascular bone necrosis	67	30 (8,5%)	121 (3,7%)	<0,0001
- Fibromyalgia	94	1 (0,3%)	223 (6,9%)	<0,0001
Pulmonary Manifestations				
- Pleural fibrosis	43	8 (2,3%)	25 (0,8%)	<0,0001
- Pulmonary thromboembolism	33	18 (5,1%)	86 (2,6%)	0,01
Cardiovascular Manifestations				
- Libman Sachs endocarditis	103	7 (2%)	28 (0,9%)	0,04
- Angina or coronary bypass	52	19 (5,4%)	50 (1,5%)	<0,0001
- Acute myocardial infarction	61	24 (6,9%)	47 (1,4)	<0,0001
- Cardiomyopathy	79	20 (5,8%)	84 (2,6%)	<0,0001
- Pericarditis	52	15 (4,3%)	59 (1,8%)	<0,0001
Peripheral vascular Manifestations				
- Claudication for more than 6 months	45	8 (2,3%)	23 (0,7%)	<0,0001
- Deep vein thrombosis	50	24 (6,9%)	119 (3,7%)	<0,0001
- Raynaud	142	80 (23,7%)	1114 (35%)	<0,0001
Renal Manifestations				
- Lupus nephritis	89	156 (44,8%)	933 (29%)	<0,0001
- HTA in the first outbreak	182	68 (20,1%)	330 (10,5%)	<0,0001
- Hematuria	247	130 (38,70%)	908 (29,5%)	<0,0001
- Creatinine clearance = 50 irreversible	112	31 (9%)	161 (5%)	<0,0001
- Proteinuria = 3,5g/24hs	126	21 (6,1%)	114 (3,6%)	0,02
- End stage renal disease	146	16 (4,7%)	82 (2,6%)	0,03
Neuro psychiatric Manifestations				
- Lupus headache	89	10 (2,9%)	204 (6,3%)	<0,0001
- Seizures	76	32 (9,2%)	156 (4,8%)	<0,0001
- Depression	89	36 (10,3%)	574 (17,8%)	<0,0001
Immunology				
- Ac anti DNA positive	99	271 (78,6%)	2342 (72,9%)	0,02
- AC anti RO positive	96	94 (27,5%)	1300 (40,8%)	<0,0001
- Positive lupus anticoagulant	1007	86 (34,11%)	547 (22,8%)	<0,0001

P5.44

Pregnancy and Patients with Preexisting Lupus Nephritis: 15 Years of Experience at a Single Center in Korea

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We investigated obstetric outcomes and comorbidities during pregnancy in females with preexisting lupus nephritis (LN) and identified predictors for renal flare. In cases of renal flare during pregnancy, we assessed the long-term post-delivery renal outcome. We performed a retrospective analysis of 183 systemic lupus erythematosus (SLE) pregnancies at prepregnancy, during pregnancy, and at 1 month, 6 months, and 1 year post-delivery. Pregnancies with preexisting LN had a greater frequency of adverse obstetric outcomes and maternal comorbidity. Renal flares occurred in 50.7% of pregnancies with preexisting LN, 89.2% of which were reactivations. Renal flare among pregnancies with SLE was predicted based on preexisting lupus nephritis (OR 17.73; 95% CI, 5.770-54.484), an active disease prior to pregnancy (OR 2.743; 95% CI, 1.074-7.004), and prepregnancy eGFR < 90 mL/min/1.73 m^2 (OR 11.151; 95% CI, 3.292-37.768).
Persistent LN 1 year after delivery was observed in 33.3% of pregnancies. The median follow-up time after delivery was 5.9 (3.1-9.7) years and chronic kidney disease (CKD) occurred in 21.4% of pregnancies with renal flare. In patients with renal flare, failing to achieve a ≥50% reduction in urine protein levels within 6 months, longer total duration of renal flare, and acute kidney injury at renal flare was associated with CKD development. Females with preexisting LN should achieve remission before pregnancy. When patients experience renal flares during pregnancy, it is important to reduce the proteinuria level by >50% within 6 months and to achieve early remission for excellent long-term renal outcomes.

P5.45

New approach to diagnosing pulmonary vasculitis in systemic lupus erythematosus

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Introduction. Ground-glass opacification (GGO) is a non-specific pattern on computed tomography (CT) scans that requires a multi-stage differential diagnosis in patients with SLE.
Purpose. To evaluate the role of different CT post-processing techniques in differentiating pleuropulmonary pathology in patients with SLE.
Materials and Methods. Between 2013 and 2015 at North-Western State Medical University named after I.I. Mechnikov (Saint Petersburg), 70 female patients, aged 40.8 ± 6.4, with active SLE underwent laboratory, pulmonary function and imaging tests (multislice computed tomography (MSCT), CT angiography and pulmonary perfusion scintigraphy). We used different post-processing techniques (MPR, MIP, mIP and color mapping) for reconstructing CT scans which were then compared with native CT and perfusion scans done by three diagnosticians.
Results. Statistics showed that the addition of post-processing techniques to native CT scans increased the sensitivity by 13.0%, specificity by 7.35% and accuracy by 5.7% in diagnosing pulmonary vasculitis. The results of color mapping correlated with CT angiogram and perfusion scans. Without clear GGO on CT scans, it helps to detect pulmonary vasculitis in 68% of patients with microvascular thrombosis (especially associated with antiphospholipid syndrome), 48% with pleuritis, 32% with pulmonary hypertension. The signs of vasculitis on color map significantly correlated with the level of anti-double-stranded DNA (r_s=0,843; p=0,005), hypocomplementemia (r_s=0,675; p=0,046), forced vital capacity rate (r_s=-0,703; p=0,013), rate of diffusion capacity (r_s=-0,813; p=0,001) and hypoxemia (r_s=0,697; p=0,034).
Conclusion. Post-processing techniques should become a routine part of radiological practice in pleuropulmonary pathology in SLE because they can be a useful addition to native CT scans.

P5.46

Overweight is a major contributor to atherosclerosis in systemic lupus erythematosus patients at apparent low risk for cardiovascular disease: a cross-sectional controlled study

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Objectives. Cardiovascular disease (CVD) is the main cause of death in systemic lupus erythematosus (SLE) patients. We aimed to determine whether overweight (defined as a BMI>25 kg/m2) contributed to subclinical atherosclerosis in SLE patients at low risk for CVD according to traditional factors.
Methods. Internal carotid wall thickness (ICWT) and carotid plaques were prospectively assessed in 49 SLE patients asymptomatic for CVD and 49 controls matched on Framingham score. Factors associated to ICWT were identified and multivariate analysis was performed.
Results. SLE patients and controls displayed a low 10-year risk for CVD according to Framingham score (mean 1.9+3.5 in SLE vs 1.8+3.2% in controls, p=0.37). ICWT (p=0.0007) and number of patients with carotid plaques (p=0.015) were however higher in SLE patients as compared to controls. In multivariable analysis, SLE was an independent risk for a carotid atherosclerosis (OR [95%CI]: 3.53 [1.36 - 9.14]; p=0.009). Older age, higher body mass index (BMI) and higher Framingham score were associated with atherosclerosis in SLE patients in univariate analysis. In multivariate analysis, only the association with overweight remained significant (OR [95%CI]: 4.13 [1.02 - 16.75]; p=0.047).
Conclusion. Overweight is a major contributor to atherosclerosis in SLE patients at apparent low risk for cardiovascular disease.

P5.47

Measurement of health status with the Patient Reported Outcomes Measurement Information System (PROMIS) instruments in adults with systemic lupus erythematosus

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Objective. Patient Reported Outcomes Measurement Information System (PROMIS) instruments allow standardized health status comparisons between different chronic disease populations. PROMIS instruments have been employed in other rheumatic diseases, but not in adult systemic lupus erythematosus (SLE). We report PROMIS scores and internal consistency in an adult SLE population.
Methods. Disease activity and damage were assessed in 129 adults with SLE. Participants then completed 8-item PROMIS short forms for each of seven health status domains. Scores were reported using a T-score metric. Internal consistency was assessed with Cronbach's alpha. PROMIS scores were compared to disease activity and damage with Spearman correlations.
Results. Participants were predominantly female (93.8%), Caucasian (52.7%), and 45.4 years old (SD=10.9). Mean SELENA-SLEDAI and SLICC/ACR scores were 2.4 (SD=2.8) and 1.7 (SD=2.2), respectively. Cronbach's alpha indicated excellent internal consistency of PROMIS instruments (alpha= 0.92-0.98, see table). Mean PROMIS T-scores were nearly one-half standard deviation worse than the United States (U.S.) population for six of seven measures. Correlations between PROMIS, SELENA-SLEDAI, and SLICC/ACR scores were low to modest, and only significant between SLICC/ACR and pain interference, depression, and physical function (r=0.27, 0.24, and -0.34, respectively).
Conclusion. PROMIS measures indicated poorer health status in our SLE population compared to the U.S. general population. Excellent internal consistency and correlations with disease damage suggest PROMIS instruments may be useful in assessing health status in SLE patients.

PROMIS Measure	T-Score Mean ± SD	Cronbach's Alpha
Fatigue	56.1 ± 9.7	0.966
Pain Interference	55.4 ± 10.1	0.980
Anxiety	54.3 ± 8.5	0.942
Depression	49.7 ± 9.0	0.946
Sleep Disturbance	56.1 ± 10.3	0.925
Sleep-Related Impairment	55.3 ± 9.0	0.916
Physical Function	43.9 ± 8.7	0.963

P5.48

B cell activating factor (BAFF) in serum and systemic lupus erythematosus disease activity using SLEDAI-2K scoring system (East Bohemian regional study)

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Objectives. BAFF serum concentration was investigated as biomarker of activity in SLE with different results, including regional. The goal is to explore the problem in prospective, comparative, cross-over study of ethnical homogenous (Caucasian) East Bohemian SLE population.
Methods. Eighty-four adult SLE (ACR/1982, update in 1997) patients and 40 age- and sex- matched healthy controls were endolled. Disease activity was assessed using SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index 2000) scoring system: a score ≥ 6 was considered clinically important. BAFF serum values were quantified using a human BAFF Quantikine ELISA (RD Systems) and compared agains SLEDAI-2K score, ESR 1 h, Hb, CRP, IgG, C3, C4, ANA/IF (maximal titre), ANA/ELISA, anti-dsDNA/IFCL (maximal titre), anti-dsDNA/ELISA and antinucleosome Abs. Data obtained were statistically processed using Medcalc-Statistical Software programme.
Results. BAFF serum concentration in 20 SLE with SLEDAI-2K≥6, and also in 64 SLE with SLEDAI-2K0.05), but significant correlation between BAFF and anti-dsDNA/IFCL (r=0.22, p<0.05) and anti-dsDNA/ELISA (r=0.22, p<0.05) was demonstrated. ROC analysis of BAFF serum values for anti-dsDNA/IFCL test: area under ROC curve 0.639, sensitivity 57.7%, specificity 68.5%, and positive predictive value 1.81.
Conclusion. Investigation of BAFF serum values in SLE (Caucasian) population under study should be useful as biomarker of serological, but not clinical activity.
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P5.49

Impact of free light-chain immunoglobulins in serum as biomarkers of disease activity in systemic lupus erythematosus

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Objectives. To explore changes of serum concentration of free light-chains (FLC) kappa and FLC lambda as putative biomarkers of SLE disease activity in a prospective, comparative, and cross-over study.
Methods. Eigthy-three adult SLE patients (ACR/1982, update 1997) and 33 age- and sex-matched healthy controls were enrolled. Disease activity was assessed using SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index 2000): a score ≥6 was considered clinically important. FLC (Freelite, The Binding Site Group) in serum were analysed by quantitative nephelometry and compared against SLEDAI-2K score, IgG, C3, C4, ANA/IF (maximal titre), ANA/ELISA, anti-dsDNA/IFCL (maximal titre), anti-dsDNA/ELISA, and antinucleosome Abs/ELISA. Data obtained were statistically processed using Medcalc-Statistical Software programme.
Results. Serum concentration of FLC kappa, FLC lambda and total FLC in 22 SLE with SLEDAI-2K ≥6, and in 61 SLE with SLEDAI-2K <6 was significantly higher against healthy controls (p=0.003-0.0001), except FLC lambda in SLE with SLEDAI-2K 0.05). In SLE with SLEDAI-2K ≥6 the concentration of FLC kappa, FLC lambda and total FLC was significantly higher than in SLE with SLEDAI-2K <6 (p<0.001). In total group of 83 SLE was found significant correlation (p<0.001) between SLEDAI-2K score and FLC kappa (r=0.56), FLC lambda (r=0.58) and total FLC (r=0.62). A strong correlation was found between antinucleosome Abs and FLC kappa (r=0.59), FLC lambda (r=0.53) and total FLC (r=0.59).
Conclusions. FLC values in serum should be useful as biomarkers of SLE disease activity.
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P5.50

Application of the 2012 Systemic Lupus International collaborating clinics classification criteria on a multicenter group of Turkish systemic lupus erythematosus patients

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Background. The Systemic Lupus International Collaborating Clinics (SLICC) group has recently proposed a new set of criteria for the classification of SLE. Our aim here was to analyze the performance of SLICC criteria compared to ACR 1997 revised criteria among established Turkish SLE cases and controls.
Methods. The study population consisted of 427 SLE cases (327 patients were enrolled at IBU; 50 at TU and 50 at KU; 387 women, 40 men; mean age at diagnosis 33.5 years range 10-81). A total of 213 controls (189 women, 24 men; mean age 40.7 yrs) were enrolled on the basis of referral to the rheumatology clinic at IBU based on positive ANA and a clinical suspicion of SLE. The controls were eventually diagnosed with the following conditions: SLE, primary Sjogren's syndrome,dermatomyositis, myelodysplastic syndrome, psoriasis, multiple sclerosis, undifferentiated connective tissue disorders, Familial Mediterranean Fever and antiphospholipid syndrome.
Results. Overall, SLICC criteria showed greater sensitivity than ACR 1997 criteria (95.5% vs 90.6%) but were less specific (84.6% vs 95.1%). The SLICC criteria resulted in fewer misclassified cases compared to ACR criteria (23 vs 44). Eight SLE patients were biopsy proven SLE and were ANA-positive but failed to fulfill four of the ACR criteria at the disease onset.
Conclusion. The new SLICC criteria provide additional sensitivity and lead to fewer misclassifications than ACR criteria. Using both criteria together will be helpful to increase sensitivity and specificity for the diagnosis of SLE, especially in early disease onset.

P5.51

Arterial wall stiffness in systemic lupus erythematosus

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Objective. Arterial stiffness has been proposed as a surrogate measure of subclinical atherosclerosis in SLE. We aimed to determine whether arterial stiffness is increased in SLE patients.
Patients/Methods. An arterial stiffness index calculated from diameter changes in the common carotid artery measured by an ultrasound method, and blood-pressure. The subjects were 302 SLE patients and 294 population controls matched for age, sex, and region of residence. Cardiovascular disease (CVD) events were defined as objectively verified coronary heart disease, cerebrovascular disease, or ischemic peripheral vascular disease.
Results. Mean age was 48±14 years in SLE patients and 49±15 years in controls (ns). Manifest CVD was more common in SLE patients (p<0.001). Systolic blood pressure was 118±17 mmHg in SLE patients and 119±16 mmHg in controls (ns). Hypertension was more common among patients (43% vs. 25%, p<0.01), 36 % of patients had anti-hypertensive treatment vs. 14 % of control subjects. The stiffness index was 6.2±3.0 in SLE patients and 5.4±3.7 in controls (p=0.05). This remained true when all subjects with a history of CVD were excluded from the analysis
Conclusions. Manifest CVD was more common among patients. Arterial stiffness measured in the common carotid artery was increased in SLE patients compared with population controls and the difference remained when excluding all subjects with known CVD.

P5.52

Systemic Lupus Erythematosus (SLE) diagnosed during hospitalization:greater disease activity, damage and short-term death

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Objectives. analyze initial and follow-up features of patients with SLE diagnosed during hospitalization.
Materials and Methods. retrospective analysis of medical records: two groups were studied, a) SLE diagnosed during hospitalization (SLEin) b) SLE diagnosed on an outpatient basis (SLEout). All the patients met the 2012 SLICC Classification Criteria for SLE.
Results. 99 patients were assessed (88 female, 11 male), average age at diagnosis was 32,8 years old; 32.3% of them were diagnosed during hospitalization and the remaining 67.7% on an outpatient basis.
Initially, SLEin had higher average SLEDAI (11.0 SD 4.6 vs 8.3 SD 3.9, p 0.003), Anti-dsDNA (81.3% vs 50.7%, p 0.007) and C3 consumption (80.6% vs 40.7%, p<0.001) than SLEout.
Within the first 6 months, the average of cumulative corticoid doses was 7155 mg (SD 3461) in SLEin vs 4067 mg (SD 3053) in SLEout (p<0.001) and immunosuppressant usage was higher (59.4% vs 26.9%, p 0.003).
Within the first year, 37.5% SLEin's kidney biopsies showed lupus GN class III, IV or V vs 16.4 % in SLEout. (p 0.02, log-rank test).
Within the first 2 years, 18.8% SLEin died vs no SLEout (p<0.001) and SLEin had more damage as measured by SLICC (Median 0, 25%-75% 0-1 vs Median 0, 25%-75% 0-0 SLEout; p 0.02).
Conclusions. SLE in SLEin is initially more active, requires higher doses of corticoids and immunosuppressants, has more significant kidney involvement, and presents more damage and greater mortality in the short term.

P5.53

Neurological disorders in Systemic lupus erythematosus

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The neurological disorders (ND) are attributable to SLE in about 14%-90%, most frequently are neuropsychiatric and cognitive dysfunction.
Objective. Demographic and clinical characterization of neurological disorders.
Methods. Study ambispective analytical, was included patients with neurological manifestations (established by ACR 1999). The statistical analysis include descriptive statistics, Pearson correlations and for differences T student and Chi square test. A value of p<0.05 was significant.
Results. We studied 131 patients with SLE, for the analysis of the neurological disorders involved only 53 patients: 98% female, mean age 35.01±14.08 years. Mean ND per patient was 1.58±0.84 and mean of follow up 6.90±6.55 years. The physical exam at the beginning was normal in 62% and 38% abnormal (20% lost muscle strength, 11% hiporeflex and 8% hipoalgesia). In order of frequency Headache is reported in 66%, Polyneuropathy 20%, Seizure 18% and Mood disorders 18% (Table I). The procedures reported in patients are: CT normal 6, calcification, cortical atrophy and hipodensity in 1; MRI hiperintensity in 7, normal and arterial narrowness in 6. The differences between the ND group and control group (73 patients with SLE without ND) was: first manifestations at time of the diagnosis and lower educational with p<0.05 and anticonvulsants use with p<0.01. Not correlation between neurological disorder and clinical/serological activity was found. The treatment more used is Cyclophosphamide in 47%, with average 7.9 monthly pulses.
Conclusion. the principal disorders are headache, seizure and mood disorders. The polyneuropathy is more frequently.

P5.54

Risk factors for the development of chronic kidney disease in lupus nephritis: assessment of a retrospective cohort from a single tertiary center in southern Brazil

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Aim. To identify the main characteristics and risk factors for the development of chronic kidney disease (CKD) in our lupus nephritis (LN) population.
Methods. We retrospectively assessed clinical, demographic and serological characteristics from 86 biopsy-proven LN patients consecutively followed from 2000 to 2014 in our center, which is a tertiary public hospital located in the southern State of Brazil. Risk factors for developing CKD were examined by univariate and multivariate Cox proportional hazards regression analyses. CKD was defined as a glomerular filtration rate < 60 ml/min/1.73 m2 for 3 months or more.
Results. Patients' main characteristics are summarized in Table I. Treatment response, complications and outcomes are described in Table II. Risk factors for developing CKD are outlined in Table III.
Conclusion. Azotemia at diagnosis, resistance to induction therapy, anticardiolipin antibodies and psychosis are risk factors for progression to CKD in our LN population. This is the first time it was assessed in our Brazilian population, hence more studies are necessary to better characterize the renal outcome and risk factors for CKD in these patients.

Table I. Patients Characteristics.

Variables	N = 86 (100%)
Sex (female)	77 (89.5)
Ethnicity (Caucasian)	62 (72.1)
Education	
Less than 8 years	36 (41.9)
Age, years	30 (± 12.4)
Nephritis classification (WHO)	
II	17 (19.8)
III	25 (29.1)
IV	25 (29.1)
V	16 (18.6)
VI	1 (1.2)
III + V	1 (1.2)
IV + V	1 (1.2)
Comorbidities	
Hypertension	61 (70.9)
Dyslipidemia	25 (29.1)
Obesity	20 (23.3)
Diabetes Mellitus	4 (4.7)

Table II. Treatment response, complications and outcomes.

Variables	N = 86 (100%)
Induction treatment	
Cyclophosphamide	50 (58.2)
Steroids (PO or IV)	21 (24.4)
Steroids + azathioprine	12 (13.9)
Mycophenolate mofetil	3 (3.5)
Drugs (other than steroids) during follow-up	
Azathioprine	68 (79.1)
Cyclophosphamide	60 (69.8)
Mycophenolate mofetil	31 (36)
Rituximab	5 (5.8)
Partial or complete remission after first induction	
Class III + IV*	45 (88.2)
Class V	13 (81.2)
Time until partial or complete remission (days)	266 (187 – 396)**
Complications	
Avascular necrosis	9 (10.5)
Tuberculosis	5 (5.8)
Total hospital inpatient days	27 (12 – 51)**
Outcomes	
Chronic Kidney Disease	16 (18.6)
End-Stage Renal Disease	3 (3.5)
Death	5 (5.8)

*Mixed classes III+V and IV+V included.
**Data is expressed as median (interquartile range).

Table III. Risk factors for CKD.

	Univariate Analysis		Multivariate Analysis*	
Variables	HR (CI 95%)	*p*	HR (CI 95%)	*p*
Sex (male)	1.248 (0.283-5.503)	0.770		
Age at diagnosis	1.019 (0.976-1.063)	0.396		
Change to an aggressive nephritis class	4.728 (1.681-13.301)	0.003		
Seizure	2.442 (0.550-10.842)	0.240		
Psychosis	4.969 (1.400-17.636)	0.013	12.944 (2.540-65.951)	0.002
Anticardiolipin Antibodies IgG/IgM	4.691 (1.628-13.521)	0.004	5.932 (1.604-21.943)	0.008
Lupus anticoagulant	2.412 (0.542-10.741)	0.248		
Laboratory profile at nephritis diagnosis				
eGFR <60 ml/min/1.73 m²	2.361 (0.856-6.509)	0.097		
Urea, mg/dL	1.017 (1.003-1.032)	0.016	1.033 (1.012-1.055)	0.003
Hemoglobin <10 g/dL	1.260 (0.448-3.544)	0.662		
Platelets <150k /µL	0.338 (0.044-2.593)	0.297		
Nephrotic range proteinuria	1.884 (0.653-5.438)	0.242		
LDL >100 mg/dL	0.995 (0.281-3.528)	0.994		
C4 <10 mg/dL	1.014 (0.339-3.030)	0.980		
C3 <90 mg/dL	1.256 (0.350-4.504)	0.727		
Response to the induction therapy				
Complete remission	0.072 (0.023-0.226)	<0.001		
Partial remission	3.422 (1.088-10.765)	0.035		
Resistance to induction therapy	7.895 (2.919-21.356)	<0.001	4.415 (1.938-10.056)	<0.001

*Multivariate anaylsis was adjusted to sex (male) and age.

P5.55

Anti -N-methyl-D-aspartatereceptor antibody is associated with fibromyalgia in patients with systemiclupus erythematosus

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Objective. The high concordance of systemic lupus erythematosus (SLE) with fibromyalgia (FM) suggests common underlying mechanisms related to pain and distress in both patient groups. This study was aimed to evaluate roles of NMDAR antibodies in development of FM in SLE patients
Methods. Sera from 104 SLE patients, 112 FM patients, and 110 healthy controls were analyzed to detect titers of antibodies to N-terminus of 2B subunit of NMDAR (GluN2B). Clinical, laboratory data and concomitant diseases were found by reviewing the patient charts. We underwent clinical examination and neuropsychiatric evaluation, and interviewed SLE patients using a structured questionnaire that included FM and neuropsychiatric symptoms.
Results. 18 patients (17.3 %) of total 104 SLE patients were revealed having FM. The titer of anti-GluN2B antibodies was significantly higher in SLE patients than FM patients and healthy controls (p<0.001). In SLE patients, patients with concomitant FM showed higher titers of anti-GluN2B antibodies (p<0.05). The titers of anti-GluN2B antibodies were correlated with tender point count (Spearman's rho = 0.238, p=0.016) and widespread pain index (Spearman's rho = 0.276, p=0.005), but not with other symptom scales. Anti-GluN2B antibody-positive SLE patients were more likely to have NPSLE and concomitant FM (p<0.05). In multivariate analysis, Anti-GluN2B antibody was independent predictor of concomitant FM and NPSLE.
Conclusion. This is the first study to present that antibodies to NMDAR may be associated with pathogenesis of FM in SLE patients.

P5.56

Cognitive Symptoms Inventory performance as a tool to trace neurocognitive deficit symptoms in patiens with systemic lupus erythematosus

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Objective. Assess CSI (Cognitive Symptoms Inventory) performance as a tool to trace neurocognitive impairment in patients with SLE.
Materials and Methods. 85 patients with SLE were assessed between 01/2013 and 06/2014. All of them completed a CSI (self-administered questionnaire which provides information about cognitive functions), and a HADS (Hospital

Anxiety and Depression Scale). The 1-hour neuropsychological test battery proposed by the ACR was performed in the Neurology Service. Patients with SD = 1.5 were considered to have neurocognitive deficit.
Results. Among the 85 patients, 70 were identified as having cognitive impairment, which represents a prevalence of 82.35% (95 % CI: 72.57, 89.77).
The area under the ROC curve of the CSI for the diagnosis of cognitive impairment was of 63.34% with a 95% confidence interval from 52.38% to 73.7%, which is above the value of no-discrimination (0.5). The area under the curve in patients with anxiety or depression was of 58.3%, and of 54% in patients without anxiety or depression. These differences are not-statistically significant, p=0.8095
Conclusions. Prevalence was 82.35%, which is high, probably because SD = 1.5 from the mean was employed as the gold standard cut-point, including patients with neurocognitive decline. CSI performed poorly as a screening method. CSI results were not biased by anxiety and depression.

P5.57

Cognitive deficit in systemic lupus erythematosus: frequency and general features.

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Objective. study cognitive impairment in patients with SLE, and its main clinical features.
Materials and Methods. 84 patients were enrolled, and a 1-hour neuropsychological test battery was performed on all of them. The sample was split into two groups: those with a score lower than 2 SD on some tests (Normal or Border) and those with scores higher than 2 SD.
Results. 84 patients were assessed (73 female y 11 male). Their average age was 32.5 years old (SD ± 12 years). Forty-three of them were Caucasian, 23 were of mixed racial origin, 15 were Amerindians, 1 was Asian, and 2 were African American. Forty-eight patients exhibited attention deficit, 38 showed memory deficit, and 2 displayed motor skills deficit. Patients had a SLEDAI (median) of 2 (RI=4), a SLICC (median) of 0 (RI=1), an average level of education of 10 years (SD 3), and disease duration (median) of 82 months (RI=87,5). 33.3% either had neurocognitive decline or were normal (GROUP 1) and 66.7% had either focal or multifocal deficit (GROUP 2).
Conclusion. patients with neurocognitive deficit had fewer years of schooling, a greater percentage received corticosteroid therapy, and the time of evolution of the disease was shorter. No differences were observed in terms of activity and damage at the time of the assessment. Levels of anxiety, depression and APS were similar.

