O001 / #406

FREE COMMUNICATIONS 01: SLE – FROM THE BEDSIDE TO THE BENCH
03-06-2025 4:50 PM - 5:50 PM

RNA DYSREGULATION AND SEIZURES IN AUTOIMMUNITY: THERAPEUTIC OPPORTUNITIES IN NEUROPSYCHIATRIC LUPUS

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Background and Aims: Neuropsychiatric systemic lupus erythematosus (NPSLE), often manifesting as seizures and cognitive impairment. The mechanisms are unclear, but Brain Cytoplasmic (BC) RNAs, which regulate synaptic protein synthesis, are implicated. BC RNA's synapto-dendritic targeting depends on its interaction with hnRNP A2 and Purα, guided by a GA motif in the 5' stem-loop. Deficiency in BC RNAs is linked to seizures. This study explores SLE autoantibodies against BC RNAs (anti-BC antibodies) as a potential cause.

Methods: Interactions between SLE anti-BC antibodies and BC RNA, along with RNA transport factor displacement, were analyzed using EMSAs. Sera or IgG from seizure-affected SLE patients were injected into mice with a permeabilized blood-brain barrier. Seizure susceptibility and mortality were assessed after auditory stimulation in the injected animals.

Results: Autoantibodies from a subset of neuropsychiatric systemic lupus erythematosus (NPSLE) patients, particularly those with seizures, target the GA motif in BC200 RNA. These autoantibodies displace RNA transport factors, leading to BC200 RNA mislocalization within neurons and its absence in synaptic regions. The presence of these autoantibodies was detected in cerebrospinal fluid (CSF) of NPSLE patients. A strong association was observed between seizure activity and elevated SLE anti-BC RNA autoantibody levels in serum. Mice injected with purified SLE anti-BC RNA autoantibodies exhibited severe seizure susceptibility with 100% mortality. However, when the mice were also given BC200 RNA decoy antigens, the seizures were completely prevented.

Conclusions: Our research identifies SLE anti-BC RNA autoantibodies as a mechanistic cause of NPSLE, suggesting BC200 RNA decoys could serve as targeted therapies for SLE-related seizures.

Keywords: BC200 RNA, Autoimmunity, Neuropsychiatric lupus

O002 / #235

FREE COMMUNICATIONS 01: SLE – FROM THE BEDSIDE TO THE BENCH
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EXPANDED CD72-CD95+B-CELLS ASSOCIATE WITH HIGH DISEASE ACTIVITY AND PERSIST AFTER RITUXIMAB TREATMENT IN SLE PATIENTS

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Background and Aims: Autoreactive B-cells are key drivers of lupus development, yet a precise characterization of their role and features remains scarce. We explored the expression of CD72, an inhibitory co-receptor, together with other markers in lupus.

Methods: Twenty SLE patients and ten healthy controls were included. Among lupus patients, nine had lupus nephritis (LN, 45%). Eight of twenty patients received rituximab (RTX) after baseline and were followed-up at 3 and 6 months. Data is represented as median and interquartile range (IQR). Cell phenotypes were analyzed by spectral flow cytometry. Correlation between B-cell subsets and Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score was assessed.

Results: Patients were mainly females (90%), of median age 38 (30-47.5) years. Flow cytometric analyses showed a decreased CD72 expression on CD19+B-cells in patients, compared to HCs. CD72 expression correlated inversely with disease activity scores (r=-0.57, p=0.04). Through unsupervised clustering, we defined a CD72-CD95+B-cell phenotype, which is enriched in plasmablast (20%) and memory cells (80%). We found higher frequencies of CD72-CD95+B-cells, with upregulated CD86 and downregulated CD20 in patients. LN patients showed increased frequencies of CD72-CD95+B-cells, compared to non-LN. In LN, expanded CD72-CD95+B-cells positively correlated with SLEDAI-2K (r=0.63, p=0.02) and inversely with C3d (r=-0.62, p=0.03) levels. In RTX-treated patients at 3 months, overall CD19+B-cells were declined, while CD72-CD95+B-cells persisted in these patients.

Conclusions: We identified an expanded CD72-CD95+B-cell subset displaying an activated phenotype in SLE patients, which associates with disease activity and

complement consumption and persists after RTX treatment suggesting a pathogenic role in the disease.

Keywords: systemic lupus erythematosus, Rituximab, B cells

O003 / #329

FREE COMMUNICATIONS 01: SLE – FROM THE BEDSIDE TO THE BENCH
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IGG AND IGA ANTI-LIN28A OUTPERFORM ANTI-DSDNA AND ANTI-SM IN DISTINGUISHING SLE FROM HEALTH AND OTHER AUTOIMMUNE DISEASES

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Background and Aims: Systemic lupus erythematosus (SLE) is characterised by the production of autoantibodies (Abs). Currently used abs either demonstrate high sensitivity across connective tissue diseases (e.g.,ANA) or high specificity yet low sensitivity (e.g.,anti-dsDNA). Our objective was to perform a broad screen of IgG and IgA antibodies to autoantigen specificities in SLE versus primary Sjögren's disease (SjD), systemic sclerosis (SSc), and healthy controls (HC) to identify novel Abs that could facilitate SLE diagnosis.

Methods: We analysed plasma samples from SLE (n=229), SjD (n=146), SSc (n=139) patients and 196 matched HC from the European PRECISESADS project (NTC02890121). Samples were screened for IgG and IgA seroreactivity against 1,609 protein autoantigens using KREX-based i-Ome arrays (Sengenics). Differentially abundant abs (daAbs) analysis was performed with the limma R-package after adjustments for age/gender, and polyspecific antibody reactivity following ROC analysis.

Results: Among 1,609 autoantigens, both IgG and IgA anti-LIN28A, were significantly elevated in SLE compared with SjD, SSc, and HC. Specifically, IgG anti-LIN28A was elevated in SLE compared with HC (sen=0.77, spe=0.69, AUC=0.80), SjD (sen=0.71, spe=0.75, AUC=0.78), and SSc (sen=0.67, spe=0.84, AUC=0.81). IgA anti-LIN28 was elevated in SLE compared with HC (sen=0.65, spe=0.83, AUC=0.80), SjD (sen=0.59, spe=0.82, AUC=0.76), and SSc (sen=0.61, spe=0.91, AUC=0.83). Anti-LIN28A

outperformed anti-dsDNA (sen=0.31, spe=1.00) and anti-Sm (sen=0.04, spe=1.00) in distinguishing SLE from HC (AUC=0.65 and AUC=0.52, respectively), SjD (AUC=0.65 and AUC=0.52, respectively), and SSc (AUC=0.64 and AUC=0.52, respectively).

Conclusions: Anti-LIN28A demonstrated high specificity and sensitivity in distinguishing SLE from HC and other autoimmune diseases. Upon validation studies, determination of anti-LIN28A could aid in improving SLE diagnostics.