	Results		
	Normal or border GROUP 1	Focal o multifocal deficit GROUP 2	*p*
Number	28 (33,3 5)	56 (66,7 %)	-
Age	32,7 (SD12)	32,3 (SD 12)	0,9
Caucasian	21,4 %	29,8 %	0,08
Years of schooling (average)	11,9 (SD 2,7)	10,1 (SD 3,1)	0,01
Time of evolution of the disease in months (median)	103 months (RI= 115, 75)	69 months (RI= 81,5)	0,02
MMSE (median)	30 (RI=1)	29 (RI=1,5)	<0,001
Treatment with HCQ	92,9 %	91,1 %	0,6
Treatment with corticoids	35,7 %	66,1 %	0,02
Treatments with immunosuppressants	17,9 %	26,8 %	0,5
APS	32%	14%	0,1
Anxiety	9,5 %	14,3 %	0,46
Deppression	3,6 %	8,3 %	1
SLEDAI (median)	2 (RI=4)	2 (R= 4)	0,5
SLICC (median)	0 (RI=1)	0 (R=1)	0,2
Graffar 4-5	17,9 %	46, 4 %	0,15

P5.58

Diet and glucocorticoid treatment in patients with SLE

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Aim. To investigate whether diet influences GC treatment in SLE patients.
Methods. This study included 114 SLE patients from SLE vascular impact cohort (SLEVIC). We linked dietary data from food frequency questionnaires with data on GC treatment from medical records. Associations between these were analyzed with logistic regression, adjusted for age and gender.
Results. Higher dietary intake of vitamin D was more common in patients treated with GC during ±1 year from inclusion (OR=2.9). Alcohol was inversely associated with GC treatment during ±1 year from inclusion (OR=0.3-0.4). Higher intake of vitamin B12, retinol, and calcium was related to unchanged/increased GC dose during ±1 year from inclusion (OR=3.0-4.6), but higher intake of fatty acid C18:2 and beta-carotene was found in patients with decreased GC dose during -1 year to inclusion (OR=0.3 and 0.2 respectively). Finally, a positive association was seen between higher intake of several nutrients and GC dose levels of >2.5, 5.0, and 7.5 mg/day.
Conclusions. Higher dietary intake of vitamin D did not protect against lupus activity. Higher intake of C18:2 (omega-6) and beta-carotene (anti-oxidant) may protect against increased GC dose. The inverse association between alcohol intake and GC treatment/lupus activity may support existing evidence on moderate intake and improved cardiovascular health in rheumatic diseases. GC treatment may have influenced dietary intake by increasing appetite. Overall, our results showed limited dietary impact on GC treatment in SLE.

P5.59

Comparison of clinical and serologicalmanifestations among juvenile-, adult-, and late-onset systemic lupuserythematosus patients in Korea

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Objectives. Patients with juvenile-onset systemic lupus erythematosus (JSLE) frequently present with severe organ involvement and higher disease activity at the onset of disease. In contrast, patients with late-onset SLE (LSLE) tend to show more insidious onset and mild initial clinical manifestations. However, few studies have investigated differences in clinical manifestations with disease onset in Asian lupus patients.
Methods. We enrolled 201 SLE patients with available clinical data at the time of onset of SLE from the lupus cohort at Chonnam National University Hospital. We divided SLE patients according to age at SLE diagnosis into three groups: JSLE (diagnosed at ≤ 18 years), adult-onset SLE (ASLE, diagnosed at 19-50 years), and LSLE (diagnosed at > 50 years), and compared baseline demographic, clinical, and relevant laboratory findings.
Results. Of the 210 patients, 27 (14.4%), 149 (74.1%), and 25 (12.4%) were JSLE, ASLE, and LSLE patients, respectively. Fever, oral ulcer, nephritis, anemia, and thrombocytopenia were more common in JSLE patients than ASLE or LSLE patients. On the other hand, Sjögren's syndrome was found more frequently in LSLE patients than JSLE or ASLE patients. Disease activity was significantly higher in JSLE patients than in ASLE or LSLE patients. Anti-dsDNA and anti-nucleosome antibodies were found more frequently in JSLE patients and less frequently in LSLE patients and decreased complement levels were more common in JSLE patients and less common in LSLE patients.
Conclusion. Our results showed that SLE patients present with different clinical and serological manifestations according to age at disease onset.

P5.60

Systemic Lupus Erythematosus Complicated by Neuromyelitis Optica

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Neuromyelitis optica (NMO) is a rare autoimmune demyelinating disease of the central nervous system, manifesting with transverse myelitis involving three or more continuous spinal segments and optic neuritis in the presence of NMO-IgG antibodies. NMO is often mistaken for multiple sclerosis and there are relatively sporadic publications about NMO and overlapping systemic or organ-specific autoimmune diseases, such as systemic lupus erythematosus (SLE).

We describe a case of a 50-year-old man who was diagnosed with SLE with cutaneous, articular and hematologic involvement. He presented with deterioration of visual acuity and localized spinal tenderness .NMO was confirmed based on MRI findings and the seropositivity for NMO-IgG. Immunosuppressive therapy was initiated with good results.
We believe that SLE and NMO are parts of the same disease spectrum. When this condition is noticed in patients with refractory, long standing SLE, prognosis is guarded.

P5.61

Pulmonary arterial hypertension and interstitial lung disease in SLE

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Objectives. Pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) can be developed in systemic lupus erythematosus (SLE) and an important prognostic factor. The aim was to assess the prevalence of PAH according to ILD in SLE.
Methods. We screened for PAH in SLE patients who had dyspnea on exertion or ILD by echocardiography in 4 hospitals. PAH was defined as pulmonary artery systolic pressure higher than 40mmHg.
Results. Among 42 patients, 16 patients had ILD, and 4 patients had PAH. There was no difference in the incidence of PAH according to the presence of ILD; 1 patients had ILD (6.3%) and 3 patients had no ILD (11.5%). In pulmonary function test, the lung diffusion capacity for carbon monoxide was 67.2±19.7%, forced vital capacity (FVC) was 86.0±21.9%, and forced expired volume in one second (FEV1) was 89.1±23.5. Only one patient had dyspnea of New York Heart Association functional class (NYHA) III, and 21 patients had NYHA II. FVC and FEV1 were lower significantly in patients with PAH compared to those without (61.9±28.3 vs 88.2±19.8, p=0.045 and 63.6±34.4 vs 91.3±20.9, p=0.049), and uric acid was higher in patients with PAH than those without (6.1±1.9 vs 4.7±1.2, p=0.03).
Conclusion. PAH is combined in 9.5% of SLE patients irrespective of ILD. SLE patients with PAH had decreased FVC and FEV1, and elevated uric acid levels compared to those without.

P5.62

The Relationship between Organ Damage and Quality of Life in Portuguese Patients with Systemic Lupus Erythematosus

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Introduction. Functional status, as assessed by health-related Quality of Life (HRQoL) instruments, is an important outcome measure in quality of care of Systemic Lupus Erythematosus (SLE) patients, increasingly recognised alongside improvement in survival and a need for humanistic and economic studies. Notwithstanding its importance, this is one of the few Portuguese studies that aim to understand the relationship between HRQoL measured by SF-36v2 and EQ-5D-3L and damage accrual.
Methods. The study was prospectively conducted in patients fulfilling the revised 1997 ACR SLE criteria, consecutively enrolled during routine clinical assessment. Age, gender, disease number/type of ACR criteria and organ damage (SLICC/DI) were recorded. Self-reported SF-36 and EQ-5D-3L Portuguese versions of questionnaires were sent by mail. Patient participation was voluntary, informed and confidential.
Results. The 43 respondents were predominantly female (95%). Mean age and disease duration were 49±15 and 10±6 years, respectively, with mean ACR criteria of 6±1. Damage occurred in 19 patients (43%), mean SLICC index 1.6±1. Overall, SF-36 reported consistently lower values in all dimensions when compared to the Portuguese population. Average values for physical and mental component summaries of SF-36 were 42.41±12.6 and 45.21±12.5, respectively. EQ-5D-3L mean was 0.64±0.2. There was no correlation between any of the QoL indices and degree of damage accrual.
Conclusion. As expected with chronic illnesses, SLE results in reduced QoL regardless of th measure used. As previously reported, HRQoL measures seem to complement rather than correlate with permanent disease damage in SLE.

P5.63

The association with Vitamin D levels and disease activation in systemic lupus erythematousus

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Backgrounds. It is controversial whether the levels of vitamin D in plasma was related with disease activity. Aim of our study is to investigate the association between disease activity and vitamin D level in SLE patients.
Patients and Methods. The medical records of total 202 patients were retrospectively reviewed. According to the levels of vitamin D, patients were divided into the low vitamin D group and the normal vitamin D group (25(OH)D <10 ng/mL and 25(OH)D ≥10 ng/mL, respectively). In addition, disease activity was evaluated with laboratory and imaging study including organ involvement of lupus during study period (between 1 year before and 1 year after check for 25(OH) D levels).
Results. The mean 25(OH)D level of 202 SLE patients was 18.44 ng/mL and the mean SLE Disease Activity Index (SLEDAI) score was 4.46. Of 202 patients, 34.2% (69) patients have been experienced lupus flares during study period and flare of lupus nephritis was observed in 18.3% (37) patients among total patients. Prevalence of patients who had history of lupus nephritis were significantly higher in the low vitamin D group (60%) compared to the normal vitamin D group (32.6%). Further, patients with low vitamin D had experienced significantly higher numbers of lupus flare and nephritis flare than patients with normal vitamin D (53.3% vs. 30.8%, 43.3% vs. 14.0%, respectively).
Conclusions. In the present study, lupus flares were more commonly observed in the low vitamin D group than in the normal vitamin D group.

P5.64

Comparison of Health-Related Quality of Life in Chilean Patients with Systemic Lupus Erythematosus, Rheumatoid Arthritis and Systemic Sclerosis

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Depressive symptoms as well as functional impairment are important in determining outcomes in rheumatic diseases. Studies of quality of life in these diseases are important for developing strategies to improve outcomes.
The aim of this study was to compare health-related quality of life scores in patients with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis (SSc), comparing them with healthy individuals.
Using a cross sectional design, comparison of Short-form (SF)-36 Health Survey was used to evaluate: patients with SLE (50), RA (96), SSc (30) and controls (30). The effects of disease activity and duration in functional ability were addressed. All patients met ACR classification criteria for RA, SLE and SSc.
The average physical component summary (PCS) and mental component summary (MCS) scores of patients with RA, SLE and SSc were lower when compared to controls. Lowest PCS score was found in RA patients and the lowest MCS score was found in SLE patients. Disease activity affects physical and mental dimensions in RA group (p<0.001 and p<0.01), no effects were observed in SLE and SSc. Exercise is associated with better physical scores in SLE (p<0.01). For PCS domain, analysis by ANCOVA adjusting by activity and disease duration showed that exercise is the main significant variable (p=0.0097).
RA, SLE and SSc showed clinically significant impairments in PCS and MCS scores, when compared to controls. Exercise is very important in improving quality of life in SLE patients. This information is important for guidance in their treatment and care.

P5.65

Dietary micronutrient intake and atherosclerosis in SLE patients

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Objective. The aim of this study was to investigate whether dietary micronutrient intake differs between SLE patients and controls, and could play a role in lupus activity and atherosclerosis in SLE patients.
Methods. This study included 111 SLE patients and 118 controls from the SLE vascular impact cohort (SLEVIC), Karolinska University Hospital, Stockholm, Sweden. Data on diet (food frequency questionnaires) were linked with data on SLAM, SLEDAI and carotid plaque. Mean dietary micronutrient intakes were compared between a) SLE patients and controls, b) SLE patients with lower and higher lupus activity, and c) SLE patients with and without carotid stable/vulnerable plaque. Association between dietary micronutrient intake and higher lupus activity, and plaque was tested through logistic regression, adjusted for potential confounders.
Results. Micronutrient levels did not differ between patients and controls, and between lower and higher lupus activity. Significantly lower intake of thiamin and niacin was found in patients with plaque. In addition, lower intake (<1st tertile) of iron, potassium and folate was inversely associated with vulnerable plaque (OR=0.3; 95% CI 0.1-1.0) after adjusting for age, LDL, glucose and hypertension. Overall association was found between higher intake (>3rd tertile) of niacin (ORcrude=0.3; 95% CI=0.1-0.8) and plaque.
Conclusions. SLE patients did not have different dietary micronutrient intake compared to controls. Dietary micronutrients were not associated with lupus activity or other manifestations. However, we found associations between some micronutrients and stable/vulnerable plaque of potential importance. Some dietary micronutrients may play a role in atherosclerosis in SLE.

P5.66

Lupus and pregnancy: A challenge !

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Objectives. To review the outcomes of the pregnancies at the SLE
Methods. Study from January 2009 to December, 2014. All the pregnant were diagnosed as SLE referring to the criteria ACR (SLE/APLS) and all have benefited from a follow-up in both specialized obstetrical center and internal specialized consulting.
Results. 25 pregnant women of average age was of 29.5 years, SLE was evolving about 2.9 years average's parity was estimated at 2.5 by pregnant; antecedent of abortion was reported in 32% ; pregnancies were programmed (28%) over one year of remission . Lupus pregnant have history of lupus nephritis (9) requiring immunosuppressive therapy (5) with residual moderate to altered renal function (4) and moderate thrombopenia (2). The APLS was associated (28%) with thromboembolisms events (4). Corticosteroid was increased to 10-15 mg prednisone daily and prophylactic doses of heparin and aspirin were required (100%). Dyslipemia (10), type 2 diabetes (4), and hypertension (4) were the most cardiovascular risks factors associated. HELLP syndrome (2), pre-eclampsia (4), fetal losses or uteri-death (5), transient ischemic strokes (4), failure kidney (2) and cardiomyopathy (1) were the main complications observed. Caesarians were required (75%) and were realized in emergency (25%). We deplore fetal deaths (7) by prematurity, respiratory distress and neo born infections . The maternal death were observed in HELLP syndrome(2).
Conclusion. Despite monitoring and long time of SLE remission the pregnancy was associated in poor prognosis. The cardio metabolic risks factors, altered kidney function, hight corticosteroid and the APLS were predictive to poor outcomes.

P5.67

Could be young age at Systemic Lupus Erythematosus diagnosis a predictive factor for neuropsihiatric involvement?

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Background. Systemic lupus erytematosus (SLE) is a multiorgan disease. Neuropsihiatric disorder can present as seizures, encephalopaty, stroke, psychosis, etc. This type of involvement has a serious impact both on disease activity, but also on damage accrual.
Objective. to determine if there is an association between young age at SLE diagnosis and neuropsihiatric involvement.
Matherial and Methods. We revised the charts of a total of 76 patients diagnosed with SLE, admitted in Sf. Maria Hospital from January 2014 to january 2015. 13 of them had at least one neuropsihiatric disorder according to the ACR nomenclature and case definitions for neuropsychiatric lupus syndromes. For statistical purposes, we matched them by age and sex with 26 SLE patients without this type of organ involvement. The statistic analysis was made with SPSS for Windows Xp.
Results. Age at SLE diagnosis was between 15 and 30 years for 38,5% of patients with neuropsihiatric involvement, wile 3 patients were less than 16 years. 46 % from the SLE patients with this type of suffering had the SLE diagnosis between 31 and 40 years and only 15,5% were older than 40 years. When compared with the patients from the sub-group without neuropsihiatric disorder, association between younger age at SLE diagnosis and neuropsihiatric involvement was significant: p 0.020 and O.R. 2.9.
Conclusions. Neuropsihiatric lupus is still a challenge for clinician and lupus patient. According to our study, young age at SLE diagnosis, including SLE in childhood, represents a predictive factor for neuropsihiatric involvement.

P5.68

What other autoimmune diseases can be associated with Systemic Lupus Erythematosus

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Introduction. Systemic lupus erythematosus (SLE) is a prototypical autoimmune disorder. Autoimmune factors may be common features of SLE and other autoimmune diseases, and both conditions may coexist within some patients.
Materials and Methods. We conducted a retrospective study on patients followed for SLE (ACR criteria) in internal medicine departement (Farhat Hached hospital - Sousse -Tunisia) over 19 years (1995 - 2013). Analyses were performed using the SPSS program, version 18.We studied associations between SLE and other autoimmune diseases.
Results. Eighty five patients are enrolled (71 women and 14 Men, mean age: 34,25 years). SLE was associated to another auimmune disease in 20 cases (23.5%). Sjögren Syndrome (SS) is the most prevalent disease associatied to SLE (14 cases). Patients with SLE associated to SS had almost the same age than patients with isolated SLE. There is no difference in the prevalence of clinical symptoms in patients with or without SS associated SLE. In contrast, Anti-SSA and Anti-SSB antibodies were more frequent in patients with SLE-SS (60% and 40% versus 50% and 40%). Anti-Sm and anti-phospholipid antibodies were less prevalent in SLE-SS (20% vs 10% for Anti-sm and 10% vs 40% for Anti-phopholipid antibodies). Moreover analysis revealed association with rheumatoid polyartrite (Rhupus) in 2 cases, and with dermatomyositis, celiac disease, Hashimoto disease and grave's disease in one case each.
Conclusion. Because of the frequent association of SLE with other autoimmune diseases and particularely with SS, we should be vigilant with some clinical and laboratory characteristics which predict the developement of SLE.

P5.69

Rhupus. The coexistence of systemic lupus erythematosus and rheumatoid arthritis

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The term rhupus is traditionally used for description of the coexistence of systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Within a group of 103 SLE cases 10 had rhupus. In 5 of these patients lupus characteristics appeared first and arthritis followed whereas in the rest arthritis appeared either simultaneously or before lupus characteristics. The aim was to describe two cases of patients with coexistence of SLE and RA or rhupus syndrome.

Two cases of rhupus are described. Both patients were female, aged 43 and 57 years, respectively.
The first patient had the typical clinical picture of RA for 15 years, ulnar hand deviation and typical radiologic RA characteristics. She developed proteinuria, hematuria, leucopenia, low complement C_3 and C_4 levels and positive ANA and anti-dsDNA. Renal biopsy revealed hyperplastic glomerulonephritis. Methylprednisolone and cyclophosphamide pulse therapy were administered followed by low dose prednisolone and mycophenolate mofetil.
The second patient, had SLE for 20 years with positive ANA, light sensitivity, fatique and diffuse arthralgias. She had taken low dose corticosteroids and hydroxychloroquine. Approximately 6 months ago she appeared with the clinical picture of seropositive RA with symmetric polyarthritis and positive anti-CCP antibodies. Methotrexate and the anti-TNFa agent golimumab were administered, the patient being now in remission.
Two cases of rhupus syndrome are described. In the first RA appeared first and SLE features with renal involvement appeared many years later, whereas in the second SLE features appeared first, RA characteristics appearing 20 years later. In patients with rhupus arthritis is a predominant feature.

P5.70

Pro-inflammatory S100 proteins are associated with glomerulonephritis and anti-dsDNA antibodies in systemic lupus erythematosus

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Objectives. Systemic lupus erythematosus (SLE) is associated with elevated levels of S100A8/A9, pro-inflammatory proteins mainly secreted by activated polymorphonuclear neutrophils (PMNs). The underlying mechanisms for increased S100A8/A9 levels and their relation to the clinical phenotype have not been carefully investigated. We assessed S100A8/A9 and S100A12 levels in SLE patient sera in relation to disease activity, clinical phenotype, presence of anti-dsDNA antibodies and ability to promote phagocytosis of necrotic cells (NC) by PMNs.
Methods. Serum levels of S100A8/A9 and S100A12 were measured by ELISA in paired samples of 100 SLE patients at time points of higher and lower disease activity. Serum-mediated phagocytosis of NC by PMNs was analysed by flow cytometry. Clinical data were recorded at time points of blood sampling.
Results. Serum levels of S100A8/A9 and S100A12 were increased in SLE patients with high disease activity compared to paired samples at low disease activity (p=0.01 and p=0.008, respectively). Elevated levels of S100A8/A9 were particularly seen in patients with anti-dsDNA antibodies (p=0.01) and glomerulonephritis before treatment (p=0.02). Immunosuppressive therapy was associated with a reduction of S100A8/A9 serum levels (p=0.002). The ability of serum to support phagocytosis of NC by PMNs was related to increased S100A8/A9 levels (p=0.01).
Conclusions. Elevated serum levels of S100A8/A9 may be used to monitor disease activity and response to treatment in SLE patients, especially in patients with glomerulonephritis. S100A12 may be a marker of disease activity in SLE. Increased S100A8/A9 levels may reflect immune-pathological processes involving phagocytosis of immune complexes by PMNs.

P5.71

Awareness of pregnancy issues and patient's options in a cohort of fertile lupus patients

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Introduction. Systemic lupus does not have a detrimental impact on fertility but in particular conditions could be associated with a negative pregnancy outcome for mother, baby or both.
Objective. To evaluate awareness of lupus pregnancy issues and possible options when poor prognosis factors are associated.
Methods. 86 consecutive fertile lupus patients (mean age 28±8.56) from 3 rheumatology centers were asked to respond to a questionnaire regarding their knowledge about possible pregnancy outcomes and their consequent options.
Results. The majority (89%) was informed by their rheumatologist about the lupus involvement in pregnancy. Most of the women, 84.84% wanted to have children before disease, but just 21% of them, a not statistically significant percentage (p=0.09, r=0.21), changed their option after diagnosis. 50% would accept the pregnancy if it would affect only them self but not the fetus, otherwise only 19.69% would accept the pregnancy if it would be dangerous just for the baby. 28.78% of patients got pregnant after the diagnosis, the number strongly correlates with females that wanted babies before getting ill (p<0.0001, CI 0.2814-0.5801). Just 12% of mothers did not respect the doctor's advice on planning the pregnancy. 83.33% would take account of their partner's option. The majority (93.93%) would prefer a team of rheumatologist and gynecologist during the pregnancy.
Conclusion. Most lupus patients are aware of issues associated with pregnancy but half of them are willing to accept the risk if it would be only for the mother and not for the child.

P5.72

Neuropsychiatric Manifestations in systemic Lupus Erythematosus

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Introduction. The prevalence of neuropsychiatric systemic lupus erythematosus (NPSLE) has been reported in 25-75%. The purpose of study is to determinate prevalence, clinical and immunological patterns NPSLE
Materials and Methods. Eighty five cases of SLE collected in the internal medicine department at Farhad Hached University Hospital of Sousse over a period of 17 years.
Results. Twenty seven patients (31, 78%) have neuropsychiatric manifestations. There were 22 women and 5 men (sex ratio = 4,4). Median age at diagnosis was 33 years ± 10. Neuropsychiatric manifestations were the first symptoms of disease in 1 case. In the other cases, mean time at SLE diagnosis was 3 years (4 months-13 years).
The most common NPSLE manifestations was as follows: seizures disorders (66,6%), psychosis (18,5 %), hemiplegia (14,8%), and polyneuropathy (7,4%) and monoplegia (3,7%). Associated manifestations were : cutaneous involvement(N= 21) , joint involvement (n=18) , pericarditis (n=10) , renal involvement (n=9) and pleural effusion (n= 3).
Anti nuclear antibodies were positive in all cases and anti Sm antibody were positive in 13 cases (46,42%).
All patients were treated by corticosteroids associated to cyclophosphamide.
The evolution was marked by the complete improvement in 18 cases (66,66%),loss of sight in 5 cases (18,5%) , stabilization of lesions in 2 cases (7,4%) and death in 2 cases (7,4%). The univariate analysis model showed association between NPSLE and anti Sm antibody (p=0,032)
Discussion. NPSLE were heterogeneous and may be difficult to detect that's why patients require careful testing to avoid underdiagnosis

P5.73

Immune cytopenias in systemic lupus erythematosus

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Introduction. In the systemic lupus erythematosus (SLE) patients, the cytopenia has emerged as a major hematologic criterion.
Materiel and Method. We retrospectively reviewed 85 patients admitted from 1995 to 2013. We identified patients who presented hematological alterations ascribed to lupus (leucopenia <4000 cells/mm3; lymphopenia <1500 cells/mm3, thrombocytopenia <100 000 cells/mm3; Autoimmune hemolytic anemia (AIHA)).
Results. Hematologic alterations were identified in 25 of 85 (29.4%) SLE patients. They were 21 female and 4 male patients. The mean age was 34 years. In the majority of patients (92%), cytopenia appeared simultaneously at the beginning of SLE. Complete blood count showed leucopenia (72%), lymphopenia (68%) and thrombocytopenia (44%). AIHA (16%) was confirmed by direct antiglobulin test. Evans syndrome was identified in 3 patients (12%). Others systemic manifestations were dermatologic (68%), rheumatologic (60%), cardiac (36%) and renal (36%). In addition, our patients had an association with antiphospholipid syndrome (24%) and another autoimmune disease (28%). Treatment was based on Corticosteroids (96%).

Discussion. Hematological involvement is common in SLE and close monitoring of cytopenia is warranted in most patients. In series, AIHA was occurred in 5-10% and thrombocytopenia in 20-40%. Autoimmune neutropenia and Evans syndrome are rare. Our results do not depart from those of the literature. Corticosteroids are considered the first line of treatment for decades and are effective in about 80% of SLE patients with hematological abnormalities.

P5.74

Cardiac manifestations of systemic lupus erythematosus

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Introduction. Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple-organ systems. The heart is one of the most frequently affected organs in SLE and any part of the heart can be affected.
Material and Method. We retrospectively reviewed 85 patients admitted from 1995 to 2013. All of the patients fulfilled the 1997 revised American College of Rheumatology criteria of SLE. Patients with heart affected were identified.
Results. Cardiac manifestations were occurred in 28 patients (33% of SLE patients). They were 25 female and 3 male patients. The mean age was 35 years. They were symptomatic only in 4 cases (dyspnea). Cardiac manifestations were discovered in 50% of cases at diagnosis. Pericardial effusion was the most common abnormality (96%). Endocarditis was found in 2 cases and myocarditis in one case. Diagnosis was based on cardiac-ultrasound (86%). Pleural effusion was present in 5 cases (18%). Antiphospholipid syndrome was associated in 13 patients (43%). Other more frequent systemic manifestations were hematologic (83%), rheumatologic (73%), dermatologic (56%) and renal (53%). Treatment was commonly corticosteroid (96%) and leads to remission in 25% of cases, relapse in 32% but others were lost sight.
Discussion. Pericarditis is the most common cardiac manifestation as in our patients. Clinically apparent lupus myocarditis is rare. Valvular dysfunction is frequently associated with antiphospholipid antibodies. It is not currently possible to predict who are at greatest risk for the cardiac involvement. Early diagnosis and initiation of treatment often leads to a rapid recovery .

P5.75

Trends of lupus nephritis in Lebanon

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Lupus nephritis is a common yet feared complication of systemic lupus erythematosus. Numerous countries have studied the trends of lupus nephritis in different populations. Similarly to most rheumatologic conditions lupus nephritis is expressed differently with varying ethnicity and geographic area. Only one previous study has documented the trends of lupus nephritis in Lebanon. This current study reflects the trends of lupus nephritis between 1999 and 2014 and compares them to the previous study, which covered the period of 1979-1999, by using a retrospective chart and pathology review of patients at the American university of Beirut medical center. The female to male ratio was 3.4:1 with a mean age of 37.85±12.35 years. Renal histology slides from these patients were assessed according to the World Health Organization classification, and were distributed as follows: class I was found in 6.8% (n=3), class II in 13.6% (n=6), class III in 9.1% (n=4), class IV in 50% (n=22), class V in 15.9% (n=7) and class VI in 4.5% (n=2). When compared to the previous study, class IV lupus nephritis remains the most prevalent class seen, and even more so in this current sample of patients. This is also depicted in different populations, from countries including India, Iran, Tunisia and Spain. All patients were on active treatment. In our series, progression to end stage renal disease was significantly associated with the level of serum creatinine. Other factors including proteinuria, gender and hypertension were not significantly associated.

P5.76

Cerebral Vasculitis in Lupus

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Introduction. Cerebral vasculitis in lupus (CVL) is an inflammation of the brain's blood vessels due to lupus activity. We report a case series with a review of literature
Case series. Four young women among 177 cases of lupus (2.25%) with high activity of SLE presented with CVL. They were seen early in the course of disease, in the first five years of disease. They presented with seizures (n=1), headaches (n=2), hemiparesis (n=1) and psychotic and bizarre behavior (n=1). Brain MRI demonstrated multiple areas with infarcts and/or vasculitis and/or signal abnormalities. The examination of cerebrospinal fluid revealed normal aspect for all patients. High dose steroids and/or cyclophosphamide were prescribed showing good outcomes without significant sequelae (recul of 6 years).
Commentar. CVL is the most serious syndrome associated with lupus. It occurs in the context of important disease activity and other serious clinical manifestations and in younger individuals.

P5.77

Evaluation of cognitive function by electrophysiological study in systemic lupus erythematosus patients with previous neuropsychiatric involvement

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Objectives. This study aimed to evaluate P300 as an electrophysiological marker of cognitive function in NPSLE patients who were diagnosed to have cognitive impairment by standard neuropsychological tests.
Methods. Event-related potentials (ERP) were assessed by the auditory and visual oddball paradigms. Amplitude and latency of P300 at the frontal (Fz), central (Cz) and parietal (Pz) regions were determined and compared to controls.
Result. Sixteen patients with previous NPSLE were identified to have cognitive impairment, defined as one or more tests below 2 standard deviations of demographically normative data, among 20 patients recruited for comprehensive neuropsychological tests. P300 detection was performed in NPSLE patients with cognitive impairment (n=9), matched SLE patients without previous NPSLE (non-NPSLE) (n=9), and healthy controls (n=15). Auditory oddball task did not show any P300 abnormality between groups. Visual oddball task revealed reduced amplitude of P300 over Fz (p=0.002) and Cz (p=0.009) electrodes in NPSLE patients compared to healthy controls and among those who had predominant memory deficit (p=0.01 at Fz). Abnormal P300 was also observed in non-NPSLE patients at Fz and Cz.
Conclusions. P300 elicited by auditory oddball paradigm was not a sensitive electrophysiological marker for cognitive impairment in NPSLE patients. Using visual oddball paradigm, abnormal P300 was found in NPSLE patients over frontal and parietal regions compared to normal controls but was not discriminative from possible subclinical disease in non-
NPSLE patients.

P5.78

Gender differences in Systemic Lupus Erythematosus patients - experience of a Portuguese Rheumatology Center

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Introduction. Systemic Lupus Erythematosus (SLE) affects females more than males, but males appear to have a more severe disease.
Gender differences have been reported for clinical, serological and hematological manifestations. Lupus nephritis seems to be more frequent and severe in males.
Objectives. To evaluate gender differences regarding clinical and laboratorial manifestations of SLE in a Portuguese cohort.
Methods. Retrospective analysis of SLE patients followed at a Rheumatology department, between 2004 and 2015. Demographic, clinical and laboratory data were obtained from medical records.

Results. We identified 79 SLE patients, 73 females (92.41%) and 6 males (7.59%). Mean disease duration was 9.51±7.60 years in females and 8.17±3.31 years in males.
Leukopenia and neurological manifestations (psychiatric symptoms and headaches) were more frequent in females, 50.7% vs 0% and 1.41% vs 0% respectively, whereas synovitis, serositis and renal disease were more frequent in males, 83.33% vs 63.38%, 50% vs 19.72% and 66.7% vs 39.44% respectively. Males with SLE tended to have more severe renal disease with worse treatment outcomes.
Prevalence of cutaneous manifestations were similar in both genders (69.01% in females vs 66.67% in males).
The most frequent presenting manifestation in females was cutaneous whereas in males it was renal. Synovitis was a common presenting manifestation in both genders.
Conclusion. Although less common in men, when it occurs, SLE tends to run a more severe course.
Our findings appear to follow what has been described in literature, with exception to neurological manifestations.

P5.79

The Risk of Mortality in Systemic Lupus Erythematosus: A General Population-Based Cohort Study

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Background. Systemic lupus erythematosus (SLE) is associated with an increased risk of mortality; however, contemporary mortality trends are unknown. We evaluated all-cause mortality among SLE patients in a general population-based setting.
Methods. We assembled a retrospective cohort of all incident SLE cases and a corresponding comparison cohort of up to 10 non-SLE controls matched on age, sex, and entry-time from the general population (1997-2012). We estimated the incidence rates (IRs) of death per 1,000 person-years (PY). We used Cox proportional hazard models to adjust for pre-existing comorbidities, healthcare utilization, and medication use. We conducted subgroup analyses by sex and age group.
Results. We identified 5,356 cases of incident SLE (mean age 49 years; 85.2% female). The IR of death among SLE patients was 33.36 deaths per 1,000 PY compared to 16.13 deaths among controls (Table). After adjusting for covariates, the HR for mortality among this patient population was 1.54 (95% CI: 1.41, 1.68). This increased risk persisted among subgroups by sex and age group, although the association was not statistically significant among patients <45 years old.
Conclusion. Our results suggest that SLE patients from the general population still have an increased risk of premature mortality.

IRs and HRs Associations between SLE and Death

	SLE Status	N	Deaths	IR (Deaths per 1,000 person-years)	Adjusted HR
Overall	Yes	5,356	821	33.36	1.54 (1.41, 1.68)
	No	53,560	3,779	16.13	1.0 (reference)
Female	Yes	4,561	611	28.19	1.48 (1.34, 1.64)
	No	45,610	2,808	13.88	1.0 (reference)
Male	Yes	795	210	71.56	1.75 (1.47, 2.08)
	No	7,950	971	30.32	1.0 (reference)
Age <45	Yes	2,154	89	8.09	1.10 (0.81, 1.48)
	No	21,660	252	2.99	1.0 (reference)
Age 45-59	Yes	1,736	206	24.54	1.40 (1.17, 1.67)
	No	17,360	784	9.40	1.0 (reference)
Age 60-74	Yes	1,086	324	77.34	1.75 (1.52, 2.01)
	No	10,750	1,414	27.71	1.0 (reference)
Age 75+	Yes	380	202	196.77	1.57 (1.32, 1.87)
	No	3,790	1,329	85.29	1.0 (reference)

P5.80

Admissions during 2014 year in patients with systemic lupus erythematosus in a tertiary university hospital in southern Brazil

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Aim. To identify factors associated to intensive care unit (ICU) admission, hospital readmission (RA) and prolonged admission (PA) in hospitalized patients with systemic lupus erythematous (SLE) in 2014.
Methods. We retrospectively reviewed clinical and laboratory features of SLE patients admitted in a tertiary public hospital in a southern State of Brazil during 2014. PA was defined as more than 10 days of hospitalization. Descriptive data including mean, standard deviation, median and percentages were calculated. Qui-square test and Fisher's exact test when appropriate were used for dichotomous categorical variables. Continuous variables were analyzed by Mann Whitney test and p value <0.05 was considered statistically significant.
Results. Forty eight patients were included in this study. Demographic and clinical data were summarized in Table I. Clinical features associated to ICU admission, RA and PA were described in Table II.
Conclusion. Higher SLICC damage index was associated with more ICU admission. Hospital RA was related with antiphospholip syndrome and cumulative dose of prednisone 12 months before the first admission. Cumulative dose of steroid and mycophenolate use were associated to PA. SLE activity and infections were main causes of admission.

Table I. Demographic and clinical features of lupus erythematosus systemic patients admitted in 2014.

Patient''s features	n=48	(100%)
Female	45	(93.8)
European-derived	43	(89.6)
Age at first admission	37 ± 15.2	
Disease duration (years)[b]	7	(2-15)
SLEDAI[b]	5.5	(2-10)
SLICC damage index[b]	1.5	(0-3)
Organ involvement	14	(29.2)
Proliferative Nephritis	33	(68.8)
Hematological	8	(16.7)
Neurological		
Antiphospholip syndrome	5	(10.4)
Treatment	9	(18.8)
Mycophenolate mofetil	32	(66.7)
Azathioprine	19	(39.6)
Cyclophosphamide	22	(45.8)
Metilprednisolone pulse therapy	4.8	(14.2-115.6)
Corticotherapy (grams)[b, c]		
Time of hospitalization (days)[b]	18	(7.2-32.2)
Hospital readmissions	18	(37.5)
Intensive care unit admission	6	(12.5)
Prolonged hospital admission[d]	33	(68.8)
Death	3	(6.2)
Causes of hospitalization	22	(45.8)
SLE activity	13	(27.1)
Infection	2	(4.2)
Cardiovascular disease	11	(22.9)
Others		

[a]years ± standard deviation; [b]median (interquartile range); [c]cumulative dose of prednisone 12 months before the first hospital admission; [d]more than 10 days of hospitalization.

Table II. Clinical features associated to admission in intensive care unit, hospital readmission and prolonged admission[a].

Clinical features	ICU admission		Hospital readmission		Prolonged admission[b]	
	Yes (n=6)	No (n=42)	Yes (n=18)	No (n=30)	Yes (n=33)	No (n=15)
APS (%)	16.7	9.5	**27.8**[c]	**zero**[c]	16.6	zero
SLICC damage index Median	**3.5**[c]	**2**[c]	2	1	2	2
Corticotherapy[d] Cumulative dose (grams)	5.4	4.8	**10.8**[c]	**3.6**[c]	**8.7**[c]	**1.3**[c]
Mycophenolate use (%)	50	14	33.3	10	**27.3**[c]	**zero**[c]

APS: antiphospholipid syndrome; ICU: intensive care unit.
[a]Chi-square test and Fisher's exact test when appropriate for qualitative variables and Mann–Whitney for asymmetric quantitative variables; [b]Prolonged admission was defined as more than 10 days of hospitalization. [c]*p* value <0.05; [d]Cumulative dose of prednisone 12 months before the first hospital admission.

P5.81

Survival analysis of patients with systemic lupus erythematosus in a tertiary hospital in southern Brazil

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Aim. To identify the characteristics and risk factors to predicts mortality and recognize the main causes of death in Brazilian patients with systemic lupus erythematosus (SLE).
Methods. We retrospectively assessed clinical characteristics from 600 patients, followed since 2001 in outpatient clinic from Hospital de Clínicas de Porto Alegre. Nineteen patients lost follow-up. Risk factors for mortality were examined by univariate and multivariate Cox proportional hazards regression analyses.
Results. Clinical features and risk factors for death were reported in Table I and II, respectively. The mean survival was 35.8 years (IC95% 32.9-38.7). The survival rate was 96.0%, 93.6% and 78.0% in 5, 10 and 30 years, respectively. The most common causes of death was SLE activity (37%) and infections (33%).
Conclusion. Antiphospolipid syndrome, elevated SLICC, advanced age at diagnosis and high dose methylprednisolone pulse therapy were risk factors for mortality . Treatment with antimalarials was a protect factor.

Table I. Baseline features of survivors and non-survivors patients with systemic lupus erythematosus in 30 years.

Variables	Non-survivors n=54 (100%)	Survivors n=527 (100%)	*p* value[a]
European-derived	31 (64.5)	389 (75.5)	0.02
Female	42 (87.5)	493 (92.4)	0.10
Age at diagnosis[b]	39.3 ± 15.7	33.3 ± 13.9	<0.001
Disease duration[b]	8.6 ± 7.1	11.6 ± 8.8	<0.001
Last SLEDAI[c]	2 (0-7)	1 (0-4)	0.02
SLICC damage index[c]	2 (1-3)	1 (0-2)	0.009
Organ involvement			
Arthritis	35 (72.9)	394 (74.6)	0.06
Nephritis	21 (43.7)	211(40.0)	0.60
Neurologic disorders	7 (14.5)	58 (11.0)	0.60
Hematologic disorders	38 (79.1)	401 (75.8)	0.30
Comorbidities			
Cardiovascular disease	18 (41.8)	80 (15.9)	0.001
Hypertension	36 (76.5)	279 (53.5)	0.02
Diabetes	10 (22.2)	34 (6.5)	0.001
Antiphospholipid syndrome	8 (18.0)	31 (6.7)	0.003
SLE treatment			
Methylprednisolone pulse therapy	20 (42.5)	140 (28.7)	0.03
Cyclophosphamide	17 (35.4)	143 (28.1)	0.30
Methotrexate	8 (17.0)	95 (18.7)	0.50
Azathioprine	18 (39.1)	240 (46.9)	0.20
Antimalarials	44 (91.6)	507 (97.5)	0.001
Mycophenolate mofetil	5 (11.9)	33 (6.4)	0.20
Cyclosporin	0 (0)	3 (5.8)	0.50
Rituximab	0 (0)	5 (9.7)	0.50

[a]Chi-square test for qualitative variables and Mann–Whitney for asymmetric quantitative variables or Student's t-test for symmetric quantitative; [b]years ± standard deviation; [c]median (interquartile range)

Table II. Cox regression models for 30-year survival rate in systemic lupus erythematosus.

Variables	Univariate Analysis[a] HR (CI 95%)	Multivariate Analysis[b] HR (CI 95%)
European-derived	0.505 (0.278-0.918)	
Sex (female)	0.533 (0.226-1.258)	
Age at diagnosis	1.049 (1.027-1.070)	1.065 (1.039-1.092)
SLICC damage index	1.220 (1.050-1.417)	1.299 (1,076-1,569)
Anti-dsDNA	0.511 (0.277-0.945)	
Arthritis	0.549 (0.288-1.050)	
Cardiovascular disease	2.651 (1.442-4.874)	
Hypertension	2.254 (1.117-4.551)	
Diabetes	2.978 (1.472-6.024)	
Antiphospholipid syndrome	2.986 (1.384-6.443)	3.021 (1.307-6.985)
Methylprednisolone pulse therapy	1.837 (1.024-3.295)	2.628 (1.283-5.383)
Antimalarials	0.288 (0.103-0.804)	0.191 (0.064-0.570)

[a]Were listed the variables with *p* value <0.2; [b]Adjusted to variables with *p* value <0.2 in the univariate analyses besides age. The variables who had a *p* value <0.01 in the multivariate analyses were considered significant.

P5.82

Preliminary studies of the LFA Rapid Evaluation of Activity in Lupus (REAL) to improve consistency and interpretabity of SLE patient progress in clinical trials and real world clinics

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Background. Clinical trial endpoints for SLE have a variety of pitfalls, and are complicated to complete and interpret, especially by busy, real world clinicians.
Methods. The LFA (Lupus Foundation of America) is developing the REAL as an application consisting of a series of efficient, landmarked, linear, 100mm scales with simple instructions. REAL rapidly integrates organ by organ SLE assessment to track progress by symptom or globally. We report a prospective study of SLE patients evaluated by a trained clinical trialist scoring SLEDAI, BILAG, PGA, and REAL as well as by another clinician who scored only REAL without special training.
Results. 99 patients were evaluated: (93% women, mean age 43.4, 34% Caucasian, with SLEDAI 5.5 (± 4.5), BILAG 6.6 (± 6.8), PGA 30.3 (± 24.5). REAL scores of both trained clinical trialists and SLE clinicians without special training correlated with other disease activity measures (see table). The intraclass correlation coefficient of REAL between trained and untrained physicians was 0.71.
Conclusions. The REAL correlates with more complicated validated disease activity measures when used by both expert lupus clinical investigators and clinicians without special training. Community input, refinement and formal validation is planned to optimize the consistency and applicability of the instrument.

	Spearman Rank Correlation Coefficients		
	SLEDAI	BILAG	PGA
Trained Investigator REAL	0.70	0.85	0.84
SLE Clinician REAL	0.58	0.6	0.71

P5.83

A Tunisian experience in Neuropsychiatric Lupus Erythematous

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Aim. In this study we aimed to describe clinical and paraclinical features and therapy approach of neuropsychiatric lupus erythematous (NPLE).
Methods. It's a retrospective comparative study of patients with SLE hospitalized with NPLE between January 2000 and December 2014 in internal medicine departments of Sahloul and Farhat Hached Hospitals in Sousse Tunisia.
Results. A total of 177 patients were included in these analyses. Of them, 55 (31.1%) developed NPLE at or after diagnosis of SLE. It was inaugural for 11 patients. . Neurological findings were headaches (n=23), CNS vasculitis or stroke (n=12), Lupus myelitis (n=1), Cognitive dysfunction (n=3), meningitis (n=1), seizures (n=14), confusion (n=5), psychiatyric manifestations (n=24) and abnormalities of the peripheral nerves (n=4).
The examination of cerebrospinal fluid revealed aseptic lymphocyte reaction in 1 case. MRI finded signal abnormalities (n=35), vasculitis (n=4), cortical atrophia (n=6), lesions of acute stroke (n=8) or cerebral veinous thrombosis (n=3).
Comparative study with 122 control patients showed that NPLE occur early in the course of systemic lupus erythematosus. NPLE associate much more inaugural respiratory manifestations (*p*=0,006) and more significant positivity of serum antiribosomal-P antibodies (*p*=0.008) and APL antibodies (*p*=0.004).
Evolution under corticosteroids and immunosuppressive showed good outcomes (60%), stabilization (20%) or aggravation of lesions in (14.5%) and death (5.5%).
Discussion. Our study show that LES in Tunisia is characterized by high frequency of NPLE with wide spectrum manifestations. NPLE accur early in the course of Tunisian SLE. NPLE remain a major cause of mortality in SLE.

P5.84

Serum Anti-Müllerian Hormone levels in SLE patients and healthy controls

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Background. Systemic lupus erythematosus(SLE) predominantly affects women of childbearing age, can lead to severe organ involvement and may require prolonged immunosuppressive therapy. Anti-Müllerian Hormone(AMH) serum levels are used as a measure of ovarian reserve, reflecting the number of primary follicles.
Aim. To compare AMH serum levels in SLE patients and healthy controls, to assess whether the presence and the severity of the disease, the type of organ involvement and the treatments used may affect the ovarian reserve.
Methods. AMH levels (Beckman Coulter kit) were measured in peripheral blood samples from 80 SLE women of childbearing age with regular menses and 80 healthy age-matched controls (p=0.6).
Results. SLE patients (mean age 30.8±6.3 years, disease duration 7.8±5.9 years, 37 with severe organ involvement, 15 treated with cyclophosphamide, 36 with other DMARDs, 29 with anti-malarials only) had lower serum AMH levels than healthy controls (4.3±3.3vs5.2±3.3 ng/ml, p=0.05). Patients with major organ involvement had AMH levels (3.3±2.8 ng/ml) lower than control subjects (p=0.02), while no difference was found for patients with minor organ involvement (p=0.33). Patients treated with cyclophosphamide showed AMH levels lower than controls (2.7±3.0ng/ml, p=0.02), while no associations with low AMH levels was found for other DMARDs. Patients treated with both methotrexate and cyclophosphamide had AMH levels (1.1±1.9ng/ml) lower than control subjects (p=0.01) and than patients treated with other immunosuppressive agents (p=0.03).
Conclusion. In SLE patients, the ovarian reserve was lower than in healthy controls and its reduction was mainly associated with the use of cyclophosphamide and the severity of the disease.

P5.85

Biomarkers in lupus nephritis: the possible role of serum Cystatin C, serum β2-microglobulin, urinary α1-microglobulin and ACR

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Background. Lupus nephritis(LN) may severely affect SLE prognosis and an effective treatment of LN requires correct diagnosis, timely intervention and early treatment of any disease relapse. Biomarkers able to early identify disease relapse are still lacking.
Aim. To evaluate if some serum (cistatin C, β2-microglobulin) and urinary (α1-microglobulin and ACR- albumin/creatinine ratio) parameters can be more useful than the conventional parameters in monitoring lupus nephritis and in predicting exacerbations of renal involvement in SLE.
Methods. 73 consecutive SLE patients with renal involvement (active or inactive at baseline) were enrolled. Serum cistatin C and β2-microglobulin and urinary α1-microglobulin and ACR levels were evaluated at baseline(T0) and after 3(T3) and 6(T6) months, along with routine clinical and laboratory examination.
Results. Of the 73 LN patients (86.3% female, mean age 38.5±12.0years, disease duration 13.0±8.8years), 49 had inactive and 24 active renal disease at baseline. Patients with active nephritis presented higher levels of SLEDAI (p<0.01), 24 hours proteinuria (p<0.01), as well as of cistatin (p=0.01), α1-microglobulin (p=0.005) and ACR (p<0.01).
During the follow-up, 11 out of the 49 patients with inactive LN at T0 presented some renal relapse. The 11 patients relapsed during the six-month of follow-up showed at baseline higher values of cystatin C (p=0.001), serum β2-microglobulin (p=0.001), urinary α1-microglobulin (p<0.01) and ACR (p<0.01), than patients with stable inactive nephritis, while no differences in traditional parameters (C3, anti-DNA, 24 hours proteinuria, SLEDAI, serum creatinin) were found.
Conclusions. This study seems to show that this biomarkers can be integrated to the conventional parameters for predicting nephritic exacerbations.

P5.86

Interstitial inflammatoryinfiltrate at renal biopsy and outcomes of class IV lupus nephritis

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Background. The role of the extraglomerular kidney interstitial involvement (tubular, peritubular, interstitial) in determining the outcome of lupus nephritis (LN) is still underestimated.
Aim. To establish the prognostic impact of interstitial immune infiltrate on the evolution of renal disease in terms of therapeutic response, number of renal flares, renal remission and chronic kidney damage development.
Methods. 64 patients with a class IV LN (ISN/RPS classification) have been considered at the onset of renal disease. Active interstitial infiltrate at renal biopsy was considered significant when above 10% of the interstitial surface. Therapeutic response at 6(T6) and 12(T12) months follow-up (FU), number of renal flares, persistent renal remission and chronic kidney damage at last FU were evaluated.
Results. Of the 73 LN patients (80.0% female, mean age 41.7±11.6 years, disease duration 8.4±6.8 years), 33 had significant infiltrate (I+) and 31 not (I-). An higher percentage of I+ patients had an active nephritis at T6 than patients without infiltrate (67.9% vs 33.3%; p=0.01), as well as at T12 (52.2% vs 11.5; p=0.002) and at last follow-up (33.3% vs 3.3%; p=0.003). Moreover, I- patients presented higher percentage of early response than I+ patients (70.4% vs 32.1%; p=0.005) and of persistent remission (74.2% vs 28.1%; p<0.01), and lower percentage of renal flare during FU (19.4% vs 59.4%; p=0.01), and of chronic kidney damage (3.2% vs 42.4%; p<0.01).
An early response to therapy (T6) and the absence of significant interstitial infiltrate are the best predictors of persistent remission at multivariate analysis.
Conclusion. The detection of interstitial infiltrate is an important step in defining the prognosis and patients stratification in predicting LN progression.

P5.87

The triple X chromosome mosaic, 45,X/46,XX/47,XXX, among women with systemic lupus erythematosus

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Systemic lupus erythematosus (SLE) is a genetically complicated illness with a sex bias in that about 90% of the patients are women. We have hypothesized that this difference is related to number of X chromosomes, not phenotypic sex. Supporting this hypothesis, we have previously shown that men with SLE have Klinefelter's syndrome (47,XXY) about 15 times more often than SLE-unaffected men. In addition, 46,XX is also increased among men with SLE. Further, we have shown that women with SLE are 3 times more likely to have 47,XXX, which is found in about 1 in 1000 live female births. In this study, we evaluated 2,133 SLE women, all of whom met the 1997 Revised ACR Criteria, for other X chromosome aneuploidies by examining B plots of the X and Y chromosome of Ilumina genome-wide association data. Abnormalities were confirmed by either FISH or kayotype. We found 3 of the SLE women had the triple mosaic 45,X/46,XX/47,XXX. The 95% binomial confidence interval of 0.00003 to 0.0041, or 1/3333 to 1/243, does not contain the estimated incidence of 1 in 25,000 live female births. Each had about 3% 45,X and 3% 47,XXX, with the remaining cells 46,XX. None of 2090 control women had the triple mosaic. We conclude that the rare X chromosome mosaic 45,X/46,XX/47,XXX is increased in women with SLE. Thus, a small percentage of 47,XXX cells is sufficient to increase risk of SLE.

P5.88

Using the American College of Rheumatology and Systemic Lupus International Collaborating Clinics Criteria to Determine Diagnosis of Systemic Lupus Erythematosus in Subacute Cutaneous Lupus Erythematosus

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Approximately 50% of patients with subacute cutaneous lupus erythematosus (SCLE) also meet criteria for systemic lupus erythematosus (SLE). Past studies have examined how such patients meet criteria for SLE using the American College of Rheumatology (ACR) guidelines. New criteria developed by the Systemic Lupus International Collaborating Clinics (SLICC) in 2012 aim to improve the ACR criteria but have not been evaluated in SCLE patients. We sought to determine which SLE criteria patients with SCLE/SLE meet according to the ACR and SLICC criteria in order to compare the two. The information was obtained from an ongoing database of lupus patients seen at the University of Pennsylvania and from their respective medical records. Using the ACR criteria, 30 patients (35%) were classified as SCLE/SLE and 55 (65%) as SCLE-only, compared with 33 (39%) SCLE/SLE and 52 (61%) SCLE-only patients using the SLICC criteria (p=0.75). Overall, SCLE/SLE patients were more likely than SCLE-only patients to have oral ulcers (ACR 60% *vs*. 9%, p<0.0001; SLICC 58% *vs*. 10%, p<0.0001), +anti-dsDNA (ACR 50% *vs*. 6%, p=0.0003; SLICC 48% *vs*. 3%, p=0.0002), and +ANA (ACR 97% *vs*. 35%, p<0.0001; SLICC 91% *vs*. 36%, p<0.0001). Patients with SCLE/SLE were also more likely than SCLE-only patients to have low complement using the SLICC criteria (58% *vs*. 9%, p=0.0003). These findings suggest that SCLE patients who meet criteria for SLE do so by meeting laboratory criteria and do not appear to have significant internal disease. Neither the ACR nor the SLICC criteria identify SCLE patients with major internal disease.

P5.89

Longitudinal, incremental direct medical costs of lupus nephritis amongst a general population-based cohort of systemic lupus erythematosus

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Objective. To estimate the incremental (extra) healthcare costs of lupus nephritis (LN) amongst a population-based cohort of incident cases with SLE compared to SLE cases without LN.
Methods. Our data captured all provincially-funded services (outpatient, hospitalizations, and all dispensed prescriptions) from 1996-2010. We used a validated algorithm to define new SLE cases from administrative health data. LN was defined using a validated case definition (>2 renal-coded encounters AND >2 nephrologist encounters), starting anytime from 12-months prior to SLE diagnosis to end-of-follow-up.
Costs for each encounter/prescription were summed from the first qualifying LN encounter, or the date of SLE diagnosis for non-LN cases, for up to 5 years. We determined the unadjusted incremental costs of LN (difference in mean per-patient-year (PY) costs between SLE-LN+ and non-LN cases), then used generalized linear models to adjust for sex, age, socioeconomic status, and baseline Charlson-Romano comorbidity index.
Results. 4,568 incident SLE cases (86% female, mean age=50±16 years) were followed for 19,139 patient-years, with 303 (7%) eventually meeting the LN definition during follow-up (SLE-LN+).
Over the five years, the unadjusted incremental costs of SLE-LN+ cases averaged $55,659/PY (2010 Canadian), with 57% from hospitalizations. Following adjustment, 5-year costs for SLE-LN+ cases were 2.8-times greater than non-LN.
Conclusion. Among newly-diagnosed SLE patients, those with LN incur, on-average, an additional $39,953 in medical costs per-patient-year over five years compared to those without LN.