Keywords: systemic lupus erythematosus, AUTOANTIBODIES, omics

O004 / #306

FREE COMMUNICATIONS 01: SLE – FROM THE BEDSIDE TO THE BENCH
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ACTIVE AND REFRACTORY LUPUS NEPHRITIS ARE CHARACTERIZED BY INCREASED FREQUENCY OF P-GP AND MRP-1 POSITIVE PLASMA CELLS AND TH17 LYMPHOCYTES IN PERIPHERAL CIRCULATION

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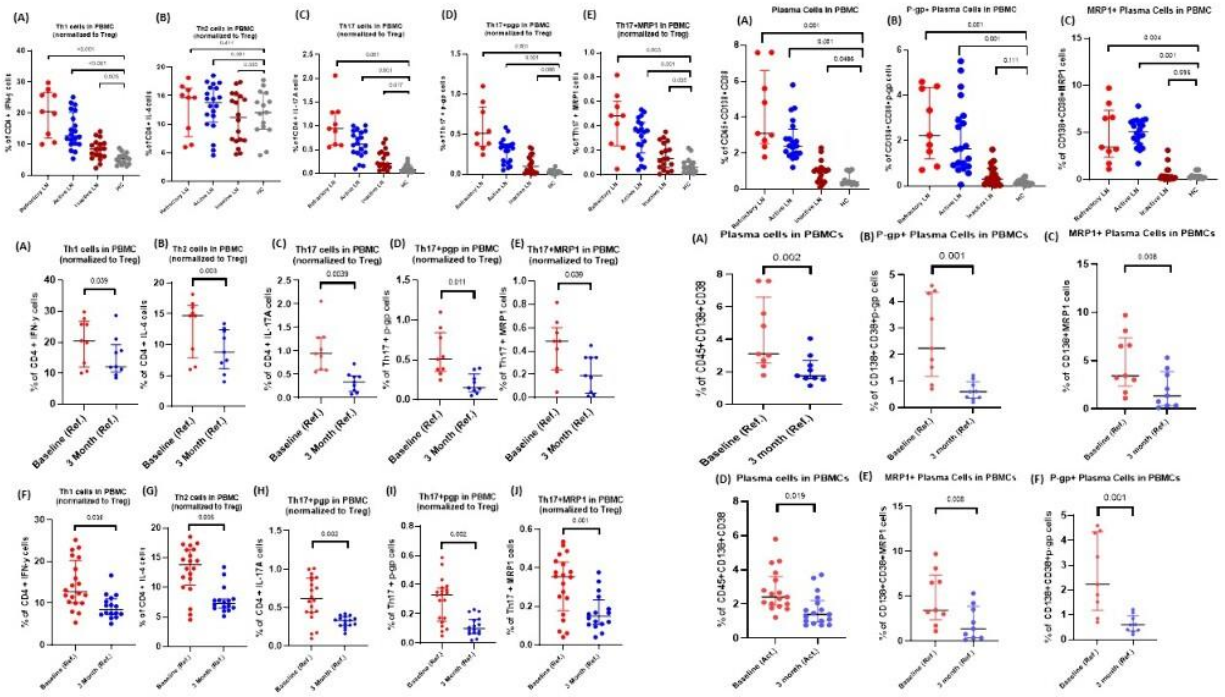
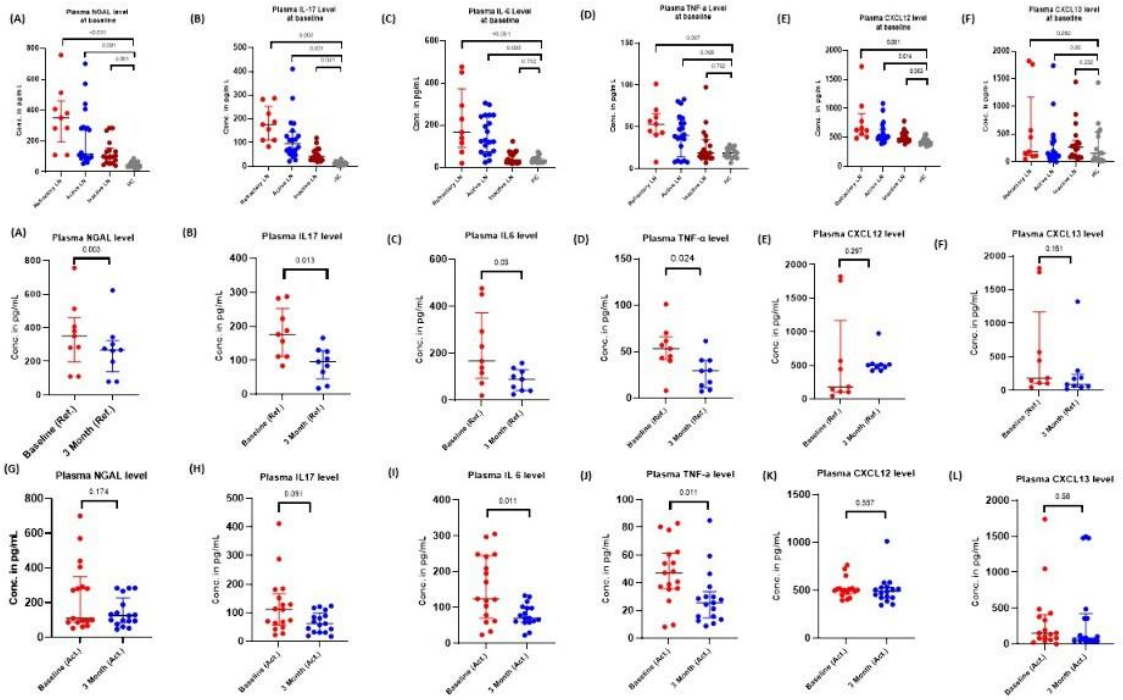
Background and Aims: Overexpression of P-glycoprotein (p-gp) and multidrug resistance protein-1 (MRP-1) on Plasma cells (PCs) and T-helper 17 lymphocytes (Th17) cells may contribute towards drug-resistant phenotype in lupus nephritis (LN). Aims: To evaluate the frequency of peripheral blood (PB) PCs and Th17 cells expressing p-gp and MRP-1 in LN.

Methods: P-gp+ and MRP-1+PCs, P-gp+ Th17/Th1/Th2 and Tregs and plasma NGAL, IL-17, IL-6, TNF-alpha and CXCL12 levels were determined.

Results: Forty-seven patients with LN; refractory n=9, active n=20 (10 treatment naïve), inactive n=18, median age 30 years, 45 females, 15 age matched healthy controls (HCs) were recruited. Ratio of Th1/Treg and Th17/Tregs were significantly increased in refractory and active LN as compared to HCs (Figure1). Th17+P-gp and Th17+MRP-1 cells were significantly increased in refractory and active LN as compared to inactive LN and HCs.



CD138⁺CD38⁺ PCs were significantly increased in refractory and active LN as compared to inactive LN and HCs at baseline (figure 2) which was significantly reduced after 3 months following treatment. Expression of P-gp and MRP-1 on PCs was significantly increased in refractory and active LN, as compared to inactive LN and HCs, which decreased significantly following treatment (figure 2).



The level of NGAL, IL-17, IL-6, TNF-α and CXCL12 in plasma of refractory and active LN were significantly raised at baseline, as compared to inactive LN and HCs, which decreased significantly after 3 months of treatment.

Conclusions: There is an increased frequency of P-gp and MRP-1-expressing PCs and Th17 lymphocytes in refractory and active LN.

Keywords: systemic lupus erythematosus, Permeable glycoprotein, Multi drug resistance protein-1

O005 / #345

FREE COMMUNICATIONS 01: SLE – FROM THE BEDSIDE TO THE BENCH
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C1Q-MIMIKING SCFV FRAGMENTS BINDING ANTI-C1Q AUTOANTIBODIES MODULATE DISEASE PROGRESSION IN MRL/LPR MOUSE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and Aims: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease characterized by tissue damage in multiple organs caused by autoantibodies and the resulting immune complexes. One possible way for complement system contribution to onset of autoimmune disorder could be realized by the impairment of C1q mediated apoptotic clearance as part of human homeostasis. The capacity of C1q to bind early apoptotic cells could be decreased or even lost in the presence of anti-C1q antibodies which are specific for epitopes within gC1q.

Methods: A phage-displayed library expressing single-chain recombinant antibodies (scFv Ab**)** was screened to select scFv specific for anti-C1q autoantibodies from different groups of lupus sera. Two groups of MRL/lpr mice were used for *ex vivo* and *in vivo* experiments.: 7 weeks old mice that are still disease free and 16 weeks old with advanced disease manifestations. We have injected the mice with 20 µg/mouse weekly of the studied scFv antibody. Blood samples were collected weekly and the sera were stored at -80 ºC for subsequent analyses. The effects of the chimeric constructs were tested using flow cytometry, ELISpot assay and ELISA methods.