	Year of Follow-Up				
	1	2	3	4	5
	Adjusted Cost Ratios (95% CI) between SLE-LN+ and non-LN SLE Cases				
Mean Per- Patient-Year Outpatient Costs	2.3 (2.1-2.5)	2.2 (2.0-2.5)	2.3 (2.0-2.6)	2.1 (1.8-2.4)	2.4 (2.0-2.8)
Mean Per- Patient-Year Inpatient Hospitalization Costs (amongst hospitalized individuals)	1.4 (1.1-1.7)	1.2 (0.9-1.6)	2.0 (1.5-2.7)	2.0 (1.4-2.9)	1.5 (0.9-2.3)
Mean Per- Patient-Year Medication Costs	2.0 (1.8-2.3)	2.1 (1.9-2.5)	2.0 (1.7-2.3)	1.9 (1.6-2.2)	2.0 (1.7-2.5)
Mean Per- Patient-Year Overall Costs	2.3 (2.0-2.7)	1.7 (1.4-1.9)	2.4 (2.0-2.8)	2.0 (1.7-2.4)	1.6 (1.3-1.9)
	Adjusted Incremental Utilization (95% CI) of SLE-LN+ cases (versus non-LN SLE cases)				
Mean Per- Patient-Year Outpatient Encounters	42.2 (37.5-46.9)	30.4 (26.5-34.2)	33.3 (29.1-37.5)	27.4 (23.1-31.6)	31.1 (25.9-36.3)
Mean Per- Patient-Year Inpatient Admissions (amongst hospitalized individuals)	0.09 (-0.41-0.60)	0.29 (-0.24-0.82)	0.40 (-0.28-1.08)	0.23 (-0.63-1.08)	0.26 (-0.54-1.05)
Mean Per- Patient-Year Prescriptions	30.6 (21.3-39.9)	26.4 (14.0-38.7)	28.5 (14.0-43.0)	30.7 (17.9-43.4)	32.8 (17.8-47.8)

P5.90

Early Lupus Project - One-year follow-up of an Italian cohort of patients with Systemic Lupus Erythematosus of recent onset

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Objective. To describe the evolution of a cohort of patients with recent onset SLE during a one-year follow-up period.
Methods. All patients with a diagnosis of SLE (1997 ACR criteria) and a disease duration lower than 12 months were consecutively enrolled in a multicentre prospective study.
Results. A total of 161 patients were enrolled; 90 patients (94.4% Caucasians, 85.5% females) were available for this study having at least 12 months of follow-up. Mean age (SD) of patients at study entry was 37.1 (13.8) years, mean disease duration (from diagnosis until study entry) was 2.8 (3.9) months. In Table I, the frequency of the manifestations included in the ACR classification criteria from onset until enrollment is compared with the frequency during the 12-month follow-up period. InTable II, the frequency of clinical manifestations and laboratory findings at study entry and during the 12-month follow-up period is reported. There was a significant reduction of the hospitalizations, from a median (IQR) of 1 (1-2) at study entry to 0 (0-0) (p<0.001), and of the days of hospitalizations, from 11 (2-18) to 0 (0-10) p<0.001 during the 12 months of follow-up.
Conclusions. During the first year after diagnosis disease course appears to be favorable

Table I. Frequency (from onset until enrollment or during 12 months of follow-up) of the manifestations included in the ACR classification criteria in the cohort of 90 patients with recent onset SLE.

ACR Criteria (%)	Baseline	12 months of follow-up	*p*-value (McNemar test)
Malar rash	36.7	23.6	0.002
Discoid rash	5.6	6.9	ns
Photosensitivity	27	19.3	0.039
Oral ulcers	10.2	9.3	ns
Arthritis	60	42.7	<0.001
Serositis	27.8	12.4	<0.001
Renal manifestations	27.8	20.7	ns
Neurological manifestations	10	8.1	ns
Hematological manifestations	57.8	36.4	<0.001
Immunological disorders	93.3	82.6	0.002
ANA	98.9	100	ns

Table II. Frequency of clinical symptoms and serological findings at study entry and during 12 months of follow-up in the cohort of 90 patients with recent onset SLE.

Clinical and serological findings (%)	Baseline	12 months of follow-up	*p*-value (McNemar test or *Wilcoxon test)
Constitutional	44.2	15.9	<0.001
Mucocutaneous	47.7	34.1	0.035
Neuropsychiatric	10.5	9.2	ns
Muscoloskeletal	59.3	38.6	<0.001
Cardiorespiratory	20.9	4.6	<0.001
Gastrointestinal	5.8	0	ns
Ophtalmic	1.2	1.1	ns
Renal	29.1	19.3	0.008
Haematological	42.4	16.3	<0.001
Low C3	74.1	80	ns
Low C4	85.7	91.5	ns
ANA	97.6	100	ns
anti-dsDNA	77.9	74.7	ns
anti-SSA (Ro)	42	54.6	ns
anti-SSB (La)	14.3	19.5	ns
anti-nRNP	21.8	30	ns
anti-Sm	16.5	17.5	ns
aCL	34.2	47.73	ns
anti-beta2GPI	27.1	42.9	ns
Lupus anticoagulant	22.1	25.6	ns
ECLAM - median (IQR)	2.5 (1.5-4.5)	0.5 (0-2)	<0.001*
SLICC - median (IQR)	0 (0-0)	0 (0-1)	ns*
VAS (quality of life) - median (IQR)	50 (20-70)	50 (10-70)	ns*

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P5.91

Antinuclear antibodies are associated with all-cause mortality and cardiovascular outcomes in the general population

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Background. Individuals with autoimmune disease, especially those with high-titer autoantibodies, have a higher risk for cardiovascular disease (CVD). Antinuclear autoantibodies (ANA) are thought to represent benign autoimmunity in up to 25% of the general population. However, the role of ANA as a potential cardiovascular risk factor in this group has not been clearly defined.
Methods. ANA were measured at baseline in 2803 participants, ages 30-65 years, in the Dallas Heart Study, a multi-ethnic population-based cohort. They were free of CVD, and had no self-reported autoimmune disease or immunosuppressive medication use. Associations of ANA with demographic characteristics, CVD risk factors, biomarkers, all-cause mortality, and incident cardiovascular outcomes, were assessed.
Results. Higher ANA were seen in females and African Americans ($p<0.0001$), hypertensive subjects ($p=0.02$), and nonsmokers ($p<0.0001$). Differences in ANA based on age, diabetes, hypercholesterolemia and metabolic syndrome were not seen. Factors independently associated with ANA included, sICAM-1, CXCL-2, Cystatin C, and sCD40L ($p<0.05$ for each). Over a median follow-up of 9.4 years, 158 total deaths, 54 cardiovascular deaths, and 157 atherosclerotic cardiovascular disease (ASCVD) events were recorded. Adjusting for traditional risk factors, increasing ANA were associated with all-cause mortality (HR 1.26 (1.10-1.46), $p=0.002$), cardiovascular death (HR 1.37, (1.10-1.73), $p=0.01$), and ASCVD (HR 1.18, (1.01-1.37), $p=0.04$). The association of ANA with all-cause mortality and cardiovascular death remained even at titers <1:160).
Conclusions. ANA are associated with inflammatory mediators and biomarkers of vascular activation. Higher ANA are independently associated with all-cause mortality, cardiovascular death, and ASCVD in an ethnically diverse, community based population.

P5.92

Longitudinal, incremental direct medical costs of systemic lupus erythematosus for the first five years after diagnosis: a general population-based cohort study

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Objective. To estimate the incremental (extra) healthcare costs of a general population-based cohort of newly-diagnosed (or incident) SLE for five years after diagnosis.
Methods. Our administrative data captured all provincially-funded outpatient encounters and hospitalizations, and all dispensed prescriptions.
Cases: We used a validated algorithm to identify a population-based cohort of incident SLE for the years 1996-2010 using ICD-9/10 codes.
Controls: Randomly-selected individuals from the general population matched to cases 5:1 on sex, age at diagnosis, and diagnosis-year.
Statistical Analysis: Outpatient and prescription costs were summed directly from billing data. Case-mix methodology was used for hospitalization costs. We estimated the unadjusted incremental costs of SLE (difference in per-patient-year (PY) costs between cases and controls), then used generalized linear models to further adjust for socioeconomic status, urban/rural residence, and Charlson-Romano comorbidity index.
Results. We matched 4,568 incident SLE cases to 22,840 controls (86% female, mean age=50±16 years).
In the first year after diagnosis, unadjusted incremental costs of SLE averaged $11,505 per-PY (2010 Canadian), with 78% from hospitalizations. Following adjustment, costs for SLE cases were 2.3-times higher than matched controls.
While hospitalization rates and costs decreased over Years 2-5, SLE was still associated with significantly-greater outpatient and medication costs (see Table).
Conclusion. Over five years, patients with newly-diagnosed SLE have three-times more medical costs than those without SLE from the general population, even after adjusting for pre-existing comorbidities.

Baseline Characteristics					
	SLE Cases		Comparison Group		*p*-value
N	4,568		22,840		n/a
N Female (%)	3,924 (86%)		19,620 (86%)		n/a
Mean Age at Diagnosis (SD)	49.6 (16.0)		49.5 (15.9)		0.54
Median Baseline Charlson-Romano Comorbidity Score (IQR)	0 (1)		0 (0)		-
Person-Years of Follow-Up	14,571		72,169		-
	Year After SLE Diagnosis				
	1	2	3	4	5
N Cases Followed	4,568	3,712	3,066	2,479	1,952
	Adjusted Cost Ratios between SLE Cases and Matched Controls (95% CI)				
Mean Per-Patient-Year Outpatient Costs	1.8 (1.7-1.9)	1.9 (1.8-1.9)	1.8 (1.8-1.9)	1.8 (1.7-1.9)	1.8 (1.7-1.9)
Mean Per-Patient-Year Inpatient Hospitalization Costs (amongst hospitalized individuals)	1.7 (1.6-1.8)	1.8 (1.6-2.0)	1.4 (1.2-1.6)	1.3 (1.1-1.5)	1.3 (1.1-1.6)
Mean Per-Patient-Year Medication Costs	1.9 (1.8-2.0)	2.0 (1.9-2.1)	1.9 (1.8-2.0)	1.9 (1.8-2.0)	2.0 (1.9-2.1)
Mean Per-Patient-Year Overall Costs	2.3 (2.2-2.4)	2.1 (2.0-2.2)	1.9 (1.8-2.0)	1.8 (1.7-1.9)	1.8 (1.7-1.9)
	Adjusted Mean Per-Patient-Year Incremental Utilization (95% CI) of SLE Cases				
Mean Per-Patient-Year Outpatient Encounters	16.9 (16.1-17.8)	13.1 (12.3-13.8)	13.1 (12.2-13.9)	12.7 (11.8-13.6)	13.6 (12.5-14.6)
Mean Per-Patient-Year Inpatient Admissions (amongst hospitalized individuals)	0.48 (0.31-0.65)	0.20 (-0.01-0.40)	0.42 (0.18-0.66)	0.26 (-0.05-0.57)	0.21 (-0.09-0.52)
Mean Per-Patient-Year Dispensed Prescriptions	11.7 (9.5-14.0)	12.6 (9.5-15.6)	14.7 (11.5-17.9)	16.2 (13.4-19.0)	17.3 (14.0-20.6)

P5.93

Factors Predictive of Flares in Systemic Lupus Erythematosus Patients: Data from a Multiethnic Latin American Cohort

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Purpose. To determine the factors predictive of flares in systemic lupus erythematosus (SLE) patients.
Methods. A case-control study nested within the GLADEL cohort was conducted. Flare was defined as an increase of at least four points in the SLEDAI. Cases were defined as patients with at least one flare. Controls were selected by matching cases by length of follow-up. Demographic and clinical manifestations were systematically recorded by a common protocol. Glucocorticoid use was recorded as average daily dose of prednisone and antimalarial use as percentage of time with antimalarial and categorized as never (0%), occasionally (>0-33%), sometimes (33-66%) and usually (≥66%). Immunosuppressive drugs were recorded as use or not use.
The association between clinical manifestations and flares were examined using univariable and multivariable conditional logistic regression models.
Results. The same number of cases and controls were included (n=465). Mean diagnosis age among cases and controls was 27.4 vs 29.9 years, p=0.002; gender and ethnic distribution were comparable among both groups (p=0.913 and p=0.886, respectively) and so was the baseline SLEDAI (10.3 vs 10.7, p=0.468). Independent factors protective of flares were age at diagnosis (OR=0.919 per every five years, 95% CI 0.867-0.973; p=0.004) and antimalarial use (usually vs never, OR=0.691, 95% CI 0.499-0.955; p=0.025) whereas azathioprine use (OR: 1.795, 95% CI 1.288-2.501; p=0.001) and neurologic involvement were predictive (OR=1.813, 95% CI 1.335-2.462; p<0.001).
Conclusions. Younger age at diagnosis, azathioprine use and neurologic involvement were predictive of flares while more frequent antimalarial use was protective.

P5.94

Diffuse alveolar hemorrhage (DAH) in patients with systemic lupus erythematosus (SLE). Analysis of 78 cases

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Background. DAH is a rare manifestation of SLE. Scarcity of cases makes hard multivariate analysis of factors associated with mortality; moreover, the benefit of therapies is dissimilar for different case series.
Methods. We assessed 78 patients with SLE and DAH from eleven hospitals. We evaluated factors associated with mortality or infections, and the benefit of therapies. Bivariate analysis was performed by X^2 or Fisher tests for categorical variables, Mann-Whitney's U test for continual variables; multivariate analysis was performed by logistic regression.
Results. From the 78 patients, 32 (41%) died. Factors associated with mortality in the bivariate analysis were higher creatinine, lower platelets, requirement of mechanical ventilation, and pulmonary infection during DAH. Independent factors in the multivariate analysis were thrombocytopenia and requirement of mechanical ventilation (Table). None of the drugs was associated with benefit of survival in bivariate analysis or adjusted for mechanical ventilation. In 29 patients (37.2%) a pulmonary infection was detected at admission. The only factor associated with infection was immunosuppressive therapy before the episode of DAH OR: 4.2 (1.3-16.3).
Conclusions. We describe thrombocytopenia, and the requirement of mechanical ventilation as independent factors associated to death in DAH with SLE. Infection is a frequent finding in DAH, mainly in SLE patients who received immunosuppressive therapy before the DAH.

Table I. Factors associated with mortality.

	Dead (n=32)	Alive (n=46)	Bivariate p-value	Bivariate OR (CI:95%)	Multivariate p-value	Multivariate OR (CI95%)
Female n (%)	27 (84.4)	39 (84.8)	1.000			
Age	23.5±17.2	23±13.8	0.651			
MEX-SLEDAI	15±8.2	11±7.8	0.0767			
Hemoglobin	7.1±2.2	7.3±2.1	0.7526			
Creatinine	2.3±1.8	0.7±0.8	0.0006		.0926	1.4 (0.9-2.1)
Platelets	120.5±135	208± 98.2	0.0014		0.0198	0.99 (0.989-0.999)
Hemoptysis n (%)	18 (56.2)	28 (60.9)	0.6833			
MV n (%)	31 (96.9)	29 (63)	0.0003201	17.7 (2.5-780.3)	0.0352	10.8 (1.2-99.6)
Infection n (%)	18 (56.2)	11 (23.9)	0.003652	4.01 (1.4-12.2)	0.0770	2.8 (0.9-9.0)
child n (%)	9 (28.1)	16 (34.8)	0.5354			
Cyclophosphamide n (%)	17 (53.1)	25 (54.3)	0.9151			
Rituximab n (%)	4 (12.5)	1 (2.2)	0.1528			
Plasmapheresis n (%)	4 (12.5)	5 (10.9)	0.8246			
Intravenous immunoglobulin n (%)	7 (21.9)	3 (6.5)	0.08159			

Results are informed as median (IQR) or otherwise informed.

P5.95

Increased Short Term Adverse Events After Total Hip and Total Knee Arthroplasty

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Background. While more SLE patients are undergoing Total Hip and Knee Arthroplasty (THA/TKA) with equivalent benefits to OA, post-surgical adverse events (AEs) may occur.
Method. Patients in our institution's arthroplasty and lupus registies were eligible. Validated SLE cases were matched 2:1 with OA by age, gender, year, and procedure. 6-month AEs were collected through chart review and self-report. Baseline characteristics were compared and regression analysis performed to determine independent predictors of AEs.
Results. 58 SLE THA were matched to 116 OA, 52 SLE TKA to 104 OA. 50% of SLE had AEs after THA vs. 19.8% OA (**p**-value <0.0001); 37.7% of SLE TKA had AEs vs. 28.2% OA (p-value =0.18). A multiple logistic regression analysis controlled for diagnosis, comorbidities, and anesthesia; SLE THA had an increased risk of AEs (OR 3.77; 95% CI 1.74-8.16), but not TKA (OR 1.52; 95% CI 0.70-3.76). Co-morbidities were not significantly associated with AE risk after either (THA: OR 1.69, 95% CI 0.76-3.76; TKA: OR 1.07, 95% CI 0.47-2.43). Conclusion: SLE is an independent risk factor for AEs after THA but not TKA. Higher THA steroid use may be a proxy for higher disease activity, increasing surgical risk, and should be considered when managing post-operative care.

Table I. Patient Characteristics Total Hip Arthroplasty Total Knee Arthroplasty.

	SLE (n=58)	OA (n=116)	*p* value	SLE (n=52)	OA (n=104)	*p* value
Age (SD)	52.0 (2.3)	50.3 (1.8)	0.57	57.9 (2.0)	58.8 (1.2)	0.67
Female, n (%)	51 (89.5%)	105 (90.5%)	0.83	52 (100%)	101 (98.1%)	0.99
BMI (SD)	27.2 (0.8)	27.0 (0.6)	0.88	30.9 (1.4)	32.7 (1.0)	0.30
Unilateral, n (%)	54 (94.7%)	109 (94.8%)	0.93	48 (92.3%)	96 (92.3%)	0.99
Charlson-Deyo Comorbidity, n (%)*			**<.0001**		**0.001**	
0 comorbidities	30 (52.6%)	100 (87.0%)		8 (15.1%)	85 (82.5%)	
1-2 comorbidities	22 (38.6%)	14 (12.2%)		17 (16.5%)	17 (21.8%)	
3+ comorbidities	5 (8.8%)	1 (0.9%)		1 (1.0%)	2 (2.6%)	
Diabetes, n (%)	2 (3.5%)	1 (0.9%)	0.26	10 (18.9%)	13 (12.6%)	0.26
Length of Stay (SD)	6.0 (0.3)	4.7 (0.1)	**0.0008**	5.4 (0.2)	5.0 (0.1)	**0.04**
Operative time (SD)	86.9 (4.4)	84.4 (3.1)	0.65	84.4 (3.6)	87.7 (2.4)	0.45
Coumadin as DVT Prophylaxis, n (%)	38 (65.5%)	30 (25.9%)	**<.0001**	50 (94.3%)	87 (84.5%)	**0.01**
Epidural Block, n (%)	47 (82.5%)	114 (98.3%)	**<.0001**	**	**	**
Pre-Operative Corticosteroid Use	26 (44.8%)	1 (0.9%)	**<.0001**	15 (28.3%)	2 (1.9%)	**<.0001**
Perioperative "Stress-Dose" Steroid Use	31 (53.4%)	2 (1.7%)	**<.0001**	16 (30.2%)	3 (2.9%)	**0.001**

*SLE excluded in comorbidity count. **Not recorded.

Table II. Adverse Events Total Hip Arthroplasty Total Knee Arthroplasty.

	SLE (n=58)	OA (n=116)	*p* value	SLE (n=52)	OA (n=104)	*p* value
Major Events						
Acute Renal Insufficiency	5 (8.6%)	0 (0%)	**0.004**	0 (0%)	0 (0%)	N/A
Arrhythmia	1 (1.7%)	0 (0%)	0.33	3 (5.7%)	4 (3.9%)	0.99
Deep Vein Thrombosis	2 (3.4%)	0 (0%)	0.11	0 (0%)	0 (0%)	N/A
Falls	6 (10.3%)	2 (1.7%)	**0.02**	1 (1.9%)	4 (3.9%)	0.52
Post-Operative Fracture	2 (3.4%)	0 (0.0%)	0.11	0 (0%)	1 (1.0%)	0.99
Dislocation	5 (8.6%)	3 (2.6%)	0.12	0 (0%)	0 (0%)	N/A
Additional Surgery	4 (6.9%)	0 (0%)	**0.01**	9 (17.0%)	13 (12.6%)	0.19
Any Major Event	15 (25.9%)	12 (10.3%)	**<.0001**	13 (24.5%)	20 (19.4%)	0.40
Minor Events						
Superficial Surgical Site Infection	4 (6.9%)	1 (0.9%)	**0.04**	3 (5.7%)	1 (1.0%)	0.07
Excessive Surgical Site Drainage	3 (5.2%)	1 (0.9%)	0.09	2 (3.8%)	4 (3.9%)	0.99
Surgical Site Ecchymosis	0 (0%)	2 (1.7%)	0.55	1 (1.9%)	3 (2.9%)	0.72
Surgical Site Erythema	3 (5.2%)	2 (1.7%)	0.33	4 (7.5%)	4 (3.9%)	0.39
Spinal Headache	2 (3.4%)	0 (0%)	0.11	0 (0%)	1 (1.0%)	0.99
Delayed Wound Healing	0 (0%)	2 (1.7%)	0.55	1 (1.9%)	1 (1.0%)	0.62
Any Minor Event	20 (34.5%)	12 (10.3%)	**0.002**	8 (15.1%)	11 (10.7%)	0.39

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P5.96

Factors associated with early damage accrual in patients with Systemic Lupus Erythematosus: 12-month preliminary results from the inception cohort of the multicenter Early Lupus Project

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Objective. To evaluate the early damage accrual and risk factors for damage in the Early Lupus Project, an inception cohort of consecutive patients diagnosed with SLE.
Methods. We report on the development and progression of damage assessed by the SLICC/ACR Damage Index (SDI) within 12-month of disease. SDI represent irreversible damage occurred after onset of SLE and present for at least 6 months; by definition, it scores 0 at disease onset.
Results. A total of 119 patients (93.3% Caucasians, 18 males) were eligible for this study having available data at 12 months of disease. Mean age at and mean disease duration from recognition of 4 ACR criteria was 36.7±14.1 years and 2.5±3.9 months (median = 1 month; interquartile range 0-3.1), respectively.
At 6 months of disease, 28 (23.5%) patients had an SDI score ≥1. At 12 months of disease, 31 (26.0%) patients had an SDI score ≥1 and only three patient had increase in pre-existing damage.
Stepwise regression models identified older age at diagnosis (p<0.01; OR 1.1 95% CI 1.0-1.3), higher number of active BILAG2004 clinical domain (p<0.01; OR 1.7 95% CI 1.2 - 2.4) and neuropsychiatric involvement at baseline (p<0.01; OR 6.7 95% CI 1.4-32.2) as independent risk factors for early development of damage in this cohort. No influence of active renal involvement and medications was detected.
Conclusions. Development of organ damage begins early in patients with SLE. Identify associated risk factors since early stages of the disease may improve short-term outcome.

P5.97

Gender influences the clinical course of lupus erythematosus (LE) - a retrospective cohort study

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Background. Gender-specific medicine aims to identify differences in disease between men and women.
Objective. To determine differences between men and women in lupus erythematosus (LE) patients were analysed in respect of clinical characteristics, laboratory parameters, and long-term outcome.
Methods. All patients diagnosed with LE from 01/2000 to 12/2013 at the outpatient clinic of dermatological autoimmune diseases from the department of dermatology and venereology (Medical University of Innsbruck) were retrospectively analysed. 83.3% (n=384) were women and 16.2% (n=74) were men. Follow-up time was mean 8.2 years.
Results. Women more frequently fulfilled SLICC criteria for systemic LE than men. Any type of internal organ manifestation was more common in women. Chronic cutaneous LE and subacute LE were equally likely to be diagnosed in both sexes. However, LE tumidus was mainly diagnosed in men and acute cutaneous LE was more frequently diagnosed in women. According to logistic regression modelling men with LE differ from women in respect of thrombocytopenia (OR 2.2), smoking (OR 2.7), malignancy (OR 2.4), and the absence of musculoskeletal manifestations (OR 0.4) and complement consumption (OR 0.4).
Limitations. A retrospective descriptive single-centre study.
Conclusion. Gender differences exist in LE. Women usually have a more severe clinical course of disease and are subject to a higher risk of internal organ involvement. However, in the long-term men should be monitored for associated malignancies.

P5.98

Disease activity patterns over time in patients with SLE - A retrospective descriptive analysis of the Hopkins Lupus Cohort

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Background. Systemic Lupus Erythematosus (SLE) is a multi-systemic inflammatory disease, characterized by an extreme variability of its expression, both between individuals and within individuals, over time. Overall disease activity appears to be an important predictor of both mortality and organ damage. It is therefore important to understand the burden of disease course over time among patients with SLE.
Objectives. To discern and describe SLE disease activity patterns over time by analyzing data from the Hopkins Lupus Cohort.
Methods. Disease activity was retrospectively studied in a cohort of 2386 consecutive SLE patients followed up quarterly for 1-28 years (10 367 person-years of followup). SLE disease activity patterns were defined using 1) Physician Global Assessment (PGA) and 2) SLE Disease Activity Index (SLEDAI), including serology: Long Quiescent (LQ), SLEDAI/PGA=0 for 1 year at all visits; Relapsing-Remitting (RR), periods of disease activity (SLEDAI/PGA>0) interspersed with periods of disease inactivity (SLEDAI/PGA=0) at 1 or more visits during 1 year; Chronic Active (CA), SLEDAI/PGA scores are >0 for 1 year at all visits. Disease activity at yearly intervals ("1-year blocks") was readily classified into 1 of the 3 major patterns for each patient. The pattern in each patient of 3 consecutive followup years ("3-year blocks") was also determined: Persistent Long Quiescent (pLQ), LQ pattern in each of the 3 years; Persistent Remissing-Remitting (pRR), RR pattern in each of the 3 years; Persistent Chronic Active (pCA), CA pattern in each of the 3 years; Mixed, at least 2 different pattern types during 3 consecutive years. The frequency of different pattern groups (LQ, RR, CA) in each "1-year-block" and pattern subgroups (pLQ, pRR, pCA, Mixed) in each "3-year-block" of followup was examined.

Results. Three major patterns of SLE disease activity were identified: LQ, RR, and CA. The RR pattern accounted for the greatest proportion of followup time for both the SLEDAI and PGA, representing 48.3% and 51.8% of total person-years, respectively. The CA pattern was the second most frequent pattern observed (SLEDAI 35.5%, PGA 38.5% of total person-years). The least prevalent pattern was the LQ (SLEDAI 16.1%, PGA 9.5% of total person-years), indicating that 655 patients experienced 1674 LQ "1-year-blocks", and 352 patients experienced 981 LQ "1-year-blocks", using SLEDAI and PGA, respectively. When disease activity was defined within 3-year intervals, the Mixed pattern was the most common for both the SLEDAI and LAI, representing 55% of total "3-year blocks". The pRR and pCA patterns were intermediate and similar in frequency (pRR 19.8%, pCA 20.7%). The pLQ was the least frequent pattern (SLEDAI: 5.7% and PGA: 2.8%). The most common discrepancy between instruments was that the PGA demonstrated CA when the SLEDAI showed an RR pattern. The SLEDAI was more likely to depict the LQ pattern than was the PGA.
Conclusion. In this large cohort, the three major patterns of SLE disease activity as originally identified by Barr et al. were confirmed. In the present study, the RR pattern appeared to be the most prevalent pattern type. Long quiescence was achieved in a subset of patients. Over a 3-year perspective almost half the patient maintained their disease activity pattern.

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

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

P5.99

How good a job are we Rheumatologists doing in screening for Hepatitis B and C before initiating Immuno-suppressive/s in SLE?

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Purpose. Various organizations have poorly defined guidelines for Hepatitis B/C screening before initiating immunosuppressive medications (ISM). We sought to quantify the prevalence and correlates of Hepatitis B and C screening among Systemic Lupus Erythematosus (SLE) patients on ISM.
Methods. Retrospective chart review of 100 SLE patients receiving ISM in rheumatology clinics was done. ISM use defined as current use of any ISM including corticosteroids(CS). Significant ISM use was defined as current use of prednisone ≥7.5 mg/day along with another ISM other than Hydroxychloroquine. Chi square test was used to compare discrete variables, while t tests were used to compare continuous variables.
Results. 86% were women; mean (SD) age was 27.9±4 yrs. 41% were on one ISM, 41% on two & 19% were on three ISM's.
Hepatitis B & C screening tests were performed in 34% and 33% patients respectively. 34/34 tested negative for Hepatitis B Surface Antigen, 12/29 had Hepatitis Surface Antibody, 2/29 Hepatitis B core Antibody & 1/33 had Hepatitis C antibody.
Screening tests were offered more frequently to younger patients, those on ≥ one ISM, those on steroids, or those on significant ISM. Among those on significant ISM, 47% were screened for HBS Ag, as compared to 22% of patients not on significant ISM (p=0.007). Likewise, 47% on significant ISM were screened for HCV Ab as compared to 20% not on significant ISM (p=0.004).
Conclusion. Hepatitis B & C screening rates are low and range from 30-50% in patients receiving ISM in SLE (<40%).

P5.100

Minorities with Lupus Nephritis and Medications: A study of Facilitators to Medication Decision-Making

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Objectives. To examine the perspectives of women with lupus nephritis on facilitators to medication decision-making.
Methods. We used the nominal group technique (NGT), a structured formative process to elicit patient perspectives. An NGT expert moderated eight patient group meetings. Participants (n=52) responded to the question "What sorts of things make it easier for people to decide to take the medicines that doctors prescribe for treating their lupus kidney disease?" Patients nominated, discussed, and prioritized facilitators to medication decisional processes.
Results. 52 women with lupus nephritis participated in 8 NGT meetings (27 African-American, 13 Hispanic and 12 Caucasian). Average age was 40.6 years (SD, 13.3) and disease duration was 11.8 years (SD, 8.3), 36.5% obtained college education and 55.8% had difficulty in reading health materials. Patients generated 280 decision-making facilitators (range= 26-42 per panel). Of these, 102 (36%) facilitators were perceived by patients as having relatively more influence in decision-making processes than others. Prioritized facilitators included, effective patient-physician communication regarding benefits/harms, patient desire to live normal life and improve quality of life, concern for their dependents, experiencing benefits and few/infrequent/ no harms with lupus medications, and their affordability. Relative to African-Americans, Caucasian and Hispanic patients endorsed a smaller percentage of facilitators as influential. Level of agreement with which patients within panels independently agreed in their selections of the three most influential facilitators ranged from 33% to 60%.
Conclusions. We identified facilitators to lupus medication decision-making. This information will be used to populate a decision aid for lupus nephritis.

P5.101

Chronic daily headache in Korean patients with systemic lupus erythematosus

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Neuropsychiatric systemic lupus erythematosus (NPSLE) includes a broad spectrum of neurologic and psychiatric manifestations. One of the most commonly observed neuropsychiatric symptoms is headache. However, the lack of specific clinical distinctions for headache in SLE has made it difficult to elucidate its pathophysiology. The aim of this study is to evaluate the neurometabolic changes using Proton Magnetic Resonance Spectroscopy (^{1}H-MRS) in patients with SLE who suffer from chronic daily headache (CDH). SLE and fibromyalgia patients with CDH and healthy controls were recruited (N = 9, N = 5, and N = 6, respectively). ^{1}H-MRS metabolite ratios were evaluated in bilateral basal ganglia (BG) and bilateral peritrigonal white matter (PWM). ^{1}H-MRS showed a significantly decreased *N*-acetylaspartate (NAA)/creatine (Cr) ratio in right BG in SLE patients with CDH compared to fibromyalgia patients with CDH and normal controls (p=0.029 and p=0.020, respectively). Left PWM NAA/Cr and Choline/Cr ratios in SLE patients with CDH were lower than those in fibromyalgia patients with CDH (p=0.019 and p=0.029, respectively). This study suggests the possibility that CDH in patients with SLE might be associated with neuronal dysfunction and neurometabolic changes.

P5.102

Anti-C reactive protein antibodies in Korean patients with systemic lupus erythematosus

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Background. We aimed to investigate the relationship between anti-CRP antibody and the disease activity markers in Korean patients with SLE.
Methods. We recruited 34 patients with SLE (31 women, 3 men; mean age 38.2 years) and 36 healthy subjects (33 women, 3 men; mean age 42 years) as normal controls (NCs). The presence of anti-CRP antibody was analyzed by enzyme-linked immunosorbent assay (ELISA). Data on clinical variables and disease activity markers, such as complement, anti-dsDNA antibody, and systemic lupus erythematosus disease activity index (SLEDAI) were recorded. The level of serum anti-CRP antibody patients were devided by the And we also compared the serum anti-CRP antibody level in SLE patients with lupus nephritis and without lupus nephritis.
Results. The level of serum anti-CRP antibody in SLE patients (11.27±5.64 μg/mL) was significantly higher than that of healthy controls (9.09±2.79 μg/mL, p=0.043). Anti-CRP antibody was positively correlated with the duration of disease(r = 0.447, p=0.004). However no difference in serum anti-CRP antibody levels was observed between the patients with lower complement levels, lower positivity for anti-dsDNA antibodies, and higher SLEDAI score and those who were not. And also there was no significant difference in the level of anti-CRP antibody between the patient with lupus nephritis and the without lupus nephritis.
Conclusions : This study shows the presence of serum anti-CRP antibody in Korean SLE patients. But there was no significant relationship between anti-CRP antibody and disease activity markers.

P5.103

Expression of serum B cell activating factor from the tumor necrosis factor family (BAFF) in systemic lupus erythematosus (SLE): relationship with disease features

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Background. B lymphocyte stimulator signaling pathway by BAFF has an important role in the selection, maturation and survival of B cells and plays a significant role in the pathogenesis of SLE.
Methods. The study included 73 pts (85% females, age 30,0 [28,0-46,0] years (median [interquartile range 25%-75%]) with SLE (ACR criteria, 1997) and 47 healthy controls (96% females, age 31,0 [26,0-49,0] years). Serum levels of BAFF (ng/ml) were measured by ELISA (Bender MedSystem GmbH, Austria). Statistical analyses were performed with STATISTICA program, version 8.0.
Results. Mean SLE duration was 5,0 [1,5-11,0] years, SLEDAI 2K score - 8 [2-13], SLICC damage index score - 0 [0-1], current prednisone dose - 10,0 [7,5-25,0] mg/day. SLE pts had no difference in BAFF level vs control (0,02 [0,01-0,64] vs 0,02 [0,01-0,03] ng/ml). In SLE pts serum BAFF level correlated with hemoglobin level (r=-0,289, p<0,05), CD19 B-lymphocytes absolute counts (r=0,655, p<0,05), erythrocyte in urine (r=0,261, p<0,05), SLE duration (r=-0,261, p<0,05) and SLICC (r=-0,286, p<0,05). SLE pts with lupus nephritis (n=29 (40%)) as compared to pts without nephritis (n=44 (60%)) had higher BAFF concentration 0,27 [0,02-0,70] vs 0,02 [0,01-0,03] ng/ml, p<0,01. SLE pts with high activity (SLEDAI 2K≥8) (n=37 (51%)) had higher levels of BAFF than the pts with SLEDAI 2K<8 (n=36 (49%)) - 0,09 [0,01-0,70] vs 0,02 [0,01-0,02] ng/ml, p<0,05.
Conclusions. In our study there is no difference in BAFF level in SLE patients and healthy control. Patients with lupus nephritis and high disease activity had higher BAFF concentration as compared SLE patients without them.

P5.104

Malignancy risk in systemic Lupus Erythematosus patients treated with cyclophosphamide

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Background. Cyclophosphamide (CYC) remains the first of choice for severe forms of rheumatic diseases but is associated with significant toxicities. For this reason, we investigated side effects of CYC in our SLE patients retrospectively. Here, we report the malignancy incidence of our group as a subgroup analysis.
Method. Data of 306 (F/M:263/43) SLE patients treated with CYC from 13 university hospitals in Turkey were evaluated. Inclusion criteria were; being older than 18 years of age, CYC usage at least 3 months and follow-up more than 1 year after CYC therapy started. Exclusion criteria were; cancer occurrence before or within 1 year of SLE diagnosis.
Results. Totally 306 SLE patients were followed in 2472 patient-years, with a average follow-up of 7 (IQR: 4-11) years. We identified 6 (1.9%) malignancy in 305 patients, with a corresponding all cancer incidence of 215/100000. The median time for diagnosis to cancer was 7.5 (range 1.3-18) years. Two patients developed hematologic malignancies, 2 solid organ cancers (lung and renal cell cancer) and 2 skin cancers. Cumulative CYC dosage and duration of CYC therapy were higher in patients with cancer than without [16(IQR:11-38) vs. 9(IQR: 6-15) gram, p=0.01 and, 21(IQR;11-48) vs. 12 (IQR; 6-18) months, p=0.02, respectively]. Malignancy risk were associated with male gender (HR: 7.7, %96CI: 1.3-44, p=0.01) and cumulative CYC dosage (p=0.008) on Cox regression model.
Discussion. We observed 6(1.9%) cancers in SLE patients treated with CYC. Malignancy risk was related with cumulative CYC dosage. In addition we found nearly seven-fold higher risk of malignancy in male patients.

P5.105

Factors associated with recognition of depression by healthcare providers in systemic lupus erythematosus

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Objective. To examine the recognition of depression by a treating physician in SLE patients with depressive symptoms.
Methods. SLE patients from a population-based cohort were screened for depression using the Patient Health Questionnaire (PHQ-9). A subset of those with moderate to severe depressive symptoms (PHQ-9 >10) cared at a large lupus clinic within the major healthcare system that serves the indigent population in Georgia, US, was examined. Electronic medical record documentation of either a diagnosis of depression, a prescription of antidepressant drugs, or a referral to psychiatric and/or a psychology practice was used to define depression recognition. The proportion of depression recognition for an observation period (OP) of 6 and 12 months before- and after-PHQ-9 completion, and factors associated with depression recognition were examined.
Results. Of 73 SLE patients with a PHQ-9 >10 and at least one lupus clinic encounter within each OP, depression was recognized in 36 (49%) and 45 (63%) within the 1- and 2-year OP, respectively.

Factors Associated with Depression Recognition: Multivariate Analysis

Sociodemographic and Disease Factors	1-year OP OR (95% CI)	p-value	2-year OP OR (95% CI)	p-value
Age (5-year increment)	1.5 (1.0 -2.1)	0.06	1.3 (0.9-2.0)	0.2
Race				
Black vs. Non-Black	3.3 (0.2-68.8)	0.4	0.6 (0.0-10.7)	0.7
Number of Outpatient Visits (3-visit increment)	0.5 (0.3-1.1)	0.1	0.7 (0.4-1.4)	0.3
Insurance				
Private or Medicare vs. No insurance or Medicaid	0.3 (0.1-1.4)	0.1	0.6 (0.1-3.1)	0.6
Education				
>=College vs. <=High school	0.3 (0.1-1.3)	0.1	0.5 (0.1- 3.0)	0.4
Organ Damage (SA-BILD)				
Severe (> 3) vs. None or Mild (0-2)	1.2 (0.3-4.6)	0.8	2.0 (0.4-9.1)	0.4
Disease Activity (SLAQ)				
Severe (> 17) vs. Mild or Moderate (0-16)	7.1 (1.1-44.4)	**0.04**	4.5 (0.5-44.2)	0.2
Duration of Disease (3-year increment)	0.9 (0.7-1.2)	0.4	0.8 (0.6-1.1)	0.2
Physician Set Clear Treatment Goals				
Yes vs. No or Do Not Know	3.6 (0.9-14.8)	0.08	20.5 (2.4- 173)	**0.006**
Primary Care Physician Visit				
Yes vs. No	2.2 (0.3-16.3)	0.4	1.6 (0.2-15.0)	0.7
Rheumatologist Visit				
Yes vs. No	0.5 (0.0-15.7)	0.7	0.3 (0.0- 8.0)	0.5
Has a Regular Doctor				
Yes vs. No	0.9 (0.1-11.2)	0.9	2.2 (0.1- 39.9)	0.6

SLAQ: Systemic Lupus Activity Questionnaire; SA-BILD: Self-Administered Brief Index of Lupus Damage.

Conclusion. Our findings suggest that patient-physician interactions and disease characteristics play major roles in the recognition of depressive symptoms among patients with SLE. While more severe disease activity may contribute to greater provider awareness of depressive symptoms in the short term, acknowledgement of patients concerns and clear definition of treatment goals may play a more significant role in the long-term.

P5.106

The association of systemic lupus erythematosus with risk of osteonecrosis - a Danish nationwide population - based case - control study

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Background. Osteonecrosis (ON) is a well known complication in patients with systemic lupus erythematosus (SLE), but population - based studies are scarce.
Objective. To investigate the impact of SLE on the risk of incident ON.
Methods. Cases consisted of all patients with a first hospitalization for ON in entire Denmark between 1995 - 2012. Ten population control subjects matched on sex, age, ethnicity and residency were randomly selected on the ON index date. We used logistic regression to estimate odds ratios (ORs) for incident ON, adjusted for other comorbidities.

Results. We included 4,107 ON case patients (median age 62 years) and 41,063 matched controls. Among ON cases, 251 patients (6.1%) had received a diagnosis of any CTD within 5 years as compared with 666 (1.6%) controls. 30 ON patients (0.7%) had SLE as underlying disorder, versus 19 (0.0%) controls. The crude OR for the association between any CTD and ON was 4.0 (95% CI 3.4 - 4.6), and the adjusted OR was 3.5 (95% CI 3.0 - 4.1). In comparison, the crude and adjusted ORs for ON associated with SLE alone were substantially higher, crude OR 15.9 (95% CI 8.9 - 28.2), and adjusted OR 9.7 (95% CI 5.3 - 17.7).
Conclusions. The risk of incident ON is almost 10 times increased in individuals with SLE, as compared to a 3.5 - fold increased risk associated with CTD in general. To our knowledge, this is the first population-based study focusing on the impact of SLE on incident ON.

P06 Antiphospholipid syndrome

P6.01

Two Cases of High Triple Positive Antiphospholipid Antibody Profile with SLE

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Antiphospholipid syndrome, is a systemic autoimmune disease characterized by venous & arterial thrombosis, pregnancy morbidity as well as presence of antiphospholipid antibodies. Anticardiolipin antibodies (aCL) are the most common antibody detected. APS can be present in 9.3 to 10% of SLE patients. We present two patients with positive ANA as well as high triple positive antiphospholipid antibodies.
Case Series. CB presented with recurrent digital gangrene & subsequent disarticulation. She was admitted due to a new ulcer at the left ankle. She is a G2P1 (1011), with a miscarriage at 12 weeks AOG. Two days after debridement, she developed interstitial pneumonitis. APS profile showed significant titers of LAC (moderately present) anticardiolipin (IgG > 120, IgM 12.3) & B2 glycoprotein (IgG >100). She was started on warfarin.
TD presented with of left sided weakness, dysarthria & and an acute frontal infarct by MRI. She is also a G2P1 (1011). Her LAC was moderately present, anticardiolipin (IgG>120, IgM 28.6), & B2 glycoprotein (IgG >100, IgM 27.7). She was also given warfarin.
Conclusion. Triple-positive APS patients have a high recurrence rate & high risk of thrombosis. Warfarin with a target INR of 2.0 - 3.0 is more effective than low-dose aspirin. Management of the thrombotic complications in these patients can be extremely challenging due to competing risks of bleeding and thrombosis.

P6.02

Does Anti-DNA positivity increase the incidence of secondary antiphospholipid syndrome in lupus patients?

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Aim of the work. to detect the incidence of secondary antiphospholipid syndrome (APS) among Systemic lupus erythematosus (SLE) patients with positive anti-DNA antibodies.
Patients and Methods. We studied 342 SLE patients; Group I: Anti-DNA positive SLE patients (n=208) and Group II: Anti-DNA negative SLE patients (n=134), with a female to male ratio of 9.39:1 and a mean age of 27.49±7.94 years and disease duration of 5.74±3.97 years. Full history taking, thorough clinical examination, laboratory and relevant radiological investigations were performed. Disease activity was assessed using systemic lupus erythematosus disease activity index (SLEDAI). Anti-ds DNA tests were carried out by indirect Immunofluorescence (IF) technique. Anti cardiolipin antibodies (IgG and IgM) and Anti-β2 glycoprotein-I antibody of IgG and/or IgM isotype were detected by ELISA.
Results. The clinical manifestations, disease activity and laboratory investigations of the SLE patients varied according to the anti-DNA antibodies. Thirty-six patients (17.3%) had secondary APS in those with positive anti-DNA antibodies while only16 (11.9%) had secondary APS in those with negative anti-DNA antibodies, with no significant differences between both groups.
Conclusion. Apparent higher incidence of secondary APS was detected in anti-DNA positive SLE patients. The non significant differences between both groups may suggest that Anti-DNA positivity cannot be considered as the only predictor of secondary APS and further studies may be needed to detect other factors which may increase the incidence of APS in SLE patients.

P6.03

Serum coagulation markers and cerebral MRI in lupus patients with antiphospholipid antibodies and cognitive dysfunction

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Cognitive dysfunction is a common manifestation of neuropsychiatric systemic lupus erythematosus (NP-SLE), and has been associated with anti-phospholipid antibodies (APLA), though the underlying mechanisms remain unclear. In this pilot study, we explore the hypothesis that cognitive dysfunction in SLE with APLA is due to cerebral microvascular thrombosis.
Nine APLA-positive patients with SLE underwent standardized neuropsychological testing, laboratory coagulation, and brain MRI with arterial spin labeling (ASL) with functional resting MRI (rs-fMRI) to evaluate brain regional blood flow and metabolism.
The study sample was 89% female, with average disease duration of 18.2 years. Median SLEDAI score and SLICC damage index were 1. Non-specific inhibitor was present in 89% of patients, anti-cardiolipin antibody in 44%, and beta-2 glycoprotein-1 in 22%.
Ongoing data analyses involve: 1) associations of T-scores on neuropsychological tests with results of coagulation biomarkers; 2) associations of ASL/rs-fMRI data with T-scores from each domain on neuropsychological testing, as well as with coagulation biomarkers.
Results from these pilot data will be discussed, with a view to informing design of a larger study which will recruit patients with SLE and APLA, as well as controls with SLE without APLA, and healthy volunteers.

P6.04

Risk of antiphospholipid nephropathy in renal transplanted lupus patients treated with mTORC inhibitors

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Objective. To study the risk of intimal hyperplasia and thrombotic microangiopathy in lupus patients with antiphospholipid antibodies receptors of kidney allograft and their relationship with mTORC inhibitors treatment.
Methods. Prospective cohort study of consecutive lupus nephritis patients with antiphospholipid antibodies who received kidney transplant. Intimal hyperplasia and thrombotic microangiopathy were evaluated in kidney biopsies at 3 and 12 months after transplant. Use of mTORC inhibitors was assessed.
Results. Thirteen patients were consecutively included. All patients were women, and their mean age was 38 years (SD=13.2). Renal biopsy was performed in nine patients at 3 months and in eleven patients at 12 months. mTORC inhibitors were prescribed in 4 (30.8%) patients.
Intimal hyperplasia was similar in patients treated with mTORC inhibitors compared to those without this treatment; at 3 months, 1/4 (25%) vs 3/5 (60%) (p=0.357), at 12 months; 1/3 patients (33.3%) vs 6/8 (75%) (p=0.279).
Thrombotic microangiopathy was not found in any patient at 3 months after transplant. At 12 months, it was found in 2/8 (25%) patients without mTORC inhibitors while it was not found in any (0/3) patient under this treatment (p=0.509).
Conclusions. Although the low number of patients precludes drawing conclusions, mTORC inhibitors do not seem to protect against the development of intimal hyperplasia in lupus patients with renal transplant and antiphospholipid antibodies.

P6.05

Clinical and immunological correlations in patients with antiphospholipid syndrome

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Background. Antiphospholipid syndrome (APS) is an autoimmune, multisystem disorder characterized by thrombocytopenia, venous and/or arterial thrombosis, pathological course of pregnancy in women in the presence of a heterogeneous group of antibodies - antiphospholipid antibodies (aPL).
Objectives. Our aim is to evaluate the correlation between aPL, antinuclear antibodies (ANA) and clinical manifestations in patients with APS.
Methods. Fourthy patients were tested for cardiolipin (aCL), β2glikoprotein1 (anti-β2GPI) and prothrombin (anti-Prothrombin), by the method of ELISA. ANA were tested by the method of immunofluorescence and are typified in subtypes according to the method of immunoblot.
Results. Secondary APS is 87.5%, primary is 12.5%. Patients with positive aCL are 85.3%, β2GPI-74,3% and 3.7% for anti-Prothrombin.The secondary APS is in the context of: SLE-74.2%, RA-8.8%, Vasculitis-8.8%, Others - 8.2%. The Pearson analysis establishes strong, statistically significant positive correlation between:
aCL and β2GPI
β2GPI and anti-M2, anti-Scl70, anti-RibP
β2GPI/aCL and anti-M2
Conclusions The frequency of secondary APS is significantly higher than the primary.APS is found mainly in women (83%), by age at the first manifestation-30.5 years.
Most often positive aPL is for aCL, followed by anti-β2GPI and most frequently anti-Protrombin.Double carrier (50%) of aPL (aCL and anti-β2GPI) is more common than one positive result (47%).Half of the patients with complicated pregnancies is found the coexistence of aCL and anti-β2GPI.In the conducted correlation analysis showed a statistically significant association between miscarriage and the presence of anti-β2GPI.Severity of clinical manifestations of APS correlates directly proportional to the titer and number of aPL.

P07 Paediatric lupus

P7.01

Epstein Barr virus immune response, viral load and association with disease activity in paediatric systemic lupus erythematous patients

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Background. Pediatric systemic lupus erythematosus (pSLE) patients tend to have more severe disease and are more susceptible to infections at presentation over time compared with their adult counterparts. Viral infections could trigger autoimmune diseases and more so in children with SLE. In this view, we have analyzed the Epstein Barr Virus (EBV) viral load and humoral auto immune response against EBV antigens and their associations with clinical manifestations in pSLE.
Methods. 40 pSLE patients (fulfilled at least 4 of the 11 revised criteria of the American College of Rheumatology) and 40 age matched controls were recruited prospectively. Viral load of EBV in the peripheral blood was measured by quantitative real-time PCR. EBV antigens were analyzed by in vitro immunoblot assays for human antibodies of the IgM and IgG classes viz. VCA gp125, VCA p19, EBNA-1, p-22 and EA-D in serum. SLE Disease activity index (SLEDAI) was calculated. Comparisons of EBV load, SLEDAI and proportions of different antibodies were performed by Chi square test.
Results. 25% (10/40) of pSLE and 10% (2/20) of controls were positive for EBV. Patients with EBV loads >2.0 x 102 copies/ml were significantly associated with disease activity and cutaneous manifestations (p<0.05). Significantly higher pSLE patients showed immune reactivity against EBNA-1(IgG), VCA (IgG) and p22 (IgG) antigens suggestive of reactivation of a latent EBV infection.
Conclusion. We have shown that relationship between EBV infection and pSLE does exist. Long term follow up of EBV infection in pSLE may strengthen this association and help to formulate therapeutic strategies.

P7.02

Effects of rituximab therapy in 9 children with refractory systemic lupus erythematosus and ANCA positive vasculitis - single centre experience

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Introduction. There are only few reports of rituximab (RTX) effects in children with autoimmune rheumatic diseases refractory to conventional therapy protocols.
Methods. Retrospective chart review of all patients with systemic lupus erythematosus (SLE) + lupus nephritis (LN) and ANCA positive vasculitis, treated with RTX at the Division of Paediatric Rheumatology and Immunology, University Hospital Centre Zagreb, during 2009. - 2014. period.
Results. Nine children were treated with RTX: 6 with SLE + LN (3 boys, 3 girl) and 3 with ANCA positive vasulitis (3 girls), median age 11.6 years (5 - 15 years). Conventional therapy included methylprednisolon, cyclophosphamide (CYC), mycophenolate mofetil, azathyoprine, in some cases plasmapheresis. In all cases RTX was introduced due to ineffectivness of conventional therapy. Median time between the begining of conventional therapy and introduction of RTX was 10.3 months (1 - 48 months). In 8 cases RTX (750 mg/m2, two doses, two weeks apart) was combined with mini pulses of CYC (350 mg/m2), in 1 case RTX was applied in dose of 375 mg/m2 per week, for 4 weeks. After RTX introduction complete, prolonged remission was achived in 6 children. In 2 patients relapses of disease required repeating of RTX therapy and one patient with ANCA possitive vasculitis died during the study.
Conclusion. Complete or partial remission after RTX introduction was achived in 8/9 (88.8%) of patients with severe autoimune diseases. To our expirience, RTX represents powerful tool in controlling SLE + LN and ANCA positive vasculitides refractory to conventional therapy protocols.

P7.03

The long-term outcome of alveolar hemorrhage in juvenile systemic lupus erythematosus: a report of five Saudi children

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Objective. Alveolar hemorrhage (AH) is a life-threatening complication of systemic lupus erythematosus (SLE). Cases complicated with AH often have active SLE with multi-organ involvement, especially lupus nephritis. In children it has been recently recognized to be even much more severe with a worse outcome compared to adult lupus patients. In this paper we aim to describe our local experience and long-term outcome
Method. patients, who were diagnosed with SLE between 2000 and 2014, were retrospectively evaluated for evidence of AH. All patients fulfilled at least four of the classification criteria of the American Rheumatism Association. Using a standardized form, we obtained data regarding the age, sex and presenting complaints of the patients, previous therapies given, clinical and laboratory features, treatment and outcome. Informed consent was obtained from all patients.
Results. During the 14-yr study period, 27 patients were diagnosed with childhood-onset SLE. Five of them (18.5%) had alveolar hemorrhage either at initial presentation (3 out of 5) or during disease course. All patients had active nephritis and two had active CNS also at time of AH. Average follow up is 5.7 years (range 3.4-7). All patients were managed aggressively in the PICU with cyclophosphamides, IV methyleprednisolone, plasmaphersis, IV immunoglobulin. Two patients received rituximab and 3 patients required mechanical ventilation, and no deaths encountered. Details of medical treatment and outcome will be presented in this paper.