Results: The data show that the scFv treatment modulates the percent of B and T cell subpopulations and splenocyte apoptosis. An increase of the proteinuria levels in the 7 weeks old MRL/lpr mice, splenocyte proliferation change and the number of plasmacytes producing anti-dsDNA antibodies in the treated group were also observed.

Conclusions: The treatment with anti-idiotypic scFv antibody has modulatory effect on lupus symptoms in MRL/lpr murine model of SLE.

Keyword: Systemic lupus erythematosus, mouse models, anti-C1q autoantibodies

O006 / #513

FREE COMMUNICATIONS 01: SLE – FROM THE BEDSIDE TO THE BENCH
03-06-2025 4:50 PM - 5:50 PM

REVOLUTIONIZING RHEUMATOID ARTHRITIS TREATMENT BY CREATING A PERSONALIZED JOINT-ON-CHIP MODEL

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Background and Aims: Rheumatoid arthritis (RA) is an autoimmune inflammatory disease affecting more than 20 million people in the world. RA is characterized by joint inflammation leading to impaired mobility and chronic pain. No cure exists for RA and there are no predictors of treatment response. Thus, 40% of patients fails to achieve RA remission. Thus, innovative trials and new drugs for RA represent an urgent unmet clinical need. To this aim, we develop a personalized next-generation joint-on-chip (JoC) that hosts RA cells derived from patient biopsies. This JoC model, by accurately replicating the complexity of a RA joint, allowed patient-specific clinical trials-on-chip.

Methods: We designed a 3D microfluidic platform capable of hosting and mechanically stimulating patient-derived tissues, including leukocyte-infiltrated synovial tissue and synovial fluid, as well as cartilage and bone. The platform also incorporates endothelialized blood vessel-like channels.

Results: Starting from synovial biopsy and blood samples, we bioprinted the microtissues in the chip, cultivated them under inflammatory conditions and successfully performed drug testing (methotrexate, celecoxib and a-TNFa).

Conclusions: Our findings mark a promising start to an ambitious project and represent a significant advancement in RA therapy research. All the partners in the FLAMIN-go project (grant agreement No. 953121) participated to this work. **Acknowledgments.**The authors would like to thank European Union's Horizon 2020 Research and Innovation programme under grant agreement No. 953121 (FLAMIN-GO) for financial support.

Keywords: Rheumatoid Arthritis, joint on chip

O007 / #425

FREE COMMUNICATIONS 02: SLE – CLINICAL ASPECTS
03-07-2025 2:10 PM - 3:10 PM

GLUCOCORTICOID-SPARING EFFECTS OF BELIMUMAB ACROSS JOINT AND SKIN PHENOTYPES OF SLE: INSIGHTS FROM THE NATION-WIDE COHORT "BELIMUMAB IN REAL-LIFE SETTING STUDY – JOINT AND SKIN".

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Background and Aims: Belimumab has shown glucocorticoid-sparing effects in SLE. This study aims to provide insight into the understudied aspect of its impact on various joint and skin phenotypes in a real-world setting.

Methods: The BeRLiSS-NeJS retrospective study in Italy enrolled adult SLE patients (≥18 years) diagnosed per 1997 ACR, 2012 SLICC, or 2019 EULAR/ACR criteria, treated with belimumab for at least six months (IV 10 mg/kg every four weeks or SC 200 mg/week) from 14 national centers. Patients were stratified by articular (NDNE, Jaccoud's arthropathy, Rhupus) and cutaneous (ACLE, SCLE, CCLE) phenotypes at baseline. Prednisone (PDN) intake was analyzed at baseline and every six months up to 36 months.

Results: Of 443 enrolled patients, 215 (49.3%) had NDNE, 30 (6.9%) had Jaccoud's arthropathy, and 21 (4.8%) had Rhupus; 112 (25.9%) had ACLE, 54 (12.5%) had SCLE, and

18 (4.2%) had CCLE. NDNE and Jaccoud's showed significant PDN reductions by 6 months, unlike Rhupus. Rhupus had significant reductions over 36 months, though less markedly. ACLE and SCLE saw significant reductions at 6 months, while CCLE did not achieve significance even at 36 months. Belimumab treatment reduced the proportion of patients taking >5 mg PDN daily and increased those achieving PDN discontinuation, particularly in NDNE, Jaccoud's, and
ACLE.

A)

Joint phenotype / PDN dose	NDNE arthritis	Jaccoud's arthropathy	Rhupus
PDN dose at baseline	10.0 (5.0 - 12.5)	8.8 (5.0 - 10.0)	10.0 (1.3 - 12.5)
Baseline vs 6 months	*p < 0.001*	*p = 0.053*	*p = 0.353*
PDN dose at 6 months	5.0 (3.8 - 7.5)	5.0 (1.3 - 8.8)	5.0 (1.3 - 7.5)
6 vs 12 months	*p = 0.154*	*p = 0.186*	*p = 0.951*
PDN dose at 12 months	5.0 (2.5 - 6.0)	5.0 (0.6 - 5.0)	5.0 (1.3 - 10.0)
12 vs 18 months	*p = 0.049*	*p = 0.777*	*p = 0.174*
PDN dose at 18 months	5.0 (2.5 - 5.0)	4.4 (0.6 - 5.0)	5.0 (0.0 - 6.3)
18 vs 24 months	*p = 0.359*	*p = 0.777*	*p = 0.805*
PDN dose at 24 months	5.0 (1.3 - 5.0)	1.9 (0.4 - 5.0)	2.5 (0.0 - 6.5)
24 vs 30 months	*p = 0.892*	*p = 0.850*	*p = 1.000*
PDN dose at 30 months	5.0 (1.0 - 5.0)	1.9 (0.5 - 6.3)	2.5 (0.0 - 6.0)
30 vs 36 months	*p = 0.118*	*p = 1.000*	*p = 0.496*
PDN dose at 36 months	3.6 (0.0 - 5.0)	1.9 (0.5 - 5.0)	1.3 (0.0 - 5.0)
Baseline vs 36 months	*p < 0.001*	*p < 0.001*	*p = 0.002*

B)

Skin phenotype / PDN dose	ACLE	SCLE	CCLE
PDN dose at baseline	10.0 (7.3 - 16.3)	10.0 (6.3 - 12.5)	6.7 (5.0 - 10.0)
Baseline vs 6 months	*p < 0.001*	*p = 0.002*	*p = 0.947*
PDN dose at 6 months	5.0 (5.0 - 7.5)	5.0 (4.0 - 7.5)	6.5 (5.0 - 7.5)
6 vs 12 months	*p = 0.227*	*p = 0.550*	*p = 0.688*
PDN dose at 12 months	5.0 (2.5 - 5.7)	5.0 (2.5 - 7.5)	5.0 (3.0 - 6.8)
12 vs 18 months	*p = 0.114*	*p = 0.329*	*p = 0.688*
PDN dose at 18 months	3.9 (2.5 - 5.0)	5.0 (2.5 - 5.0)	4.6 (3.8 - 5.0)
18 vs 24 months	*p = 0.711*	*p = 0.614*	*p = 0.789*
PDN dose at 24 months	3.3 (1.1 - 5.0)	5.0 (2.5 - 5.0)	5.3 (2.5 - 7.5)
24 vs 30 months	*p = 0.505*	*p = 0.950*	*p = 0.947*
PDN dose at 30 months	3.9 (1.3 - 5.0)	5.0 (2.5 - 5.0)	5.0 (4.3 - 5.0)
30 vs 36 months	*p = 0.786*	*p = 0.592*	*p = 0.423*
PDN dose at 36 months	10.0 (7.3 - 16.3)	5.0 (2.5 - 5.0)	3.9 (2.5 - 5.0)
Baseline vs 36 months	*p < 0.001*	*p < 0.001*	*p = 0.082*

Table 1. Daily prednisone reduction over time across the various joint (A) and skin (B) phenotypes. Prednisone doses are shown as the median with interquartile range. The statistical significance of the dose comparisons between each pair of timepoints was assessed using Friedman two- way analysis of variance by ranks for related samples (α = 0.05).

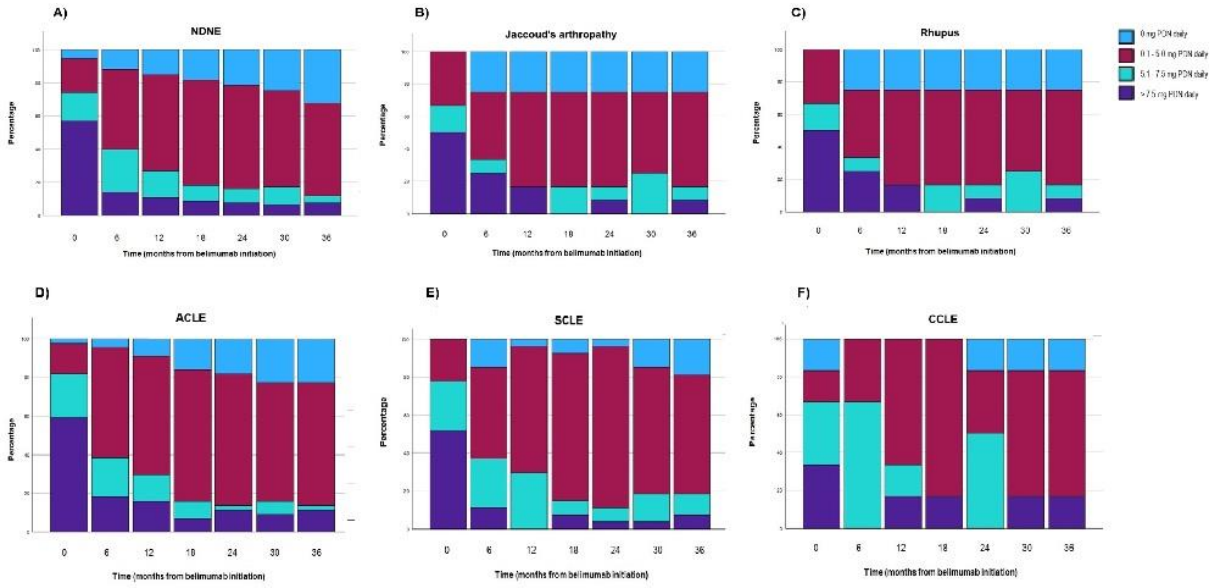

Table 2. Stacked bar chart of prednisone doses over time of joint (A-C) and skin (D-F) patients. Bars represent the percentage of patients stratified into different tiers of daily oral prednisone intake at any given timepoint.

Conclusions: Belimumab significantly reduced daily prednisone intake over 36 months in all SLE joint and cutaneous manifestations except CCLE. NDNE and Jaccoud's showed stronger, faster reductions than Rhupus. Overall, belimumab enabled steady tapering and discontinuation of prednisone, particularly in NDNE, Jaccoud's, and ACLE.

Keywords: systemic lupus erythematosus, Belimumab, Real-life study

O008 / #139

FREE COMMUNICATIONS 02: SLE – CLINICAL ASPECTS
03-07-2025 2:10 PM - 3:10 PM

MUCOCUTANEOUS DISEASE ACTIVITY AND DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM THE ASIA-PACIFIC LUPUS COLLABORATION LONGITUDINAL COHORT STUDY.

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Background and Aims: To describe prevalence, associations and health-related quality-of-life (HRQoL) impact of mucocutaneous manifestations (MCMs) in SLE.

Methods: Data from the Asia-Pacific Lupus Collaboration (APLC) cohort were analysed (2013-2020). Mucocutaneous activity items were rash, alopecia and mucosal ulcers, defined by the SLEDAI-2K and deemed persistent if present at ≥2 consecutive visits. Mucocutaneous damage items were chronic skin ulceration, scarring alopecia and skin/panniculum scarring, defined by the SDI. HRQoL was measured by SF36. Multivariable regression was used to determine correlates of mucocutaneous activity at each visit. Time varying covariate survival models were used to determine predictors of mucocutaneous damage.

Results: 1499/4102 (36.5%) had mucocutaneous activity (rash n=105; alopecia n=731; mucosal ulcers n=352) and 606/3655 (16.6%) had persistent mucocutaneous activity, during a median of 2.5 (1.0-5.1) years follow-up. These patients were more likely to record worse mean mental (45.5 v 47.6, p=0.003) and physical-component SF36 scores (45.3 v 49.0, p<0.001). Being Caucasian, smoking, serologic activity, serositis, vasculitis and nephritis were risk-factors for mucocutaneous activity. 157/3346 (4.3%) accrued mucocutaneous damage (chronic ulceration n=30; skin/panniculum scarring n=53; scarring alopecia n=98). These patients had worse mean mental (44.00 v 47.51, p=0.03) and physical component SF36 scores (41.6 v 48.8, p<0.001) and were more likely to be Caucasian and smokers.

Conclusions: Mucocutaneous activity in SLE was prevalent and more likely in smokers, while mucocutaneous damage was uncommon. Possible explanations include under-reporting, and/or limitations in damage-items captured by the SDI. MCMs were associated with worse HRQoL. Our findings highlight unmet-needs in treatment of mucocutaneous activity and measurement of mucocutaneous damage in SLE.

Keywords: systemic lupus erythematosus, cutaneous lupus erythematosus, Unmet clinical needs

O009 / #168

FREE COMMUNICATIONS 02: SLE – CLINICAL ASPECTS
03-07-2025 2:10 PM - 3:10 PM

PREVALENCE AND PROGNOSTIC FACTOR OF LUPUS NEPHRITIS, END STAGE KIDNEY DISEASE, AVASCULAR NECROSIS AND MORTALITY IN PATIENT WITH SLE IN THE RECENT ERA

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Background and Aims: Systemic lupus erythematosus (SLE) is an autoimmune disorder associated with increased risks of chronic kidney disease (CKD), avascular necrosis (AVN), and mortality. However, recent data on the prevalence and risk factors for these conditions in SLE remain limited. This study aimed to address these gaps in contemporary SLE management.