Inititial presentation, treatment and outcome of SLE patients with AH

patient	Sex	Age at diagnosis in years	Initial treatment	Additional features at diagnosis of AH	Subsequent treatment	Outcome
1	F	8.5	MPred, IVIg, pred. Rituximab,	fever, sever hypertension, nephritis, status seizure, skin vasculitis, serositis	MMF, Pred.HCQ	12 years old well controlled
2	M	1.6	MPred, IVIg,IV CPM., Plasmaphersis, ECMO, Rituximab.	fever, sever hypertension, nephritis, skin vasculitis, arthritis	IV CPM (6month) Pred, HCQ, MMF	5 years old developed minimal change nephrotic syndrome subsequently went to remission
3	M	5	MPred, IVIg,IV CPM, Plasmaphersis, ECMO, pred.	Fever, skin vasculitis, sever hypertension nephritis, arthritis	IV CPM (6month) MMF, Pred, HCQ	9 years old In Remission
4	F	10	MPred,IVIg, IV CPM, pred. mechanical vent.	Fever, status seizure, sever hypertension nephritis, arthritis	IV CPM (6month) Pred, HCQ, MMF	18 years old poor response CRF on dialysis Failed renal transplantation
5	M	6.5	MPred,.IVIg, IV CPM plasmaphersis, pred	fever, arthritis, nephritis, skin rash, hypertension	IV CPM (6month), Pred, HCQ, MMF	17 years old well controlled

P7.04

Juvenile Systemic Lupus Erythematosus (jSLE) activity at diagnosis and organ damage during follow-up

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Background. JSLE is a severe multisystemic auto immune disease. The clinical manifestations can change at diagnosis and during disease course. There are different scales to assess disease activity. SLEDAI (Systemic Lupus Erythematosus Disease Activity Measure) is one of the most used and the organ damage is established using Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI).
Objectives. Describe the clinical manifestations, activity index at diagnosis and damage during follow-up in a group of jSLE patients in Bogota, Colombia.
Methods. Descriptive study. Disease activity was established using SLEDAI and damage using SDI.
Results. This series included 66 jSLE patients, 81.8% female. The mean age of illness onset was 11.4 years (7-15).The mean follow-up time was 44.8 months (6-108). 77.3% of patients have SLEDAI values greater or equal to 6 at diagnosis. Relapsing-remitting was the most common type of course (69.7%), followed by the long-term stability (18.2%) and continuous chronic activity (12.1%). The frequency of organ damage at the last consultation was 43.9%. The most common type of damage was growth failure (75,8%). The frequency of organ damage was greater after the second year of follow up (p 0.044), disease onset before 10 years (OR 4 (CI 1.3-12) p 0.01) and SLEDAI ≥12 at diagnosis (OR 2.9 (IC1.1-8.1) p 0.03)
Conclusions. Is common high activity index at jSLE diagnosis. Survival has improved considerably but long term damage from disease and treatment is important. Early diagnosis and proper monitoring are keys in reducing organ damage.

P7.05

Differences in clinical features and mortality between childhood-onset and adult-onset systemic lupus erythematosus: prospective single-center cohort study

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Objectives. To compare differences in clinical features and mortality between childhood-onset systematic lupus erythematosus (cSLE) and adult-onset SLE (aSLE) from large single center cohort.
Methods. A total, 1,112 SLE patients (133 cSLE and 979 aSLE) were enrolled and followed from 1998 to 2012. American College of Rheumatology (ACR) classification criteria for SLE, autoantibodies, disease activity measured SLE Disease Activity Index (SLEDAI-2K) and Adjusted Mean SLEDAI, and damage measured by the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI), and medication were compared between two groups. Mortality was compared as the standardized mortality ratio (SMR). Predictors of mortality in SLE were evaluated using Cox proportional hazard models after adjusting for age, sex, and disease duration.
Results. After mean 6.3 years of follow-up, cSLE had higher number of cumulative ACR criteria and higher adjusted mean SLEDAI (p<0.001 and p=0.001, respectively), but no difference in SDI (p=0.797). High dose intravenous corticosteroid was more treated in cSLE (p=0.037), but other medication were not different.
The SMR (95% confidence interval [CI]) of cSLE was 18.8 (8.6-35.6), and significantly higher than aSLE (SMR 2.9, 95% CI 2.1-3.9). cSLE was independent predictor of mortality (hazard ratio 3.8, 95% CI 1.5-9.6). Hemolytic anemia (HR 10.1, 95% CI 3.4-30.1) and positivity of anti-phospholipid antibodies (HR 3.9, 95% CI 1.3-11.6) significantly increased the mortality for cSLE patients compared to aSLE.
Conclusion. cSLE patients had worse clinical outcomes with higher mortality than aSLE patients. Special attention is needed when cSLE is combined with hemolytic anemia or positivity of anti-phospholipid antibodies.

P7.06

Digital vasculitis survey in 852 childhood-onset systemic lupus erythematosus patients: a multicenter cohort study

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Objective. To study prevalence, risk factors and morbidity of digital vasculitis (DV) in a large population of childhood-onset systemic lupus erythematosus (cSLE) patients.
Design. Retrospective multicenter cohort study.
Setting. Clinics of 10 Pediatric Rheumatology centers of São Paulo State, Brazil.
Patients. 852 patients diagnosed with cSLE according to American College of Rheumatology criteria.
Measurements and Main Results. An investigator meeting was held to define the protocol and clinical parameters definition. Clinical DV cases were classified based on ulceration, gangrene, tender finger nodules, periungual infarction or splinter hemorrhages according to SLEDAI-2K. Demographic, clinical, laboratorial data, disease activity (SLEDAI-2K), cumulative damage (SLICC/ACR-DI), treatment and outcomes were also evaluated. DV were observed in 52/852 (6.1%) cSLE patients. Periungual hemorrhage was diagnosed in 24 cSLE patients, periungual infarct in 14, ulceration in 13, painful nodules in 3 and gangrene in 1. The median of disease duration was lower (0.0 vs. 54 months, p<0.0001), with a higher current SLEDAI-2K [19.5 (0-44) vs. 2 (0-45), p<0.0001] and higher current prednisone dose [40 (5-80) vs. 10 (1-90) mg/day, p<0.0001] in patients with DV compared to those without DV. Logistic regression analysis revealed that SLEDAI-2K (OR=1.135; 95%CI=1.083-1.190; p<0.0001), current dose of prednisone (OR=1.053; 95%CI=0.828-1.339; p<0.0001), mucocutaneous involvement (OR=0.034; 95%CI=0.004-0.280; p<0.0001) and disease duration (OR=0.983; 95%CI=0.970-0.996; p=0.039) were independent risk factors for DV (R^2 Nagelkerke 0.540).
Conclusions. To our knowledge, this study included one of the largest studies of cSLE patients. We identified that disease activity and mucocutaneous involvement were the main risk factors for these severe morbidity outcome.

P7.07

Chronic arthritis survey in 852 childhood-onset systemic lupus erythematosus patients: a multicenter cohort study

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Objective. To assess chronic arthritis (CA) in a large population of childhood-onset systemic lupus erythematosus (cSLE) patients.
Design. Retrospective multicenter cohort study.
Setting. Clinics of 10 Pediatric Rheumatology centers of São Paulo State, Brazil.
Patients. 852 patients diagnosed with cSLE according to American College of Rheumatology criteria.
Measurements and Main Results. An investigator meeting was held to define protocol and clinical parameters definitions. CA was diagnosed in the presence of fixed arthritis in at least one joint, for at least six weeks. "Rhupus" was classified as overlap of juvenile idiopathic arthritis (ILAR criteria) and cSLE. Demographic, clinical, and laboratorial data, disease activity (SLEDAI-2K), cumulative damage (SLICC/ACR-DI), treatment and outcomes were evaluated. CA were observed in 32/852 (3.7%) cSLE patients. Chronic monoarthritis was diagnosed in 4 patients, oligoarthritis in 8 and poliarthritis in 17 (3 were unknown). Joint deformity and radiographic changes were present in 12 patients (25%). Four cSLE patients were rheumatoid factor positive (13% of cSLE patients with CA). Rhupus was observed in 3 cSLE patients. Median of disease duration was shorter (1.5 vs. 55 months, $p<0.0001$), with higher current SLEDAI-2K [11 (4-29) vs. 2 (0-45), $p<0.0001$] and higher current prednisone dose [0.5 (0.1-7.5) vs. 0.2 (0.02-30) mg/kg/day, $p<0.0001$] in patients with CA compared to those without CA.
Conclusions. To our knowledge, this was the first study that evaluated a large cSLE population and clearly demonstrated that CA was a rare manifestation. We identified that disease activity was the main risk factor associated with CA in early disease course.

P7.08

Validating the Pediatric Automated Neuropsychological Assessment Metrics Cognitive Performance Scores in the screening of neurocognitive impairment in childhood-onset systemic lupus erythematosus

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Background. Neurocognitive impairment is an important morbidity in childhood-onset systemic lupus erythematosus (cSLE); however, the gold standard formal neurocognitive testing is difficult to access. Screening for neurocognitive impairment (NCI) using computerized testing with the Pediatric Automated Neuropsychological Assessment Metrics (PedANAM) is a more feasible option. Four recently derived cognitive performance scores (CPS) use PedANAM derived data and differing statistical methods to establish suggested cutoff values for patients requiring further evaluation.
Objective. To examine external, concurrent, criterion and diagnostic validity of the PedANAM-CPS scores using a single-centre multiethnic cohort.
Methods. Patients were recruited within 18 months of cSLE onset, and all had formal neurocognitive testing and PedANAM testing on the same day. Validation of the PedANAM-CPS scores utilized sensitivity and specificity analyses in addition to other nonparametric statistical comparisons.
Results. 29 cSLE patients without premorbid NCI completed the study procedures. Median age at testing was 15.2 years, 83% were female. Six (21%) patients had NCI identified by formal testing. All four CPS scores were significantly different (worse) in patients with NCI, and predetermined cutoffs were reached only in patients with NCI. Two of the 4 CPS scores (one using an unweighted average and the other a logistical regression model) had 100% sensitivity to detect NCI, while the CPS based on principal components analysis had the highest specificity (87%) for detecting NCI. Confidence intervals were wide owing to the small cohort size.
Conclusions. PedANAM-CPS scores are useful to identify cSLE patients who require referral for formal neurocognitive assessment.

P7.09

PKCd at the gate of autoimmunity: B cell deficiency and severe autoimmunity caused by deficiency of protein kinase C delta

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Systemic lupus erythematosus (SLE) is the prototype of a systemic autoimmune disease. Despite intense research efforts, the molecular disease mechanisms remain only partially understood.
We investigated a consanguineous family with an index patient suffering from early-onset SLE with severe autoimmunity. Combined homozygosity mapping and exome sequencing identified a biallelic splice-site mutation in protein C kinase delta (PRKCD), causing absence of the corresponding protein product. On a cellular level, PKCδ deficiency is associated with increased IL6 mRNA levels and decreased phosphorylation of myristoylated alanine-rich kinase substrate a downstream target. Our study uncovers human PRKCD deficiency as the first cause of monogenic SLE. In the meantime, 4 additional patients have been published and extended our understanding of the phenotypic range of human PRKCD deficiency. PKCδ-deficient patients present with a broad spectrum of autoimmunity, lymphoproliferation, butterfly-rash as well as multiple autoantibodies.
Although several studies have investigated PKCδ function in the immune system, a systematic view has remained elusive. We thus performed tandem affinity purifications to identify novel interaction partners of PKCδ. We identified both known interactors and novel interactors with regulatory function in lymphoid cells. These results will be further validated using co-immunoprecipitation experiments.
Severe gene disruptions characteristic of monogenic diseases often highlight essential players in complex disease networks as illustrated here for PKCδ deficiency. Therefore it is not surprising that also adult-onset multifactorial SLE patients display reduced PKCd levels, evidenced by multiple studies. PKCδ can be considered a key regulator in SLE, of relevance far beyond Mendelian SLE as an extreme phenotype.

P7.10

Serum biomarkers of inflammation, fibrosis, and cardiac function associate with diagnosis and severity of cardiac neonatal lupus

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Background. Cardiac manifestations of neonatal lupus (cardiac-NL) include congenital heart block and cardiomyopathy. Identification of maternal and fetal biomarkers that associate with development and morbidity of cardiac-NL should provide clues to pathogenesis with translational implications for management. Several candidates were chosen for examination based on potential roles in cardiac dysfunction, inflammation and fibrosis: C-reactive Protein (CRP), NT-proBNP, troponin-I, matrix metalloproteinase-2 (MMP2), urokinase plasminogen activator (uPA), urokinase plasminogen activator receptor (uPAR), plasminogen, and vitamin D.
Methods and Results. 139 cord and 135 maternal blood samples collected during a pregnancy at risk for cardiac-NL were available for study. Levels of cord CRP, NT-proBNP, MMP2, uPA, uPAR, and plasminogen were higher in cardiac-NL compared to unaffected cases and positively associated with a disease severity score derived from known risk factors for mortality, independent of maternal rheumatic disease, season at highest risk of cardiac-NL, and medications taken during pregnancy. Cord troponin-I levels did not differ between groups. Cord and maternal vitamin D levels were not associated with cardiac-NL or severity, but average maternal vitamin D level during pregnancy positively associated with longer time to postnatal pacemaker placement.
Conclusion. These data support fetal reactive inflammatory and fibrotic components to the development and morbidity of cardiac-NL. CRP and NT-proBNP can be followed after birth to potentially monitor for severity and progression of cardiac-NL. MMP2 and the uPA/uPAR/plasminogen cascade provide therapeutic targets to decrease fibrosis. Although decreased vitamin D levels did not confer increased risk, maternal levels should be optimized given the positive influence on postnatal outcomes.

P7.11

The CHILL-NL study, very long term outcome of childhood-onset SLE: Education and Work participation

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Background. Childhood onset SLE (cSLE) is a severe, lifelong autoimmune disease. Studies looking at the effects of cSLE on education and work participation are scarce.
Methods. Adults with cSLE were seen by the CHILL-NL (CHILdhood Lupus in the NetherLands) study team for a single study visit containing a structured history and physical examination. Education and work status were assessed by structured and validated questionnaires.
Results. 47 cSLE patients (44 female) were analyzed, median disease duration was 16 years (range 1 – 36). 62% of people had an SDI of ≥1.
Education was reported to be affected by the disease by 61% of patients, 58% reported their career choice to be affected.
None of the patients worked full-time and 27% worked part-time, compared to the female Dutch norm population of which 23% worked full-time and 69% worked part-time. 46% of patients never had paid employment. SLE fully or partially influenced the decision to work less or quit completely in 38% of cases. The majority (92%) of patients who were fully unable to work, and 52% of the patients who worked part-time had an SDI of ≥1.
Conclusion. cSLE has a clear impact on education and work participation. Patients are often not able to follow their education or career of choice due to their disease. Additionally, cSLE patients are often unable to work, the majority of them having disease damage . Better control of disease including prevention of disease damage is of great importance to facilitate patients to participate in our community.

Table 1. Baseline characteristics.

Variable (n=47)	Outcome	
Female	94%	
Caucasian	68%	
Age at diagnosis in years (median + range)	14 (7 – 17)	
Disease duration in years (median + range)	16 (1 – 36)	
Current SLEDAI-2K score (median + range)	4 (0 – 14)	
SLICC-DI ≥ 1 (range 1-8)	62%	
Musculoskeletal damage	28%	
Neuropsychiatric damage	23%	
Renal damage	21%	
Patients still using immunosuppressive drugs	87%	
Medication use	Ever	Current
-Prednisone	98%	67%
-Hydroxychloroquine	81%	63%
-MMF	46%	22%
-Azathioprine	65%	24%
-ACE-I or ARB	64%	43%
Patients ever hospitalised due to infections	49%	
Quality of Life (measured with the Short-Form36, n=44)	cSLE	Dutch Norm
-Physical Functioning	74±25*	83±23
-Role Physical	62±39*	76±36
-Role Emotional	84±34	82±33
-Social Functioning	77±22*	84±22
-Bodily Pain	66±22*	75±23
-Mental Health	78±19	77±17
-Vitality	53±19*	67±19
-General Health_	48±25*	71±21
Female patients that had a pregnancy wish but not anymore	15	
Number of patients giving up child-wish due to SLE only	4 / 15 (27%)	
Number of patients giving up child-wish partially due to SLE	3 / 15 (20%)	
Patients ever pregnant	12 / 45 (27%)	
Total number of pregnancies	27	
Time to pregnancy in months (median + range)	3 (0 – 84)	
Complications during pregnancy	12%	
Pregnancy induced hypertension	12%	
Pre-eclampsia	4%	
Premature birth	12%	
Other		

[1]Anti-hypertensive drugs, antiepileptic drugs. *$p<0.05$.
ACE-I: Angiotensin-converting-enzyme inhibitors; ARB: Angiotensin II blocker.

P7.12

The CHILL-NL study, very long-term outcome of childhood-onset SLE: disease activity, damage, quality of life and fecundity

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Introduction. Childhood-onset systemic lupus erythematosus (cSLE) is a severe multi-system autoimmune disease. Little is known regarding outcomes in adult life. This study addresses these very long-term outcome of cSLE.
Methods. Adults with cSLE were seen for a single study-visit, which included a structured history and physical examination. SLEDAI-2K and SLICC-Damage Index (SDI) were assessed. Health-related quality of life (HRQoL) and fecundity were determined by validated questionnaires. Information was supplemented with all previous medical records.
Results. So far, 47 cSLE patients (94% female, 68% white) were analysed (Table I). Median disease duration was 16 years (range 1 - 36), median SLEDAI was 4 (range 0 - 14). The majority had an SDI of ≥1, neuropsychiatric and renal damage comprised 44% of all damage. Most patients (87%) were still using immunosuppressants. HRQoL was lower in most domains compared to Dutch normative data. Fifteen female patients did not have a pregnancy-wish anymore, 7/15 gave up their child-wish completely or partially due to SLE. Twelve patients were ever pregnant, median time to pregnancy was 3 months (range 0-84). Complications were reported in 40% of pregnancies.
Conclusions. Our results underline the severe disease course that cSLE can have, reflected in i) the damage accrued, ii) many patients not achieving drug-free remission and iii) significantly lower quality of life. Additionally the disease influenced pregnancy-wish, and many pregnancies had a complicated course.

P7.13

IL-6 and IL-10 levels in childhood-onset systemic lupus erythematosus: are they different in the active and inactive forms of the disease?

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Objective. To determine Th1, Th2 and Th17 cytokines profile in a cohort of childhood-onset SLE (c-SLE) patients and healthy controls. To elucidate the association between cytokines and disease activity.
Methods. We included 51 patients with c-SLE, mean age [15.3 years (range 5-20)] and 47 healthy controls [mean age 15.4 years (range 6-21)]. Disease activity was evaluated according to SLEDAI-2K. Score ≥4 was considered as active disease. Th1 (IL-2, IFN-γ and TNF), Th2 (IL-4 and IL-10) and Th17 (IL-6 and IL-17) cytokines were measured by cytometric bead array (CBA). Non-parametric tests and Spearman's correlation were used.
Results. Plasmatic levels of IL-6 (p=0.0002) and IL-10 (p=0.0002) were increased in c-SLE patients when compared to healthy controls. IL-6 (p<0.0001) and IL-10 (p<0.0001) levels were also increased in patients with active disease when compared to patients with inactive disease and the control group. In the correlation study among cytokines, it was observed in the control group a complex network of correlation among various cytokines: a low correlation between IL-6 and IL-10 (r=0.28; p=0.04) and a mild positive correlation between each of those cytokines with IL-2 (r=0.42; r=0.54), IL-4 (r=0.33; r=0.61) and TNF (r=0.37; r=0.53) respectively. In patients with disease activity, the above-mentioned correlations were insignificant.
Conclusion. IL-6 and IL-10 play an important role in the pathogenesis of c-SLE, mainly in the active phase of the disease, where the complexity of interactions among cytokines was lower than in the control group.

P7.14

Cyclophosphamide use in Juvenile Systemic Lupus Erythematosus (JSLE) in a tertiary care center in Saudi Arabia, a retrospective study

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Introduction. Cyclophosphamide is an important treatment modality in severe JSLE.
Objectives. To Describe our experience in the use of cyclophosphamide in JSLE, its outcome and safety.
Methods. A retrospective analysis of data for all children, aged 14 years or less, diagnosed with JSLE who received cyclophosphamide in a tertiary care center in Saudi Arabia between 2000-2014. SLEDAI and SLICC scores were measured to evaluate patients' responses to treatment and end-organ damage respectively pre-treatment, after 6th, & 12th doses.
Results. A total of 71 patients received Cyclophosphamide, 61 were females (86%). The mean age of disease onset, disease diagnosis, and cyclophosphamide initiation was 9.2, 9.6, and 10.4 years respectively. Mean duration of follow-up was 6.6 years. Nephritis (49.3%) then cerebritis (18.3%) were the main indications. Comparisons of SLEDAI and SLICC of the whole cohort pre and post treatment were statistically significant with *p*-values of 0.001 and 0.006 respectively. No statistical significant difference was found after comparing SLEDAI and SLICC scores after 6th & 12th doses.
49 patients (69%) had no major side-effects. Major side effects encountered included: 7 patients had herpes zoster infection (10%), 3 had significant alopecia (4.2%), 2 had skin abscesses in 2, 1 had recurrent lung abscesses, 1 had recurrent urinary tract infection, and 1 had allergy to mesna.
Conclusion. Cyclophosphamide is still considered important effective treatment in severe JSLE. It is relatively well tolerated among children however infections remains a major infrequent problem so shorter course is recommended.

P7.15

Long-term outcomes of diffuse proliferative lupus nephritis and the significance of global and segmental subclasses in children

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Data on global (IV-G) and segmental (IV-S) subclasses of diffuse proliferative lupus nephritis (DPLN) in children are lacking.
To compare clinicopathology and prognosis, 56 children aged <18 years from 2004 to 2014 were analyzed. The median follow-up was 6 years (range 1-11). Clinical endpoints were 1) complete remission (CR), 2) chronic kidney disease (CKD) defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 or end-stage renal disease (ESRD), and 3) death. The ratio of IV-G to IV-S was 2:1. Proteinuria and activity index was higher in IV-G ($p<0.05$). Global endocapillary proliferation and leukocyte exudation were predominate in IV-G whereas segmental endocapillary proliferation was predominate in IV-S ($p<0.005$). Overall CR rate was 53.6%. Four of 16 patients with CKD had ESRD. Overall renal survival rates, defined as eGFR ≥60 mL/min/1.73 m^2, at 1,5 and 10 years were 93%, 78% and 64%, respectively. Three deaths occurred (all in IV-G). Patient survival rates at 1,5 and 10 years were 98%, 96% and 91%, respectively. Table shows outcomes by subclass of children with DPLN. Patient and renal survival rates did not significantly differ between both groups.
IV-G and IV-S displayed some clinical and histopathological disparities but rendered similar outcomes in children. The majority of children with DPGN reached adulthood but accrued significant renal damage. Thus, treatment regimens which can slow the progression of CKD are needed.

Outcomes of global (IV-G) and segmental (IV-S) diffuse proliferative lupus nephritis in children

Outcomes	IV-G (n = 36)	IV-S (n = 20)	*p*
Months after biopsy (median, interquartile range)	99.7 (47.9 - 118.2)	78.3 (27.6 - 107.3)	0.34
Complete remission (n, %)	18 (50.0)	12 (60.0)	0.47
Chronic kidney disease (n, %)	11 (30.6)	5 (25.0)	0.66
Renal survival rate (%, 95% CI)			0.81
1 year	91 (75 - 97)	95 (69 - 99)	
5 year	85 (67 - 93)	70 (43 - 87)	
10 year	63 (40 - 80)	70 (43 - 87)	
ESRD (n, %)	3 (8.3)	1 (5.0)	0.64
ESRD-free rate (%, 95% CI)			0.76
1 year	94 (79 - 99)	95 (69 - 99)	
5 year	94 (79 - 99)	95 (69 - 99)	
10 year	88 (64 - 96)	95 (69 - 99)	
Death (n, %)	3 (8.3)	0 (0)	0.18
Patient survival rate (%, 95% CI)			0.24
1 year	97 (82 - 100)	100 (100 - 100)	
5 year	94 (77 - 98)	100 (100 - 100)	
10 year	87 (63 - 96)	100 (100 - 100)	

P7.17

Advanced Proteomics for Lupus Nephritis Biomarker Discovery

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Introduction. There an ongoing need for high-quality biomarkers of lupus nephritis(LN) damage and activity. Isobaric-Tags for Relative and Absolute Quantitation (iTRAQ)is an advanced proteomic method that quantifies and compares protein expression among samples by mass spectrometry in a single experiment. We aimed at discovering biomarker candidates for LN activity and chronicity,using iTRAQ.
Method. Urine was collected from children with proliferative LN (N=16) at the time of kidney biopsy; LN activity as per the NIH-activity index (score:0-24) were categorized as low (<5), moderate (5–15), high (15–20) and very high (>20) and damage as per the NIH-chronicity index (0-12) was considered low (<1), moderate (2–3), or high (>4). iTRAQ experiments compared protein composition in4urine samples from different LN-activity or LN-chronicity categories,respectively. Using Gene-spring,the relative expression of proteins differentially excreted was tested for significant differences using a log-rank test, using unweighted means of protein levels in the low LN-activity or low LN-chronicity as reference controls.
Result. Patients had a mean age of 17±5.01years (80% female) and there are 5 patients in each LN-class,and iTRAQ detected112differentially expressed proteins. Statistically significant differences between LN-activity and LN-chronicity categories are shown below.
Conclusion. iTRAQ revealed eight proteins that are differentially excreted in the urine depending on the degree of LN-activity or LN-chronicity. These biomarkers-candidates will need further validation using specific assays to assess their clinical usefulness.

Proteins differentially excreted with LN-activity and LN-chronicity.

	Activity	Chronicity
Proteins	Vitamin D-binding protein Alpha-2-macroglobulin Antithrombin-III Alpha-1-antichymotrypsin Transthyretin Ig gamma-1 chain C region	Alpha-1-antichymotrypsin SERPINA3) Antithrombin-III (SERPINC1)

P7.18

Rituximab therapy in neuropsychiatric manifestations of juvenile systemic lupus erythematosus

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Introduction. Up to two-thirds of patients with paediatric systemic lupus erythematosus (SLE) show involvement of the nervous system. It is a major cause of morbidity. There are a wide variety of neuropsychiatric manifestations that generally present within the first year of diagnosis.
Treatment needs to be directed toward the presumptive pathophysiologic mechanism. Most patients will require symptomatic and immunosuppressive therapies, using an induction and maintenance approach. However, many cases are resistant to therapy.
Case report. A 14-year-old boy was admitted with a 1-year history of intermittent arthralgia, constitutional symptoms, Raynaud phenomenon and dysphagia. Upon further investigation, he was diagnosed with SLE-scleroderma overlap syndrome, with class V membranous nephritis.
Shortly after, he developed symptoms of anxiety and cognitive dysfunction - executive functions, memory impairment and acalculia. Electroencephalograms and brain imaging were normal. Cerebrospinal fluid analysis detected a mild IgG elevation and pleocytosis. Antiphospholipid and anti-ribosomal P antibodies were positive.
He started methylprednisolone, cyclophosphamide, hydroxychloroquine, enoxaparin and gabapentin.
Because of clinical deterioration, with mutism alternating with psychomotor agitation and acute confusional state, haloperidol and rituximab were added.
There was rapid clinical response, with resolution of the neuropsychiatric symptoms and improvement in proteinuria.
After 20 months of follow-up, no evidence of neuropsychiatric recurrence was found.
Discussion. The diagnosis of primary neuropsychiatric SLE can be challenging, Immunoserologic testing and brain imaging may contribute to an earlier and more specific diagnosis.
Rituximab has shown effectiveness in treating severe refractory neuropsychiatric SLE, namely in cases with acute confusional state and cognitive dysfunction.