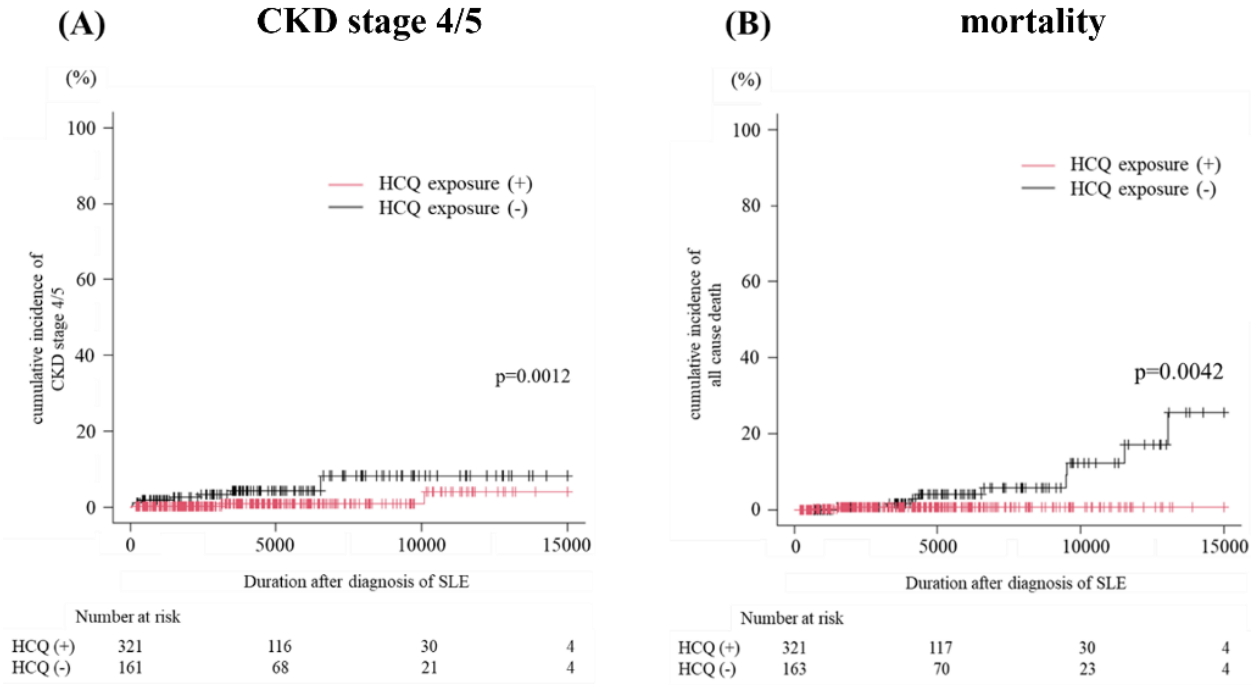
Methods: We analyzed data from SLE patients treated at a tertiary referral center from April 2006 to February 2023. We evaluated the prevalence and risk of lupus nephritis, CKD progression to stage 4 or 5, AVN, and all-cause mortality.

Results: We included 484 SLE patients in the study. Lupus nephritis was observed in 26.2% of the patients. AVN was observed in 4.8%, CKD stage 4 or 5 in 2.7%, and 2.5% of the patients died during the follow-up period. Lupus nephritis was more common in patients diagnosed before age 20, while CKD progression and mortality were higher in those with older onset SLE. Hydroxychloroquine usage was shown to be a protective factor against CKD progression and all-cause mortality (CKD stage 4 or 5: HR 0.21, 95% CI 0.056-0.80, p=0.022; all-cause death: HR 0.14, 95% CI 0.031-0.66, p=0.013). Methylprednisolone pulse therapy was identified as a risk factor for AVN but not for CKD progression (AVN: HR 6.10, 95% CI 2.42-15.35, p<0.001).

Conclusions: The prevalence of CKD, AVN, and mortality has improved in recent SLE cohorts. Hydroxychloroquine appears protective against CKD progression and mortality, while methylprednisolone pulse therapy is a risk factor for AVN.

	Biopsy confirmed LN			Biopsy confirmed LN class III/IV		
factor	HR	95% CI	p value	HR	95% CI	p value
Age of diagnosis< 20yo	**1.75**	**1.19-2.56**	**0.0037**	**1.81**	**1.14-2.89**	**0.011**
Sex (male)	1.44	0.81-2.57	0.21	1.74	0.90-3.38	0.10
Asian ethnicity	1.23	0.50-3.02	0.65	1.32	0.42-4.20	0.63
anti-dsDNA Ab (%)	**2.21**	**1.44-3.40**	**<0.001**	**3.75**	**2.03-7.00**	**<0.001**
anti-RNP Ab (%)	1.21	0.82-1.78	0.34	1.28	0.80-2.05	0.30
anti-Sm Ab (%)	1.07	0.64-1.77	0.80	0.89	0.50-1.60	0.70
anti-Ro/SSA Ab (%)	1.06	0.64-1.77	0.81	1.46	0.72-2.94	0.29
Low C3	**2.45**	**1.64-3.66**	**<0.001**	**4.36**	**2.44-7.76**	**<0.001**
Low C4	**2.48**	**1.60-3.86**	**<0.001**	**3.41**	**1.88-6.19**	**<0.001**

	CKD stage 4/5			All cause mortality		
factor	HR	95% CI	p value	HR	95% CI	p value
Diagnosis age <20yo	0.862	0.22-3.33	0.83	NA	NA	NA
Diagnosis age≥40yo	**4.17**	**1.24-14**	**0.021**	**11.69**	**3.05-44.78**	**<0.001**
Sex (male)	2.77	0.60-12.86	0.19	**5.77**	**1.50-22.17**	**0.011**
Asian ethnicity	0.46	0.06-3.64	0.46	NA	NA	NA
Joint/muscular	1.20	0.32-4.52	0.79	1.18	0.33-4.17	0.80
Skin/mucocutaneous	0.52	0.15-1.78	0.30	0.76	0.20-2.85	0.68
Renal manifestation	**4.01**	**1.06-15.2**	**0.041**	1.60	0.49-5.28	0.44
LN class III/IV	2.46	0.69-8.74	0.17	0.38	0.048-3.03	0.36
Serositis	2.42	0.64-9.15	0.19	1.52	0.33-7.05	0.60
Neurological	0.93	0.12-7.36	0.95	1.72	0.37-7.94	0.49
Hematological	0.37	0.11-1.20	0.098	0.94	0.28-3.20	0.94
anti-DNA Ab	1.69	0.45-6.40	0.44	NA	NA	NA
anti-RNP Ab	0.82	0.23-2.92	0.75	1.29	0.38-4.33	0.68
anti-Sm Ab	0.68	0.14-3.29	0.63	NA	NA	NA
anti-Ro/SSA Ab	0.50	0.13-1.92	0.31	1.362	0.16-11.35	0.78
anti-La/SSB Ab	2.66	0.33-21.31	0.36	2.62	0.34-23.54	0.34
LAC	2.29	0.66-7.92	0.19	1.331	0.35-5.10	0.68
anti-CL Ab	1.46	0.39-5.52	0.58	1.678	0.43-6.51	0.45
anti-CLβ2GPI Ab	2.034	0.26-15.98	0.499	2.278	0.29-18.11	0.44
Low C3	2.21	0.58-8.34	0.24	2.918	0.78-10.88	0.11
Low C4	1.62	0.43-6.11	0.48	1.573	0.47-5.3	0.47
HCQ use	**0.21**	**0.056-0.80**	**0.022**	**0.144**	**0.031-0.66**	**0.013**
BEL use	1.48	0.39-5.59	0.56	NA	NA	NA



Keywords: systemic lupus erythematosus, mortality rate, chrinicl kidney disease

O010 / #477

FREE COMMUNICATIONS 02: SLE – CLINICAL ASPECTS
03-07-2025 2:10 PM - 3:10 PM

CONVENTIONAL IMMUNOSUPPRESSANTS, AND NOT B-CELL DIRECTED BIOLOGICS, INCREASE THE RISK OF HERPES ZOSTER INFECTION IN SLE

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Background and Aims: SLE is characterized by an increased risk of Herpes Zoster (HZ) infection compared to the general population. To analyse HZ infection rate, characteristics, and risk factors in a cohort of SLE patients in the pre-non-live-recombinant vaccine era.

Methods: HZ episodes occurring after SLE diagnosis were collected from 2008 to 2024. Demographics, disease assessments prior to/after HZ episodes, hypogammaglobulinemia, lymphocyte subpopulation cytopenias, and characteristics of HZ episodes were registered. Patients with HZ infection were compared with those without (controls).

Results: Among 586 SLE patients, 112 HZ episodes occurred in 109 patients: prevalence rate 19%, incidence rate 0.84 per 100 patients/year. Characteristics of patients and HZ event features are summarized in Tab1. Although renal, neurological, and vascular involvement did not differ between HZ-patients and controls, HZ patients displayed a higher disease activity, as expressed by higher exposure (ever) to immunosuppressants (0.033), lower prevalence of prolonged remission (0.046), and less frequent discontinuation of immunosuppressants (0.021). Notably, exposure to belimumab or rituximab (current or in the previous year) did not increase HZ risk. In addition, leucopenia was more common in HZ-patients (0.045). At multivariate analysis, MMF was independently associated with HZ infection (OR 3.02, 95%CI 1.23-7.43, p=0.016). Among HZ-patients, higher clinical-SLEDAI (0.027), higher glucocorticoid cumulative dose (<0.001), and lymphopenia (0.01) were associated with post-herpetic neuralgia or HZ multi-site involvement. At multivariate analysis, no independent predictors

emerged.

Tab1 - HZ events and patients characteristics at HZ (n= 112)			
N° of patients	109	Post-herpetic neuralgia	19 (18.6%)
Mean age at HZ	43.2 ± 18.8	Other complications	3 (3%)
Mean disease duration at HZ	13.2 ± 8.4	HZV therapy	
Gender at birth - Female	93 (82.3%)	None	5 (5.9%)
Ethnic group		Topical	5 (5.9%)
Caucasian	93 (82.3%)	Oral	70 (82.4%)
Afro-American	7 (6.2%)	Intravenous	2 (2.4%)
Asia	4 (3.5%)	Topical+ Oral	3 (3.5%(
Arab	3 (2.7%)	Mean cSLEDAI	2.4 ± 4.2
American native/Hispanic	6 (5.3%)	N° of patients on clincal remission	52 (46%)
Localization		Mean SLICC at episode	1.0 ± 1.2
Trunk	43 (50%)	Patients off GC	31 (29.5%)
Head and Neck	15 (17.4%)	Patients on Low-dose GCs	43 (38%)
Limbs	16 (18.6%)	Patients off any IS	32 (80.8%)
Multiple sites	12 (14%)	Patients on HCQ/CQ	32 (30.5%)

Conclusions: SLE disease activity and treatment with conventional immunosuppressants increase the risk of HZ. In contrast, belimumab and rituximab did not show the same burden.

Keywords: SLE, herpes zoster, DMARD

O011 / #256

FREE COMMUNICATIONS 02: SLE – CLINICAL ASPECTS
03-07-2025 2:10 PM - 3:10 PM

ADMINISTRATION OF BELIMUMAB IN EARLY ACTIVE LUPUS PATIENTS HINDERS ACCRUAL OF EULAR/ACR CRITERIA WITHIN THE FIRST 12 MONTHS OF TREATMENT

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Background and Aims: Background. Addition of biologic drugs to standard of care (SoC) in SLE is advised in refractory patients. Evidence is needed on the effectiveness of early biologic use in influencing SLE course. **Objective.** To assess the effect of belimumab administration on disease progression in early active lupus patients.

Methods: Methods. We performed a multicentric observational study on patients with early SLE receiving either belimumab or SoC alone and compared the rate of EULAR/ACR 2019 criteria (1) accrual between the two groups as a measure of lupus progression over time. Patients were defined as early active if they were diagnosed within 12 months from treatment initiation and displayed up to two EULAR/ACR criteria, excluding major organ involvement, with active serology . All the data were collected in an anonymized fashion at baseline and at 3, 6, and 12 months. Kaplan-Meier curves with log-rank comparison were used to assess criteria accrual throughout the first 12 month of follow-up.

Results: Results. We included 57 early active SLE patients, 24 (42.1%) receiving SoC alone and 33 (57.9%) receiving add on belimumab to SoC and followed up for at least 12 months from baseline. The groups were comparable in terms of age, gender, disease duration and disease activity at baseline. Patients doomed to early belimumab displayed higher mean SLICC and steroid daily dosage (Table 1). Table 1. Baseline clinical and demographic features of early SLE

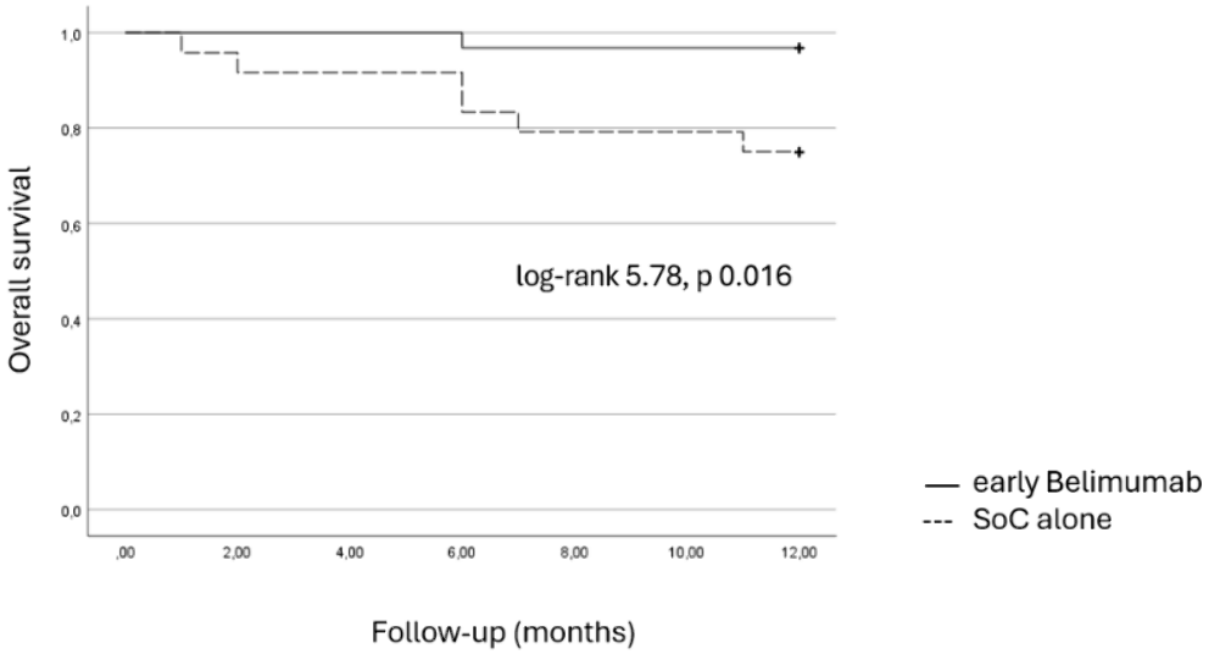
patients

	Belimumab	SoC	P
Age	30.12±11.64	39.39±15.96	0.085
Gender, F (%)	29 (87.9)	23 (95.8)	0.385
HCQ n (%)	30 (90.9)	17 (70.8)	0.077
IS n (%)	26 (78.8)	21 (87.5)	0.494
PDN mg/d	8.75±6.67	5.00±10.61	0.054
Anti-dsDNA titers (kU/L)	201.04±282.95	88.91±46.86	0.020
C3 mg/dl	79.54±27.41	82.48±23.91	0.348
C4 mg/dl	12.00±5.12	10.77±3.53	0.180
cSLEDAI-2K	5.42±1.76	5.75±1.33	0.227
SLICC	0.12±0.42	0.00±0.00	0.052

Continuous variables expressed as mean±SD

Conclusions: Conclusions. Timely use of belimumab in patients with early active SLE can significantly delay disease progression, potentially preventing development of severe manifestations.