P08 Miscellaneous

P8.01

Identification of a systemic lupus erythematosus risk locus spanning the genes ATG16L2, FCHSD2, and P2RY2 in Koreans

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Systemic lupus erythematosus (SLE) is a chronic, heterogeneous autoimmune disorder that has a strong genetic contribution to the disease etiology. In this study, we performed a genome-wide association scan to identify loci associated in 1174 Korean SLE cases and 4248 population controls. Eleven regions outside the HLA exceeded the genome-wide significance threshold of $p<5x10-8$. A novel SNP-SLE association was also identified peaking at rs11235667 located between FCHSD2 and P2RY2 ($p=1.0x10-8$, odds ratio (OR)=0.59, 95% confidence interval (CI)=0.50-0.71) on a haplotype spanning 33kb upstream to ATG16L2. Replication was tested for rs11235667 in an independent set of 1,412 SLE cases and 1,163 population controls of Korean and Chinese ancestries resulting in Pmeta-rep=0.001 and Pmeta-overall=6.67x10-11 (OR=0.63, 95% CI=0.55-0.72). Within the HLA region, association peaked within the Class II region at rs116727542 with multiple independent effects. Classical HLA allele imputation identified HLA-DRB1*1501 and HLA-DQB1*0602, both highly correlated, as most strongly associated with SLE. The ten remaining regions were previously established as SLE risk loci that replicated in this study: STAT1-STAT4, TNFSF4, TNFAIP3, IKZF1, HIP1, IRF5, BLK, WDFY4, ETS1 and IRAK1-MECP2. Of the established SLE risk loci, independent second effects not previously reported were observed in TNFAIP3 and TNFSF4, and differences in the association for a putative causal variant were identified in the WDFY4 region. Further studies are needed to determine if any other suggestive loci are true SLE risk effects and to identify the causal variant(s) in the region of ATG16L2, FCHSD2, and P2RY2.

P8.02

Genome-wide analysis of DNA methylation in systemic lupus erythematosus

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Introduction. In recent years there has been progress in identifying genetic loci contributing to risk for systemic lupus erythematosus (SLE), but a large proportion of susceptibility still remains unexplained. Epigenetics is starting to emerge as an important contributing factor in SLE, and could act as a link between the environment and the genome.
Aim. To investigate the impact of DNA methylation variation on SLE susceptibility.
Patients and Methods. DNA extracted from blood from 600 Swedish SLE patients and 600 healthy controls was analysed on the Illumina HumanMethylation 450k array, covering 485,000 CpG sites in the genome. The Minfi R package was used for quality control, normalization of intensity data and calculation of methylation beta values. Blood cell type proportions were estimated based on publicly available reference DNA methylation signatures of flow sorted cells. Differential cell count estimations, age and sex were included as covariates in the association model.
Results. We find that methylation at thousands of sites in the genome is perturbed in SLE. We observe large methylation differences between patients and controls at interferon regulated genes which exhibit decreased methylation in SLE. Significant hypomethylation in interferon regulated genes was for example observed at the genes *IFI44L* and *MX1* consistent with results in fractionated blood cells from SLE patients.
Conclusion. Our results further emphasize the role of the type I interferon system in SLE.

P8.03

The role of musculoskeletal ultrasound in the stratification of SLE; a multicenter crosssectionalstudy

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Background. Musculoskeletal symptoms in SLE are common and cause substantial morbidity. Musculosketelal ultrasound (US) has a potential role in assessing these symptoms. However, There is still limited data on the nature and severity of US findings in SLE.
Objectives. to determine the characteristics and severity of US abnormalities in SLE and to correlate these abnormalities with the clinical findings.
Methods. Patients with SLE had hand US examination and clinical and blood assessments. Any patient who had Rhupus was excluded.

Results. A total of 55 patients were recruited. Among them, 18%, 18%, 55% and 9% of patients were BILAG A, B, C and D respectively. In those with inflammatory joint symptoms (BILAG A-C), 58.3% had significant US finding (GS ≥2 and/or PD ≥1). All BILAG A had moderate-severe PD (i.e.PD≥2). However, a substantial number of patients who had BILAG B (*i.e.* clinical synovitis) were judged not to have significant US findings. In contrast, many patients with BILAG C did have significant US abnormality (Table). Erosions were found in about one third of BILAG A patients(Table). There was a moderate positive correlation between presence of PD and presence of erosions (Correlation Coefficient= 0.44 (p<0.001)). Neither inflammatory markers nor SLE immunological markers appeared to be associated with joint inflammation.

Frequencies of different ultrasound abnormalities in Different BILAG groups

Ultrasound abnormality	A (n=10)	B (n=10)	C (n=30)	D (n=5)
GS ≥ 2 and/or PD≥1	100%	80%	38%	0%
PD≥1	100%	80%	20%	0%
PD ≥2	100%	40%	7%	0%
Erosions	33%	20%	7%	0%
Tenosynovitis	45%	30%	11%	0%

Conclusions. US may be more sensitive than clinical examination and BILAG in classifying joint pathology in SLE.

P8.04

An explanation for the failure of whole blood interferon signatures to represent SLE disease activity

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IFN activity is measured using whole blood IFN gene signature (IFNGS) but does not consistently correlate with disease activity or predict response to IFN-blocking therapy.
Objective. To compare IFNGS between unsorted PBMC and sorted cell subsets in healthy controls and SLE patients.
Methods. PBMCs from 12 patients and 16 controls were sorted using multiparameter flow cytometry into Monocytes, NK cells, T cells and B cell subsets. Gene Expression PreAmp with Fluidigm® PreAmp Master Mix and TaqMan® Assays (96 assays) were used.
Results. We compared known ISGs in PBMCs between SLE and HC. Although some ISGs were elevated in SLE patients (*e.g. HERC5, IFI6, USP18,* all p<0.01), others were no different from healthy controls (e.g. *BST2, CXCL10, EIFAK2, IFIH1, IFIT1, XAF1*). ISGs that were higher in PBMCs were mainly those strongly expressed in monocytes. However, some of these ISGs were elevated in individual subsets, but not PBMCs. For example, *EIFAK2* and *XAF1* in B cells, T cells and monocytes. Expression of these genes correlated with other subset-specific markers of cell function. Notably, in B cells, *IGJ* (representing antibody synthesis) correlated with *IFIH1* (r=0.594, p=0.006) and *IFIT1*(r=0.447, p=0.048).
Conclusion. We identify a group of ISGs whose expression is elevated in B cells and correlates with secretory function but are not detected in unsorted blood, which instead predominantly represents monocytes' IFN response. Fundamental pathogenic pathways of IFN and B cells cannot be measured unless cell-specific assays are used. This may explain the limitations of whole blood IFN signatures.

P8.05

Comparison of discoid versus subacute cutaneous lupus reveals overlapping and distinct interferon regulated pathways

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Cutaneous lupus rashes can be substantial, disfiguring, and often refractory to usual lupus therapies. Phenotypic presentation and risk of systemic lupus manifestations differs by rash subtype, thus we chose to examine the transcriptional differences between discoid (DLE) and subacute cutaneous (sCLE) lupus rashes. Formalin-fixed paraffin-embedded (FFPE) tissue blocks of 22 DLE and 24 sCLE rash biopsies were acquired from the University of Michigan Anatomic Pathology repository. Five 10 micron sections were cut and RNA was isolated and analyzed via Affymetrix ST 2.1 array. Gene expression changes were compared to 8 similarly treated and isolated healthy control biopsies. Using a stringent fold-change filter of 2 and a q-value <0.01, 569 genes were commonly regulated in both rash subtypes. Analyses using Genomatix and Ingenuity software confirmed enhancement of known lupus-associated pathways, and transcription factor analysis revealed important gene regulation by STAT1, STAT2, STAT4, IRF1, and IRF8. Upregulation of TLR2 and inflammasome-associated genes were also noted. A total of 180 and 216 genes were uniquely regulated in DLE and sCLE respectively. Unique to DLE, a strong upregulation of interferon (IFN) gamma associated pathways was highlighted and IL-4 appeared a likely prominent regulator of DLE-specific gene expression. In sCLE, type I IFN signaling predominated and unique expression of CD14 and the chemokines CCL20 and CCL2 were seen. These data suggest that DLE and sCLE have overlapping and unique transcriptional expression signatures which may guide therapeutic and diagnostic decisions. Further analysis of these specific profiles may identify targets for novel therapies to treat cutaneous lupus.

P8.06

Thrombotic thrombocytopenic purpura in patients from the Systemic Lupus Erythematosus registry of the Spanish Society of Rheumatology (RELESSER)

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Background. In our area, SLE patients present haematologic manifestations in 70% of cases. Some of them are rare so there are no large series to provide relevant information.
Objectives. To study SLE patients with TTP in a large sample.
Methods. SLE patients from RELESSER were studied. We analysed SLE manifestations of activity (BILAG and SELENA-SLEDAI indices) and damage (SLICC/ACR DI), before, during and after the TTP episode until the last assessment of the patient, and treatments, recurrences and deaths by this entity.
Results. 3,656 patients from 45 Rheumatology Units were studied. We found 19 cases of PTT (&lt 1%). 100% women, 94.7% Caucasian. Mean age (±SD) at diagnosis was 28.9±11.4 years. Patients were divided into 3 groups according to chronology between TTP and SLE. In group (G) 1 patients developed TTP and later SLE. In G2 both conditions were simultaneous. In G3 patients developed SLE and then TTP. G2 and particularly G3 showed high SLE activity at PTT

diagnosis (SLEDAI &gt 6). Afterwards patients maintained SLEDAI scores of 3.8±5.3 at G2 and 2.4± 0.7 at G3.
Detailed data are shown in Table I.
Conclusions. TTP is rare (&lt 1%) in SLE. It can be severe and fatal. TTP should be suspected in SLE patients with anemia and thrombocytopenia so treatment can be started without delay.

Table I. Detailed Data.

	Group 1	Group 2	Group 3
Number of patients	3 (15.8%)	5 (26.3%)	11 (57.9%)
Time between TTP and SLE (months)	TTP to SLE: 25.3 (±8.5)	Simultaneously	SLE to TTP: 73.6 (±60.5)
Time between TTP and last assessment (months)	227.3 (±117.8)	157.2 (±105.8)	196.9 (±65.6)
Age at SLE diagnosis (years)	25.5 (±10.3)	36.5 (±6.5)	26.4 (±9.4)
Age at TTP diagnosis (years)	23.3 (±9.6)	36.5 (±6.5)	33.3 (±11.6)
Number of organ systems affected by SLE before TTP diagnosis	Not applicable	Not applicable	6.55 (±2.5)
Number of organ systems affected by SLE at TTP diagnosis	Not applicable	4 (±2)	4.72 (±2.8)
Number of organ systems affected by SLE until last assessment	6 (±3)	3.8 (±2.3)	2.2(±1.8)
Haemoglobin levels at TTP diagnosis (g/dl)	10 (±3.2)	7.7 (±2.1)	7.4 (±1.8)
Platelets levels at TTP diagnosis	10,667 (±7,506)	25,200 (±38,590)	22,909 (±18,387)
SLEDAI//SLICC-ACR DI at TTP diagnosis	Not applicable	13.2 (±5.7)//0	21.7 (±15.2)//1.45 (±1.1)
SLEDAI//SLICC-ACR DI 1 year after TTP	Not applicable	3.8 (±5.3)//0.8 (±1.3)	2.4 (±0.7) //1.7 (±1.1)
SLEDAI//SLICC ACR DI at last assessment	0.7 (±1.1)// 0	4 (±3.7)//1.8 (±2.7)	2.26 (±0.7) // 2.7 (±1.6)
Number of treatment lines	1 (±0)	2.8 (±2)	2.4 (±1.7)
Number of treatments administered	2 (±1)	5.4 (±2.9)	3.8 (±2.5)
Most frequent treatment	Glucocorticoids (100%)	Glucocorticoids (100%) Plasma Exchange (80%) Cyclophosphamide (60%)	Glucocorticoids (81.8%) Plasma Exchange (72.7%) Cyclophosphamide (41.8%)
Number of Recurrences	0	0	2
Number of Deaths	0	0	2

P8.07

Lupus like glomerular disease associated with Human Immunodeficiency Virus (HIV) in the era of highly effective antiretroviral therapy (HAART) in a high complexity university hospital between the years of 2006 and 2012

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We report 10 cases of glomerulonephritis with pathological findings similar to lupus nephritis in patients with HIV and antibodies ANA and Anti positive DNA, with benign evolution with adequate control of their infectious pathology without therapy renal replacement; unknown whether these findings are similar to those found in lupus nephritis or are part of the spectrum of systemic lupus erythematosus.
Design. Descriptive, retrospective study carried out at a high complexity level University Hospital. We reviewed patient records between January 1st 2006 and July 1st 2012. Inclusion criteria for the study were: HIV infected adults of Latin American origin, who developed renal impairment which was defined by an abnormal serum creatinine value or by the presence of proteinuria, and in whom renal biopsy was performed.
Results. See Tables. Conclusion: In our study population (Latinamerican) found 10 cases of lupus-like glomerulonephritis in 30 renal biopsies studied, finding a high frequency of this pathology has not been described in other populations and where its pathophysiology, treatment and prognosis is still to be defined

Patients' clinical characteristics and laboratory data on their last medical visit.

Variable	
Mean time in years between renal biopsy and last medical check-up	2.8 years (SD)
Mean proteinuria on last medical check-up	1500 mg/24 hours (SD)
Presence of hematuria on last medical check-up	None
Mean serum creatinine on last medical check-up	1.5 mg/dl (SD)
Mean GFR on last medical check-up (calculated by MDRD)	58 ml/min (SD)
Receiving HAART	29 patients (96%)
CD4 count higher than 200 on last medical check-up	10 patients (33%)
CD4 count between 100-200 on last medical check-up	7 patients (23%)
CD4 count lower than 100 on last medical check-up	13 patients (43%)
Undetectable viral load on last medical check-up	24 patients (80%)
High viral load on last medical check-up	6 patients (20%)
C3 or C4 low	19 patients (63%)
Presence of antinuclear antibodies or Anti DNA	24 patients (80%)

Microscopic Diagnosis

Type of Nephropathy	Number of patients
Non-collapsing focal and segmental glomerulosclerosis	13 (39%)
Lupus-like glomerulonephritis	10 (30%)
Chronic interstitial nephritis	4 (12%)
IgA nephropathy (Berger's Disease)	4 (12%)
Minimal change glomerulonephrittis	1 (3%)
Collapsing segmental and focal glomerulosclerosis	1 (3%)

P8.08

New classification criteria for systemic lupus erythematosus correlate with disease activity

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Aim. To determine the prevalence of American College of Rheumatology (ACR) and Systemic Lupus International Collaborating Clinics (SLICC) classification criteria among systemic lupus erythematosus (SLE) patients; to determine disease activity and severity; and to investigate the correlation of classification criteria with disease activity, and of disease activity and damage index with disease duration.
Methods. We performed a cross-sectional study on 110 SLE patients from the Division of Rheumatology and Clinical Immunology, University Hospital Centre Rijeka, Croatia in the period from September to December 2013 and determined disease duration and the total number of ACR and SLICC classification criteria. Disease activity was assessed by Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) index and organ damage by Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index.
Results. The number of SLICC classification criteria met per patient was significantly higher than the number of ACR criteria (7 [IQR 6-8] vs 5 [IQR 4-6], $p<0.001$). Moderate correlations were detected between the number of SLICC classification criteria and disease activity index, both in case of active ($r=0.48$, $p=0.003$) and inactive disease ($r=0.43$, $p<0.001$). We neither found a correlation between the number of ACR criteria and disease activity nor between disease activity and disease duration. However, there was a good correlation between SLICC/ACR damage index and disease duration ($r=0.63$, $p<0.001$).
Conclusion New SLICC classification criteria correlate with disease activity because they capture more manifestations also included in the SLEDAI index. Patients with longer disease duration had a larger damage index score.

P8.09

Urinary concentrations of chemokines and cytokines in lupus patients

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Objective. Urinary concentrations of specific chemokines and cytokines were assayed in lupus patients.
Method. One hundred and one lupus urine samples were assayed for urinary MCP-1, VCAM-1, CXCL16, TNFR-1, p-selectin, TWEAK, Lipocalin and Adiponectin using ELISA kits. Patients were classified into "active nephritis", "inactive nephritis" and "non-nephritis" groups. Urine infections were excluded. The unpaired T test was used for comparison of cross sectional data. A p value of <0.05 is considered significant.
Results. In the "active nephritis" group, MCP-1 (p=0.0007; p=0.0002), TNF-R1 (p=0.0005; p=0.00002), VCAM-1 (p=0.0004; p=0.0000004) and Lipocalcin (p=0.0001; p=0.00002) concentrations were elevated compared to the other 2 groups. The "inactive nephritis" group had higher MCP-1 (p=0.04), VCAM-1 (p=0.0007) and Adiponection (p=0.02) concentrations than the "non-nephritis" group. Urinary concentrations of TWEAK, CXCL-16 and p-selectin did not show any significant difference between the groups.
Conclusion. Lupus patients with active nephritis showed a profile of significantly elevated urinary MCP-1, TNF-R1, VCAM-1 and Lipocalcin concentrations. Clinically inactive lupus nephritis patients exhibit elevated concentrations of MCP-1 and VCAM-1 compared to patients with no nephritis, suggesting the possibility of an ongoing low grade inflammatory process in the kidneys.

Mean urinary concentrations of chemokines and cytokines

Nephritis	MCP-1 (pg/ml)	TWEAK (pg/ml)	TNF-R1 (pg/ml)	CXCL-16 (pg/ml)	VCAM-1 (pg/ml)	Lipocalin (pg/ml)	P-Selectin (pg/ml)	Adiponectin (pg/ml)
Active (n=12)	755	15	1732	95	3192	5520	314	3592
Inactive (n=28)	172	11	913	52	2503	4062	320	3690
Non-Nephritis (n=61)	77	15	676	47	1720	3672	320	2312

P8.10

Both contact system and neutrophil extracellular traps take part in the pathogenesis of lupus nephritis

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Objective. To detect the serum levels of high molecular weight kininogen (high molecular weight kininogen, HK) and citrullinated histone H3 (cH3, neutrophil extracellular trap symbol protein) in patients with lupus nephritis (LN).To explore their pathogenic effects in this disease.
Methods. Serum samples from 70 patients with LN, among those,10 uninfected LN patients with both activity stage and remission stage serum, 16 patients at activity stage with infection;8 patients with chronic glomerulonephritis and 22 healthy controls were collected. Serum HK and cH3 were detected using commercial ELISA kits. The association among serum HK, cH3 and SLE-DAI, urine red blood cell count, 24-hour urinary protein excretion,complement were furthure analyzed.
Results. (1)The serum level of HK in LN patients at activity stage were all lower than those at remission stage (117.58±87.01ug/ml vs 273.96±194.82ug/ml, p<0.001) and chronic kidney disease group (280.96±116.91ug/ml, p<0.001) and healthy controls (253.04±94.58ug/ml, p<0.001). The serum level of cH3 in LN patients at activity stage are all higher than those at remission stage(446.14±219.33pg/ml vs 315.81±239.48pg/ml, p<0.001) and chronic kidney disease group (277.14±24.76pg/ml, p=0.001) and healthy controls (309.11±147.82pg/ml, p<0.001). (2) Sequentialy detecting the 10 LN patients which both activity and remission serum, the serum level of HK at activity stage (101.42±84.05ug/ml) were lower than that at remission stage (298.20±186.20ug/ml, p=0.01)), while the serum level of cH3 at activity stage (528.35±255.51ug/ml)are higher than that at remission stage (276.67±164.07, p=0.02). (3) At activity stage the serum level of HK and cH3 in LN with infection were both showed no significant difference with those in LN patients without infection.
Conclusion. Both contact system and neutrophil extracellular traps participate in the pathogenesis of LN.

P8.11

Level and significance of serum peptidylarginine deiminase type 4 in patients with systemic lupus erythematous

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Objective. To detect the serum level of peptidylarginine deiminase type 4(PAD4) in patients with systemic lupus erythematous (SLE), and explore its pathogenic effect in the disease.
Methods. 14 patients with SLE on active stage and 8 patients with SLE on remission stage were enrolled in this study. 11 patients with rheumatic arthritis (RA) on active stage and 11 patients with RA on remission stage were considered as positive controls. 8 patients with primary chronic kidney disease (CKD) were considered as disease controls. 12 healthy volunteers were considered as normal controls. All of their serum samples were collected. Serum PAD4 was detected using commercial ELISA kits. The association between serum PAD4 and SLE-DAI, 24-hour urinary protein excretion, erythrocyte sedimentation rate (ESR) in SLE patients was further investigated.
Results. The serum levels of PAD4 on active stage and remission stage of SLE patients were respectively elevated than that of the normal controls, 75.99 (60.44, 99.16) kU/L,76.29 (62.79, 119.14) kU/L vs 32.58 (26.13, 41.46) kU/L (both p<0.05). The serum level of PAD4 in patients of SLE on activity and remission stage were higher than that in CKD group, 75.99 (60.44, 99.16) kU/L,76.29 (62.79, 119.14) kU/L vs 53.11 (47.69, 58.83) kU/L (both p<0.05).
Conclusion. PAD4 was kept a higher level in SLE patients, it might involve in the pathogenesis of SLE.

P8.12

Changes in the monocyte subsets phenotype are associated with HMGB1+ microparticles isolated from Systemic Lupus Erythematosus patients

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Background. Microparticles, (MPs), cellular fragments that include membrane and cellular derivatives, are considered to play a critical role in immune responses, due to their ability to transfer and modulate a variety of components. MPs are recognized by monocytes affecting their maturation, migration, and function. Interactions between MPs and monocytes have not been described in SLE.
Methods. MPs and monocyte subsets from SLE and healthy controls were characterized by multiparametric flow cytometry.
Results. MPs from SLE patients had higher amounts of HMGB1, C1q, and IgM. We did not observed differences in the number of MPs, or in the content of DNA, RNA and phosphatidylserine compared to healthy controls. Regarding monocyte subsets, the percentage of non-classical was reduced in SLE patients, classical and intermediate monocytes from patients have significantly reduced expression of CCR2, CCR5, CX3CR1, CD11b, CD36, and HLA-DR; non-classical monocytes have reduced expression of CD36. The FcR CD64 and CD86 were significantly increased in classical monocytes. Regarding C1qR, CD93 was reduced in all subpopulations and CD35 was reduced in classical and in intermediate monocytes. Remarkably, HMGB1+ MPs have a negative correlation with the expression of CCR2 and CX3CR1 on classical and intermediate monocytes.
Conclusions. MP recognition and activation by the specific monocyte subsets should be altered in view of its FcR, CD36 and C1qR expression. The associations indicated that in addition to their ability to form immune complexes (C1q+ and IgM+) in SLE patients, MPs could affect the interaction of monocytes with the endothelium, and their recruitment into inflamed tissue.

P8.13

Ki-67 proliferation index in renal biopsy samples of patients with systemic lupus erythematosus

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Introduction. Renal involvement is the most significant prognostic factor in patients with systemic lupus erythematosus (SLE). Renal biopsy findings play an important role in treatment decisions. Ki-67 is a monoclonal antibody that is only found in proliferative cells. We investigate the proliferation activity in

renal biopsy specimens by using Ki-67 monoclonal antibody, and to compare the proliferation index between different subgroup of patients.
Material-Method. Renal biopsy specimens of 29 patients with SLE were retrospectively evaluated. Ki-67 immunostaining was performed. For each specimen 1000 cells were counted and the number of Ki-67 positive cells was determined. Ki-67 proliferation index was compared with disease activity, serum creatinine, complement levels, protenuria and anticardiolipin antibodies.
Results. A positive correlation between Ki-67 proliferation index, creatinine levels and SLE disease activity index were found. In subgroup of lupus nephritis, Ki-67 is correlated with class III and IV. Allthough conventional activity indexes were low in 3 of 9 patients with class II lupus nephritis, Ki-67 proliferation indexes were high indicating proliferation in also class II patients.
Conclusion. Ki-67 can be used as a proliferation marker in renal biopsy specimens of patients with SLE and may support the conventional activity indexes.

P8.14

Activity and damage in systemic lupus erythematosus patients during follow-up period

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Objectives. to describe the outcomes and predictors for development of damage in a large cohort of SLE patients. Materials: this was a prospective longitudinal study of a cohort of SLE patients between 1999 and 2010. Disease activity, damage and treatment data were collected. Death information was provided by phone survey.
Results. the study included 280 patients (184 females, 96 male) with mean age 29.2±10.9 years. Antiphospholipid syndrome (APS) was verified in 151 patients (F 111; M 40). There were 22 072 assessments and total follow-up period of 4958 patient-years. It was registered 500 items of damage (in 143 patients) and 48 deaths. In 10 years 24 patients were excluded because of the lack of information. The overall standardized mortality ratio was 2.0 (95% CI 1.5, 2.8). A multivariate regression model confirmed male sex (HR 1.83, p=0.04), age of first symptoms under the 40 years (HR 1.0, p=0.04) and valvular heart disease (HR 2.5, p=0.01) as independent risk factors of death. The most common causes of death were acute damage of the vascular bed (43%) with subsequent multiorgan symptoms, infection (27.8%), terminal kidney diseases (17%) and malignancy (9%). The next predictors for damage accrual were more frequent prior damage: APS, male sex, older age at diagnosis, SLE activity, corticosteroid and cyclophosphamide exposure. Patients with the predictors were more likely to develop new damage earlier in their disease than later.
Conclusion. SLE patients have premature mortality. Concomitant APS, male sex, SLE activity, corticosteroid and cyclophosphamide exposure were associated with damage development.

P8.15

At pre-clinical stage; connective tissue disease is indistinguishable from other inflammatory arthritis on ultrasound in CCP-negative early arthritis patients

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Background. ANA positivity is a common finding in patients presenting with inflammatory joints symptoms without connective tissue disease (CTD) features or satisfactory RA classification criteria. There are limited data on long-term prognosis on this subgroup of patients.
Objectives. To assess if musculoskeletal ultrasound (US) can predict future diagnosis in ANA positive CCP negative arthralgia.
Methods. Patients with new inflammatory joint symptoms where recruited into IACON study. Data of ANA positive patients who neither satisfied OA nor CTD diagnosis at presentation were analysed. Patients had a baseline clinical and US assessment and were followed up over 1-4 years.
Results. A total of 151 ANA positive patients were recruited; 73 (48.3%) were CCP negative, of whom 17 (23%) satisfied the RA classification criteria while 45 (61%) were diagnosed as undifferentiated inflammatory arthritis (UA). Of these 45 UA patients, after 1-4 years of follow up, 10 (22%) were ultimately diagnosed as CTD. In those with UA at baseline, 33.3% of endpoint CTD patients had synovitis (GS ≥2 and/or PD ≥1) at baseline in comparison to 45% of endpoint inflammatory arthritis, 50% of endpoint UA. GS and PD scores at baseline did not differ between endpoint diagnoses (Table I).
Conclusions. In absence of CCP, patients with early onset inflammatory arthritis that were ultimately diagnosed as a CTD were clinically and sonographically indistinguishable from those were ultimately diagnosed as seronegative RA or SpA.

Table. Median (1st-3rd Quartile) of total GS and PD score in different diagnosis groups.