Figure 1. Kaplan-Meier curves depicting criteria-free survival in patient groups



Keyword: SLE, belimumab, early

O012 / #334

FREE COMMUNICATIONS 02: SLE – CLINICAL ASPECTS
03-07-2025 2:10 PM - 3:10 PM

POST-HOC ANALYSIS OF THE BERLISS-NEW JS REGISTRY: EFFICACY OF BELIMUMAB ON THROMBOCYTOPENIA

Margherita Zen[1], Greta Hulej[1], Marisol Bracalenti[1], Martina Tizian[1], Elena Ruffato[1], Roberto Depascale[1], Alberto Cauli[2], Lorenzo Cavagna[3], Rossella De Angelis[4], Giacomo Emmi[5], Roberto Gerli[6], Marcello Govoni[7], Renato Lo Gullo[8], Simone Negrini[9], Luca Quartuccio[10], Maurizio Rossini[11], Carlo Salvarani[12], Paola Tomietto[13], Angelo Vacca[14], Luca Iaccarino[1], Andrea Doria[1]
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Background and Aims: Belimumab has demonstrated efficacy in various domains of SLE, but real-world data showing its effectiveness on the hematologic aspect are scarce. To evaluate the efficacy of belimumab on hematologic manifestations in a national cohort of SLE patients.

Methods: We considered all patients with thrombocytopenia (n=44), defined as a count <150,000/mmc, enrolled in the Italian multicenter lupus cohort BeRLiSS, treated with Belimumab IV 10 mg/kg monthly or SC 200 mg weekly as an add-on therapy. The efficacy of belimumab was evaluated as an improvement in mean platelet count and as the percentage of patients achieving normalization of platelet count. The average daily dose of corticosteroids was also calculated. We conducted univariate analyses using paired sample t-tests and repeated measures, utilizing SPSS version 29.

Results: In the 44 patients with thrombocytopenia a significant improvement in platelet count was observed during a mean follow-up of 36±24 months (Greenhouse-Geisser sig. p=0.039); normalization of platelet count was achieved at 6, 12, 24, 36, and 48 months by 50%, 57%, 52%, 63%, and 55% of patients, respectively. Additionally, belimumab demonstrated a glucocorticoid-sparing effect (p=0.004). The glucocorticoid-sparing effect and improvement in platelet count were independent of the co-administration of a conventional immunosuppressant.

Conclusions: Add-on therapy with belimumab led to clinical improvement in a significant proportion of patients with hematologic involvement in a real-world setting, associated with a glucocorticoid-sparing effect. This effect does not appear to be independent of the co-administration of a conventional immunosuppressant.

O013 / #490

FREE COMMUNICATIONS 03: OPEN ISSUES AND NOVELTIES IN ARD
03-07-2025 2:10 PM - 3:10 PM

THE STRATEGY OF CHOICE FOR ESTIMATING 10-YEAR CV RISK IN ITALIAN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE CORDIS STUDY GROUP

Fabio Cacciapaglia[1], Gian Luca Erre[2], Matteo Piga[3], Elena Bartoloni[4], Andreina Manfredi[5], Ennio Giulio Favalli[6], Maria Sole Chimenti[7], Serena Guiducci[8], Eleonora Celletti[9], Addolorata Corrado[10], Alessandro Giollo[11], Simone Parisi[12], Ivan Giovannini[13], Elisa Gremese[14], Francesca Spinelli[15], Garifallia Sakellariou[16], Ombretta Viapiana[17], Fabiola Atzeni[18]

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Background and Aims: Patients with rheumatoid arthritis (RA) have an increased cardiovascular (CV) risk, which is often underestimated by traditional risk models due to RA's inflammatory nature. This highlights the need for better screening methods to prevent major cardiovascular events (MACE). The CORDIS-SIR study aimed to evaluate different CV risk estimation tools in Italian RA patients to identify the most effective model for primary prevention.

Methods: A cross-sectional cohort of RA patients without prior CV events was observed from January 2019 to December 2023. The study assessed CV risk using three models: SCORE-2, Progetto Cuore (PGC), and the Expanded Risk Score for RA (ERS-RA). Patients aged 35-69 were stratified into low-, intermediate-, or high-risk categories, with multiple comparisons between the models.

Results: Data from 971 RA patients (79.5% female; mean age 58) revealed varying risk estimates. SCORE-2, PGC, and ERS-RA predicted 10-year MACE probabilities of 4.3%, 5%, and 7.2%, respectively. ERS-RA showed stronger correlations with PGC and SCORE-2. PGC classified the most patients as low-risk, SCORE-2 categorized the most as intermediate-risk, and ERS-RA identified the highest number of high-risk patients. The incidence rate of

fatal and non-fatal CV events was 0.25/100 patient-years.The models generally overestimated observed CV risk, though no statistically significant differences were found.

Conclusions: Overall, PGC appeared to be the most appropriate model for the Italian RA population. However, the study highlighted the need to consider model differences when estimating CV risk in RA patients.

Keyword: rheumatoid arthritis, CV risk, major cardiovascular events, CV risk scores, CV events

O014 / #435

FREE COMMUNICATIONS 03: OPEN ISSUES AND NOVELTIES IN ARD
03-07-2025 2:10 PM - 3:10 PM

SYNOVIAL TISSUE PATHOTYPES DIFFERENTIATE REFRACTORINESS TO DMARDS IN PSORIATIC COMPARED TO RHEUMATOID ARTHRITIS

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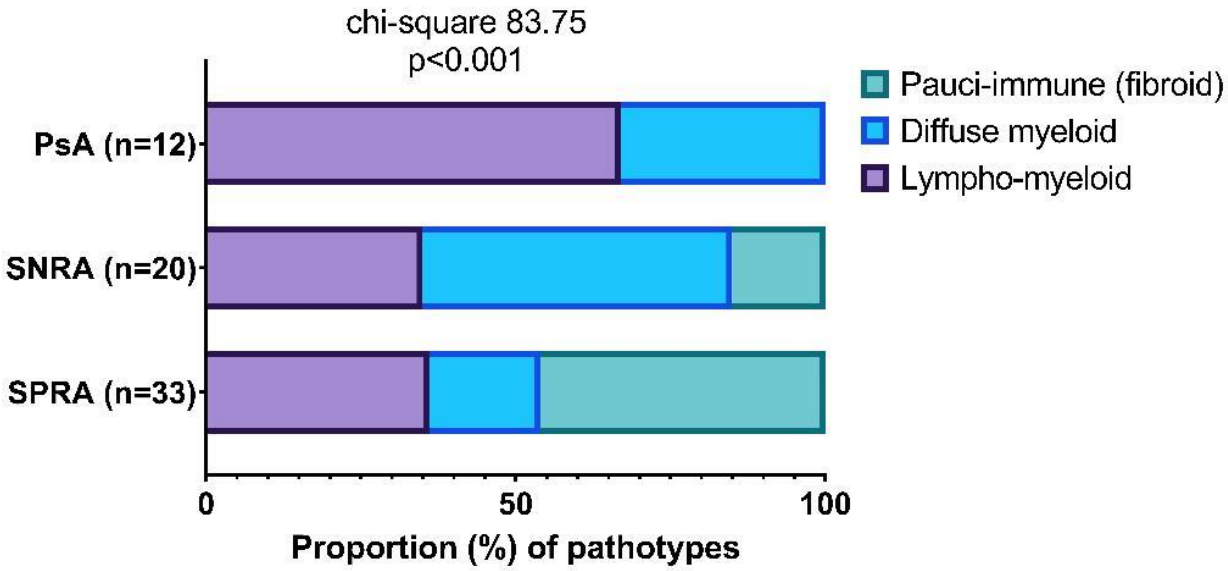
Background and Aims: This study aimed to compare synovial features of refractory PsA with refractory seropositive and seronegative rheumatoid arthritis (SPRA, SNRA)

Methods: Patients with inadequate response to DMARDs and at least one clinically active joint that underwent ultrasound-guided synovial biopsy. Disease activity was evaluated with SDAI for RA and DAPSA for PsA. Ultrasound synovitis was graded according to GLOESS. Histopathological assessment included Krenn Synovitis Score (KSS) and immunohistochemistry (IHC) for CD68, CD20, CD138, CD3, and CD34. According to the IHC, the synovial pathotypes were classified as myeloid, lymphoid, or pauci-immune.