Ultimate diagnosis	GS Median (1st-3rd Q)	PD Median (1st-3rd Q)
CTD	10 (3.5, 12.5)	0 (0, 2)
IA	7 (6, 17)	0 (0, 2)
UA	11.5 (5.3, 14.8)	0.5 (0, 2)
Non-inflammatory	8 (6, 13)	0 (0, 2)

P8.16

Profile of male Systemic Lupus Erythematosa observed in Internal Medecine

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Introduction. The male 's systemic lupus erythematosa (SLE) is characterize by its rarity and by its severity
Objectives. To analyze the clinical, biological and evolutive profile of the male lupus.
Patients and Methods. Retrospective study from January 1996 to December 2014 Diagnosis of SLE is established according to the criteria of the ACR.
Results. on 214 cohort of SLE we collected 11 cases of male lupus (5%) with average age of 31 years (19 - 54). Main clinical manifestations prevail by the joint (5) or skin achievement (7), hematological manifestations (5) type of sever to moderate thrombopenia (2) and hemolytic anemia (4). Severe manifestations observed were glomerulonephritis (7) myocarditis (1), pleural effusion (4) pericarditis (4) and neurological manifestations (2).
Immunological tests are associated in phospholipids syndrome in 4 patients.
The course is characterized by thromboembolisms (4), failure kidney and (4).
The major infections having justified a hospitalization, appeared as nosocomial and arising under immunosuppressive are frequent (5) so we noted tuberculosis (4), visceral leishmaniasis (1) , septicemia and/or septic arthritis (1). The specific treatment was dictated by the severity of the visceral localization and the clinical context. We deplored 2 death (septicemia and mutiivisceral failure in activated macrophagia) , 2 patients developed failure kidney and were transferred in hemodialysis and 2 developed osteonecrosis hip.
Conclusion. Renal and hematologic manifestations characterized revealing men SLE
The poor prognosis is associated in thrombo-embolisms events, renal failure and a high increased susceptibility in the infections.

P8.17

The association between type I Interferon Response, complement activation and clinical findings in Systemic Lupus Erythematosus

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Background/Objectives. We evaluated some biomarkers associated with type I IFN response and complement activation in SLE; and determined their relationship with clinical findings.
Methods. We included 94 SLE patients (88F, 6M, mean age: 39) and 101 healthy controls (87F, 14M, mean age: 38). Complement factor H, complement fragments Bb, C3a-des-arg, ficolin-2, sCXCL-12 (SDF-1), sCXCL-10 (IP-10), neutrophil activation-related LL-37, and BLyS levels were determined with ELISA.
Results. SLE patients had significantly higher sCXCL-12 (646.9±859.1 vs. 242.8±240.8, p=0.001), sCXCL-10 (469.6±537.9 vs. 262.9±351.4, p=0.012), and complement fragments Bb (4.36±2.2 vs 3.68±2.5, p=0.046) levels than healthy controls. C3a-des-arg (4.14±2.2 vs. 4.94±1.4, p=0.003) and LL-37 (3.74±1.8 vs. 5.5±1.6, p<0.001) levels were significantly lower in SLE group than in the control group. Ficolin-2 and BLyS levels were similar in both groups. When SLE patients whose SLEDAI scores were active and inactive were compared, it was seen that sCXCL-10 was significantly higher in the former group (p=0.023). SLE patients with arthritis had significantly higher sCXCL-12 (p=0.003), BLyS

(p=0.03), sCXCL-10 (p=0.001) and complement fragments Bb (p=0.004) levels than SLE patients without arthritis. SLE patients with neurologic involvement had significantly lower C3a-des-arg level when compared to other SLE patients (p=0.022). BLyS was found to correlate with LL-37 (r=0.27, p=0.033) and disease duration (r=0.39, p=0.002).
Conclusions. Our results support the roles of type I IFN response and complement activation in the pathogenesis of SLE. sCXCL-12, sCXCL-10, C3a-des-arg, LL-37, and complement fragments Bb might be used as biomarkers in SLE and they might be useful to define certain clinical subgroups.

P8.18

Increased serum Tie-2 Level in Systemic Lupus Erythematosus patients and related factors

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Background/Objectives. In this study, we evaluated biomarkers related to endothelial injury, angiogenesis (tyrosine-kinase with Ig-like and epidermal growth factor-like domain 2, Tie-2) and NF level. In addition, we investigated the association between this parameters and clinical findings in our SLE patients.
Methods. Age-and-sex matched 60 SLE patients (56F, 4M, mean age: 39.5±11.5) and 34 healthy subjects (29F, 5M, mean age: 38.2±10.9) were included into the study. Plasma Tie-2 and neurofilament level were evaluated by ELISA method. NF level was converted to its log level, because the distribution of its level was not normal.
Results. Tie-2 level was significantly lower in SLE patients than in healthy controls (19.03±11.9 pg/ml vs. 31.3±15.1 pg/ml, p=0.001). Neurofilamentin level was similar in SLE patients and controls (median: 5.08 (range: 3.09-6.35) pg/ml vs. 5.12 (3.08-5.7) pg/ml, p>0.05). Serum Tie-2 level in SLE patients with major organ involvement was significantly lower than in patients without major organ involvement (13.6±7.8 vs. 20.5±12.4 pg/ml, p=0.05). In the healthy control group, serum Tie-2 level correlated significantly with NF level (r=-0.66, p=0.003). In the SLE group, these parameters did not seem to correlate with each other.
Conclusions. Serum Tie-2 level in SLE patients was significantly lower. Decreased Tie-2 level may be related to major organ involvement in SLE.

P8.19

Description of Vitamin D enzymatic machinery in Systemic Lupus Erythematosus

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Background. Vitamin D deficiency is associated with a variety of autoimmune condition. Local production from inactive form is very important in order for vitamin D to contribute to immune regulation.
Objective. to realize a complete description of all the enzymatic machinery implicated in activation and functioning of vitamin D at the cellular level.
Material and Methods. 20 consecutive patients with SLE and 12 matched by gender and age healthy donors (HDs) were evaluated. Sera and peripheral blood mononuclear cells (PBMCs) from SLE patients and HDs were analyzed for total 25-hydroxyvitamin D [25(OH)D] and for the transcripts of 1α-hydroxylase (CYP27B1) - the activating enzyme, 1α,25-dihydroxyvitamin D3 24-hydroxylase (CYP24A1) - the inactivating enzyme and Vitamin D Receptor (VDR). The statistical analysis was made with SPSS programme.
Results. Except CYP27B1 mRNA, which was decreased, all other experimental markers were higher in SLE patients than in HDs: p 0.034 for VDR, p 0.024 for CYP 27B1, p 0.021 for CYP24A1. An imbalance in VDR, CYP27B1 and CYP24A1 mRNAs expression in SLE PBMCs was suggested by significant correlation between them only in HDs (Table I). Moreover, SLE patients with 25(OH)D lower than 20ng/ml showed increased CYP24A1 mRNA expression compared to HD (p 0.008).
Conclusions. This data demonstrate the abnormal expression of enzymes involved in vitamin D metabolism in SLE patients.

Table I. Normal functioning of vitamin D enzymatic machinery found only in HDs.

mRNA	CYP27B1	CYP24A1
VDR SLE		
VDR HDs	r 0.682	p 0.021
CYP27B1 SLE		
CYP27B1HDs		r 0.591
		p 0.056

P8.20

Associations of SNPs located in STAT4, TNXB and ITGAM genes with susceptibility to Discoid and Systemic Lupus Erythematosus

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Lupus Erythematosus (LE) is a complex, heterogeneous autoimmune disease that manifests with a variety of clinical symptoms. Some LE types, like Discoid Lupus Erythematosus (DLE) affect only skin, whereas the others like Systemic Lupus Erythematosus (SLE) affect many organs. Despite previous studies revealing that some single nucleotide polymorphisms (SNPs) might be the risk factors for the SLE, little is known whether that susceptibility loci are associated with development of the skin types of the disease. In the present study, we have analyzed three SNPs located in ITGAM (rs1143679), TNXB (rs1150754) and STAT4 (rs7574865) genes in 35 SLE and 15 DLE patients from Polish population. The control group included 50 healthy donors from Polish population. SNPs were genotyped using TaqMan assays by Real-Time PCR on ViiA™ 7 Real-Time PCR System. Differences in allele and genotype frequencies were calculated with two tailed Fisher's exact test using STATISTICA 12.5 software. P values < 0.05 were considered as statistically significant. The allele A of rs1143679 (ITGAM), as well as the allele A of rs1150754 (TNXB) were significantly associated the with SLE, but not with the DLE compared to unaffected controls. Significant associations were also observed for the AA + AG genotypes of rs1143679 (ITGAM), as well as for the AA + AG genotypes of rs1150754 (TNXB) and the SLE, but not the DLE. In contrary, the TT genotype of rs7574865 (STAT4) was significantly more frequent in both SLE and / or DLE patients than in healthy controls.

P8.21

Factors implicated in development ofatherosclerotic plaque in SLE

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Subclinical atherosclerosis and early atherosclerotic lesions have an increased prevalence of SLE patients compared with the general population, and injuries occur at a younger age.
Objective. Assessment of risk factors and their influence in development of atherosclerotic lesions - plaque, in patients with SLE.
Material and Method. The study which included 97 patients with SLE, diagnosed in according to ACR 1997 criteria and 64 persons in control groups matched sex and age. Atherosclerosis lesions have been evaluated using the carotid intimae-media thickness (IMT), which was measured at the common carotid artery, using B-mode ultrasound. We evaluated traditional risk factors (hypertension, smoking, sex, age, cholesterol, etc) and disease activity was assessed by the SLEDAI index (SLE Disease Activity Index), and BILAG score.
Results. All the patients were female, mean age 43, 14±10,40SD (years), and 43, 31±10,80SD control groups, mean disease duration of 9, 05±5, 21 (years) of SLE groups. Mean value IMT in patients with SLE showing atherosclerotic plaque is 0.598±0,038mm, (p=0.0001), higher than the average IMT value group of patients without plaque (0.537±0,036mm). ROC curve analysis shows that traditional risk factors have a lower contribution in the development of atherosclerotic plaques in the patients with SLE compared with controls (0.90 vs AUROC AUROC = 0.72) and specific risk factors present major impact on them (AUROC = 0.89).
Conclusion. Traditional risk factors have little impact compared with lupus disease specific risk factors in atherosclerosis.

P8.22

Jessner lymphocytic infiltration of the skin or lupus erythematosus?

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Jessner lymphocytic infiltration of the skin is a rare benign yet chronic T-cell infiltrative disease. The condition remains poorly understood, some authors considering it a variant of lupus erythematosus. The aim was to describe the case of a patient presenting with manifestations of Jessner lymphocytic infiltration of the skin.
A patient, male, aged 44 years, presented with a relapsing skin eruption over the trunk and upper extremities. The rash presented initially during the summer, lasted for 5 months and remitted without any specific treatment. A year later the rash presented during the summer, relapsing during the winter. Corticosteroids were administered locally and hydroxychloroquine was administered orally. A skin biopsy was performed, which showed Jessner lymphocytic infiltration of the skin without any evidence of lupus erythematosus. Treatment was stopped. The patient is without any specific treatment the skin rash having periods of flare and remission. At the moment the patient has an erythematous rash in the trunk without pruritus, pain or exfoliation. There are no systemic manifestations.
Jessner lymphocytic infiltration of the skin is a benign chronic condition, considered by some authors to be a variant or a manifestation of lupus erythematosus. The cause of the disease is unknown. It follows a benign course with flares and remissions.

P8.23

The cardiovascular risk associates in systemic lupus erythematosus patients

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Background. Systemic lupus erythematosus (SLE) patients present with a particularly increased cardiovascular risk (CVR).
Objectives. The aim of this study was to evaluate the relation of the CVD with SLE-related particularities.
Methods. Patients diagnosed with SLE according to SLICC 2012 criteria were successively included. SLE disease activity was assessed using SLAM score and the damage accrual by the SLICC index. CVR was assessed in all patients by the Reynolds risk score (RRS) and the Framingham Risk Score (FRS).
Results. 84 patients were included, with a mean±SD age at inclusion of 44.7±12.1 years, age at diagnosis of 35.6±10.9 years and net feminine predominance (87%). The presence of secondary antiphospholipid syndrome (APS), but not of Raynaud or Sjögren syndrome, was associated with a significant increase in CVR as assessed by both RRS and FRS [med (inf; sup) 1.8 (0.2-7.9) vs 0.9 (0.2-7.9), respectively 10.6 (0.5-28.5) vs 3.3 (0.5-24.8); $p<0.05$].
The CVR assessed by RRS and FRS was found to be significant correlated with the SLICC index results ($p=0.016$; r=0.264, respectively $p<0.001$; r=0.375), but not with SLAM score ($p<0.05$).
In patients with present hydroxychloroquine treatment the CVR computed by RRS and FRS was significant lower [med(inf;sup) 0.9(0.2-7.9) vs 1.2 (0.2-7.7), respectively 1.2 (0.2-7.7) vs 8.6 (1.7-28.5), $p<0.05$].
Not other similar relation was observed for any other treatment. However, the length of corticosteroid therapy was correlated with the CVR scores ($p=0.031$, r=0.238).
Conclusion. The presence of secondary APS, accrual damage and the length of corticosteroids therapy is associated with an increase of CVR in SLE patients. On the contrary, hydroxychloroquine might be protective.

P8.24

Renal biopsy complications in patients diagnosed with Lupus Nephritis - experience of a Portuguese Rheumatology Center

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Introduction. Renal involvement in patients with Systemic Lupus Erythematosus (SLE) has major prognostic implications due to increased morbimortality. Clarifying lupus nephritis (LN) class with percutaneous renal biopsy (PRB) is an imperative step that allows adequate therapeutic management.
Macroscopic haematuria is the most frequent complication of PRB but more severe complications, such as perirenal haematoma and major haemorrhage, may occur and be life threatening.
Objectives. to evaluate complications following PRB in a Portuguese cohort of LN patients.
Methods. retrospective study on LN patients submitted to PRB between 2004 and 2015. Information on renal complications along with demographic, clinical and laboratory data were obtained from medical records.
Results. In a cohort of 79 patients with SLE, we identified a total of 18 with renal involvement, 14 females (77.78%) and 4 males (22.22%), with present mean disease duration of 11.86±7.93 years in females and 9.00±3.92 years in males. 16 underwent PRB and had LN according to the OMS classification, 4 class III, 8 class IV, 4 class V.
Only 2 out of 16 patients had complications following PRB, both were males. Both presented perirenal haematoma and one had severe haemorrhage requiring blood transfusion and renal artery embolization. This patient had positive anticardiolipin antibodies and was posteriorly submitted to renal transplantation.
Conclusion. Although being a minimally invasive procedure, PRB carries risks and risk/benefit has to be carefully weighed. PRB performed with imaging support, namely echography, and preceded by platelet transfusion and desmopressin protocol, when indicated, may decrease complications.

P8.25

Unusual Manifestationsof SLE Observed in Internal Medicine Cohort

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Objectives. To analyze through cohort of SLE patients some atypical manifestations.
Patients and Methods. Retrospective study from January 1994- to December 2014 of SLE patients following in specialized consultation and/or in hospitalization .The diagnostic of SLE is established ACR criteria. All patients have beneficiate of autoimmunity tests and have an average follow-up of 24 months.
Results. On 214 studied cases, average age of revealing disease was about 25.9 years Revealing forms of SLE were feverish cytopenia in a macrophagic activation syndrome (5), Kikuchi adenitis (4) mimicking lymphoma (1), acute pancreatitis (4), chronicle parotid hypertrophy (2) and acute panniculitis (2). The opportunist infections were tuberculosis (5) or visceral leishmaniasis (7). We observed in the following up liver steatosis attested by histopathology data (5) as well as liver regenerative nodular's hyperplasia (1), infiltrative pneumopathy (4), pulmonary arterial hypertension (2), calcinosis (5), acute crisis of recurrent angioedeme (4), reversible posterior cerebral angeitis (2), increases of chronic colic pseudo-obstructions (2), eye infringements with altered vision by vasculitis (2), spontaneously reversible hypothermia and paralysis diaphragmatic (2). Celiac disease (5), autoimmune hepatitis (7) and type 1 diabetes (4), rheumatoid arthritis and scleroderma (9) were main autoimmune diseases associated to SLE. Iatrogenic adverse effects were pancreatitis in Ibuprofen (1), cutaneous reactions in antimalaria drugs (7).
Conclusion. The unusual clinical expressions represent 25% of the cases of SLE and constitute diagnostic wandering when they inaugurate the disease (feverish cytopenia, abdominal emergency….)so relevance the perpetual revision of criteria diagnosis and prognostic of this systemic multidisorder disease of plural expressions.

P8.26

Capabilities of European lupus Groups: members of LUPUS EUROPE

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Background. Lupus groups will have a significant role to play in healthcare. LUPUS EUROPE is an umbrella organization of 24 national lupus groups in Europe.
Objectives. To identify the different structures and capabilities among European lupus groups.
Methods. An online survey was distributed to validated contacts within member groups. It had four sections: (i) group aims, structure and funding (ii) resources and network (iii) the situation for people living with lupus in the country (iv) the lupus group needs and wishes in capability building nationally and on European level. Questions offered single answer, multiple response or commentary.
Results. 14 groups (58%) responded from Belgium (2), Cyprus, Denmark, Finland, Greece, Italy, Iceland, Netherlands, Norway, Spain, UK, Sweden and Switzerland. Key results included:
• 13/14 groups have an elected board of volunteers, 11/14 are run by volunteers
• 9 of the 14 groups are affiliated with the arthritis and/or rheumatism associations in the country
• 12/14 groups cited membership subscriptions as the main source of funding
• 8/12 groups identified need for capacity building in political lobby activities
More than 2/3rds of the groups expect LUPUS EUROPE to support member groups in their advocacy work and provide scene and opportunity to have more people educated and engaged in improving lupus patient interests in research and political work.
Conclusions. There is a diverse range of capabilities and needs amongst national European lupus groups; some are very well established with significant capabilities, while others need capacity building in priority areas.

P8.27

Are vitamin D levels in lupus patients associated with non-scarring alopecia?

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Background. Non-scarring alopecia is one of the new Systemic lupus erythematosus (SLE) criteria. Although it is not specific, alopecia is common during active lupus disease.
Objectives. The aim of this study was to determine the relationship between vitamin D levels and alopecia in SLE.
Methods. Sixty patients were included in the study. Vitamin D levels were measured by HPLC reverse-phase chromatography and confirmed by mass spectrometry.
Results. Forty of the 60 SLE patients (66.7%) had low vitamin D levels, while 35 of all patients (58.3%) had alopecia. Vitamin D levels were not significantly different between patients with and without alopecia (Table). Twenty-six of the patients with alopecia and 14 of the patients without alopecia revealed low vitamin D levels (Table). Alopecia incidence was relatively in patients with decreased vitamin D level higher than in patients with normal vitamin D level (Odds ratio: 2.27, 95% confidence interval: 0.76-6.78, p=0.142).
Conclusions. Vitamin D levels are associated with systemic inflammatory diseases. In our study, vitamin D level was relatively lower and the incidence of decreased vitamin D level was relatively higher, in SLE patients with alopecia compared to patients without alopecia. However, there is need for a larger cohort to verify this association.

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Vitamin D levels in lupus patients with and without alopecia

Alopecia	Present (n=35)	Absent (n=25)	*p*
Vitamin D level, mcg/L	13.5±11.8	16.9±13.7	0.254
Decreased vitamin D level, n (%)	26 (72)	14 (56)	0.142*

*Odds ratio: 2.27, 95% confidence interval: 0.76-6.78.

P8.28

Hair mercury is inversely related to disease associated damage in systemic lupus erythematosus

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Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease. Numerous studies support a specific gene-environment interaction in the development and progression of SLE. *In vitro* and animal studies strongly implicate inorganic and organic mercury as one such environmental factor. The aim of this study is to investigate the relationship between disease activity and damage in SLE with exposure to inorganic mercury primarily derived from mercury vapour (Hg^0) from dental amalgams and exposure to methyl mercury (MeHg) from fish consumption.
Methods. We measured total Hg concentrations in urine (biomarker of Hg^0exposure) and hair (biomarker of MeHg exposure) in fifty two SLE patients. Disease activity was assessed using the British Isles Lupus Assessment Group index (BILAG) and severity of damage was measured using the Systemic Lupus International Collaborating Clinics/ American College of Rheumatology (SLICC/ACR).
Results. There was no relationship between urinary Hg and disease activity or damage.A significant negative correlation was observed between hair Hg and BILAG (R= -0.323, 95% CI: -9.808, -0.513). Hair Hg was also negatively correlated with SLICC/ACR (R= -0.377, 95% CI: -1.568, -0.046).
Discussion. Low dose exposure to Hg^0, primarily from dental amalgams was not associated with disease activity or damage in SLE patients. There was an inverse relationship between hair Hg levels and disease activity and damage in SLE. This may be due to hair Hg being a surrogate marker for individual exposure to fish and therefore the associated consumption of various nutrients, including anti-inflammatory n-3 polyunsaturated fatty acids (PUFAs).

P8.29

Another image of lupus in men

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Systemic lupus erythematosus (SLE), a chronic autoimmune inflammatory disease, with unknown etiology, is generally considered to be uncommon among men. We report a case of SLE, in a middle age man, miner, presenting with arthritis, adynamia, fatigue, weight loss, continuous fever, Raynaud phenomenon, whose diagnosis was delayed due to history of tick bite (Lyme disease). The lack of response to antibiotic treatment and the presence of systemic manifestations (persistent fever, impaired of joints, kidney, cardiopulmonary, severe anemia) associated with inflammatory syndrome required immunological assessment that highlight the presence of a large number of antibodies in particular of lupus. After exclusion of cancer disease, hepatitis, immunodeficiency syndrome, endocarditic disease and other infections, was administered cortisone and immunosuppressive therapy (hydroxychloroquine, azathioprine) with favorable evolutions.
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P8.30

Systemic Lupus Erythematosus and mother's breast feeding status

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Objectives. To evaluate the likelihood of breast-feeding in patients with Systemic Lupus Erythematosus (SLE).
Methods. It was a prospective study of 44 cases of postpartum course of the disease in 43 women with documented SLE (ACR 1997), 5 of which had the antiphospholipid syndrome. Patients were observed at V.A. Nasonova Research Institute of Rheumatology from February 2011 to August 2014y., all gave written informed consent to participate in the study. Therapy after delivery consisted of 2-32mg/day Metypred- 43 (97.7%) patients and 200-400mg/day Hydroxychloroquinum - 35 (79.5%) patients. Patients were subjected to thorough examination at 1, 3, 6 and 12 months after delivery. Data are presented as Me [IQR].
Results. 31 out of 44 (70.5%) patients did not discontinue breastfeeding. The duration of lactation was from 2 weeks to 24 months (Me = 8 [3.14] months). The lactation was suppressed immediately after birth in 13 cases: in 4 - due to the high activity of SLE, in 4 - on mother's request, in 2 - because of perinatal death of the child and in 3 - due to the state of the child. Natural curtailment of the lactation was the main reason for not breastfeeding in 23 (52.3%) cases. Twelve (27.3%) patients were breastfeeding for 12 or more (up to 24) months. All these patients had low SLE activity (n = 3) or SLE remission (n = 9).
Conclusions. Lactation in SLE patients is possible in the absence or the low activity of disease.

P8.31

The carotid intima-media thickness - role of assessment clinically silent atherosclerosis in patients with on long-term corticosteroid treatment

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Objectives. In inflammatory joint diseases(IJD)- proven amplifying the risk of acute coronary syndrome by 1.5 times compared to the general population . In systems connective tissue diseases, there are secondary atherosclerotic changes during the course of carrying out the treatment with systemic corticosteroids(SCS).
Aim. To assess of subclinical atherosclerosis in patients receiving continuous treatment with SCS./>Methods: CIMT is measured by B-mode color Doppler ultrasound, 7-10 MHz with 7,5 MHz linear probe with an ultrasonographic mashine "Essaote" of 67 patients aged 40 to 60 years that are maintenance treatment of a SCS- a dose of 10 mg Prednisolon over 5 years. The 34 patients with IJD and 33 patients with systemic lupus erythematosus (SLE) control group of 39 patients. Systematic Coronary Risk Evaluation(SCORE)- assesment the Framingham Health Study Scale . />Results: In the first group with IJD - CIMT was 1,3mm ± 0,1 / p<0.05 / and SCORE was 10% by 12 patients and 15% by 22 patients.
In the second group with SLE - CIMT was 1,28 mm± 0,21/ p<0.05 /, SCORE was 10% by 8 patients and 29% by 25 patients.
In the control groupe - CIMT was 1,24 mm ± 0,1 / p<0.05 / and in the patients, SCORE was 10% by 16 patients and 20% by 23 patients.
Conclusions. The carotid sonography miniinvasive method for assessment and prevention of atherosclerotic complications patients . The levels CIMT correlate with the degree of risk may be markers for clinical non-declared atherosclerosis in high risk patients.

P8.32

Comparison of the responsiveness and minimal important differences (mid) of the lupusqol and the SF-36 in patients with Systemic Lupus Erythematosus (SLE) after treatment of a moderate or severe flare

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Objective. With improving survival in SLE patients, patient-reported health-related quality of life (HRQoL) has become an important outcome. The LupusQoL is a reliable and valid HRQoL measure and this study evaluates the responsiveness and minimal important differences (MID) for each of the 8 domains of the LupusQoL and SF-36 in SLE patients.
Methods. SLE Patients who flare were recruited from nine UK centres. HRQoL were assessed using LupusQoL, SF-36, and Juniper global change score at baseline and at monthly visits for nine months. The responsiveness of the LupusQoL and the SF-36 were explored when patients reported an improvement, no change or a deterioration of health status between consecutive time-points. MID were estimated as mean changes when minimal change was reported on the Juniper scale.
Results. 101 patients were recruited [94% female, 62.6% white Caucasians, mean (SD) age 40.9 (12.8) years.] For all LupusQoL domains, mean HRQoL worsened when patients reported a deterioration in health status, improved when patients reported an improvement and was stable when little change was reported; SF-36 domains showed comparable responsiveness. The estimated MID for the LupusQoL for deterioration ranged from -2.4 to -8.7 and for improvement 3.5 to 7.3; for the SF-36, -2.0 to -11.1, and 3.8 to 10.9 respectively.
Conclusion. All LupusQoL domains are sensitive to change when patients report a deterioration or improvement in their health status. LupusQoL items were informed by patients and provide the advantage of SLE specific domains that are important to the patients which are not captured by the SF36.

P8.33

Pattern of Lupus Nephritis in the Military Hospital: A histological and immunofluorescence study

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Introduction. Lupus nephritis (LN) is the most common and serious manifestation of systemic lupus erythematousus (SLE).There is a wide variation in the natural history of systemic lupus erythematosus (SLE) among different ethnic and geographical groups. Studies in Arabs are few and those in North Africans and especially in the Sudanese population don't exist. This study aims to characterize the pattern of Lupus nephritis among Sudanese patients.
Objectives. To demonstrate the clinical,laboratory features of the disease.The study was conducted at the Renal Dialysis unit at The Military Hospital,Sudan. From April 2009-May 2010.Atotal of 34 patients were studied.
Results. Of the 34 patients there were 33 females and one male between 10-75 years with a median age of 24 years.The histological pattern of lupus nephritis using World Health Organization classification, class I (n=2,5.9%); class II (n=7,20.6%); class III (n=9,26.5%); class IV (n=8, 23.5%); class V (n=3,8.8%); class VI (n=5, 14%).There was no significant correlation between immunoglobulins & complement components performance and the WHO classes (p value >0.05 for all classes).The most common significant features at the time of biopsy were ≥3.5g of 24 hours urine protein detected in (94.1%)of the patients and edema in (73.5%) of them.
Conclusion. I conclude that focal segmental glomerulonephritis (class III) is the most common histopathological pattern of Lupus nephritis.The Sudanese pattern resembles that reported in some Arab countries such as Kuwait and KSA and differs from those reported in African countries and other parts of the world.