Results: 65 patients were enrolled in the study (33 SPRA, 20 SNRA and 12 PsA). Demographics, disease activity and prior DMARD use were similar across groups, except for PsA patients having shorter disease duration compared to SNRA (p=0.008) and SPRA (p=0.011) and lower prevalence of erosions compared to SPRA (p=0.02) (Table 1). While overall KSS scores were similar, PsA had a higher stromal density subcomponent (p = 0.02). PsA patients also had significantly lower occurrence of fibroid pathotype compared to SPRA (0% vs. 46%, p=0.04) and higher occurrence of lymphoid pathotype (66% PsA vs. 36.5% SPRA, p=0.010, vs. 35% SNRA, p=0.14).


chi-square 83.75
p<0.001
PsA (n=12)
SNRA (n=20)
SPRA (n=33)
0
50
100
Proportion (%) of pathotypes
Pauci-immune (fibroid)
Diffuse myeloid
Lympho-myeloid

				P values		
	SPRA n = 33	SNRA n = 20	PSA n = 12	SPRA vs SNRA	SPRA vs PSA	SNRA vs PSA
Age, median IQR	62 (15)	55.5 (25.5)	58.5 (15.2)	0.29	0.40	0.089
Female sex (%)	26 (78.8)	17 (85)	10 (83.3)	0.72	1	1
BMI, mean (SD)	25 (4.2)	23.9 (3.5)	23.2 (4.3)	0.29	0.22	0.65
Disease duration	13 (11)	10.5 (14.5)	5.5 (4.4)	0.70	0.008	0.011
Number of prior csDMARD	2 (2)	2 (2)	2 (1)	0.94	0.49	0.94
Number of prior b/tsDMARD	1 (2)	1 (3)	0.5 (2)	0.78	0.39	0.58
Current GCs (%)	15 (45.5)	12 (60)	5 (41.7)	0.40	1	0.47
CRP (mg/L)	3.2 (9.8)	4.35 (14.7)	5.7 (26.8)	0.72	0.28	0.50
ESR	31.5 (42.8)	29 (38)	30.5 (45.5)	0.41	0.97	0.62
TJC	4 (5)	3 (3.3)	3 (7)	0.54	0.99	0.86
SJC	4 (6)	2.5 (3.3)	2 (2.25)	0.36	0.19	0.43
PGA-VAS	70 (34.2)	67.5 (31.2)	60.5 (50)	0.74	0.72	0.81
PHGA-VAS, mean (SD)	58.9 (22.6)	59.7 (19.2)	49.2 (31.1)	0.88	0.34	0.31
Disease activity (%)						
High	12 (36.4)	4 (20)	4 (33.3)	0.24	1	0.43
Moderate	18 (54.6)	15 (75)	5 (41.7)	0.16	0.51	0.13
Low	3 (9.1)	1 (5)	3 (25)	1	0.32	0.14
Failed 2 b/tsDMARDs	14 (42.4)	8 (40)	5 (41.7)	1	1	1
GLOESS	2 (1)	2 (1)	2.5 (1)	0.91	0.75	0.85

Table 1. Demographic and clinical features. Data are presented as median and interquartile range (IQR) or mean and standard deviation (SD). Abbreviations: BMI, body mass index; csDMARDs, conventional synthetic disease modifying drugs; b/tsDMARDs, biologic or targeted DMARDs; GC, glucocorticoid; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; TJC, tender joint count; SJC swollen joint count; PGA, patient global assessment; PhGA, physician global assessment; VAS, visual analogue scale; PIRRA, persistent inflammatory refractory rheumatoid arthritis; NIRRA, non-inflammatory refractory rheumatoid arthritis; GLOES, global OMERACT-EULAR score system.

				P values		
	SPRA n = 33	SNRA n = 20	PSA n = 12	SPRA vs SNRA	SPRA vs PSA	SNRA vs PSA
KSS, median (IQR)	4 (3)	5 (2.3)	6 (1)	0.44	0.06	0.15
Hyperplasia	1 (1)	2 (1)	2 (1)	0.20	0.28	0.85
Density	1 (1)	1 (1)	2 (0.5)	0.57	0.06	0.02
Infiltrate	1 (2)	2 (2)	2 (1)	0.45	0.18	0.45
Follicular lymphoid aggregates (%)	15 (45.5)	8 (40)	9 (75)	0.78	0.10	0.08
Pathotype (%)						
Diffuse myeloid	6 (18.2)	10 (50)	4 (33.3)	**0.02**	0.42	0.47
Fibroid	15 (45.5)	3 (15)	0	**0.04**	**0.004**	0.27
Lymphoid	12 (36.4)	7 (35)	8 (66.6)	1	0.10	0.14

Table 2. Comparative analysis of synovial features of refractory seropositive rheumatoid arthritis (SPRA), seronegative (SNRA) and psoriatic arthritis (PsA). Data are expressed as median and interquartile range (IQR). Abbreviations: KSS, Krenn Synovitis Score.

Conclusions: The observed differences in synovial features between refractory disease states may guide tailored treatment strategies.

Keywords: Refractory, synovial biopsy, rheumatoid

O015 / #183

FREE COMMUNICATIONS 03: OPEN ISSUES AND NOVELTIES IN ARD
03-07-2025 2:10 PM - 3:10 PM

RARE CONNECTIVE TISSUE DISEASES IN PATIENTS WITH C1-INHIBITOR DEFICIENCY HEREDITARY ANGIOEDEMA: FIRST EVIDENCE ON PREVALENCE AND DISTRIBUTION FROM A LARGE ITALIAN COHORT STUDY.

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Background and Aims: In Hereditary Angioedema (HAE) related to primary C1 inhibitor deficiency (C1INH), the defective clearance of immune complexes and apoptotic materials potentially leads to autoimmunity. No large population studies focus on rare connective tissue diseases (RCTDs) in C1INH-HAE. We aim at evaluating for the first time distribution of Systemic Lupus Erytematosus (SLE), primary Sjogren Syndrome (SjS), primary

antiphospholipid syndrome (APS), Systemic Sclerosis (SSc), and mixed connective tissue diseases (MCTD) in a large Italian cohort of C1INH-HAE patients.

Methods: A multicenter observational study includes C1INH-HAE patients from ITACA Centers throughout Italy. Inclusion criteria are i. a defined diagnosis of type I or II C1INH-HAE; ii. age ≥15 years (puberty already occurred); iii. enrollment in the ITACA Registry. The diagnosis of SLE, primary SjS, primary APS, SSc, and MCTD are made in accordance with international classification criteria.

Results: From a total of 855 C1INH-HAE patients referring to 15 ITACA Centers, patients with concomitant RCTDs were 2.1% (n=18) with F:M ratio 3.5 and a prevalent type I C1INH-HAE (87.2%). SLE is the prevalent diagnosis (44.5%, F:M=3; age at SLE diagnosis 21 ± 8.3 y.o.), while the remaining diagnoses are SjS (22.2%), APS (16.6%), SSc (11.2%), and a single MCTD. HAE-long term prophylaxis (LTP) is significantly prevalent in RCTDs than in the whole population ($p<0.01$), in 58.4% of cases already administered at the time of RCTD diagnosis.

Conclusions: A relevant prevalence of RCTDs is documented in C1INH-HAE patients, mainly SLE. Patients with RCTDs are on LTP in a significant proportion supporting the idea of a bidirectional link between C1INH-HAE and autoimmunity.

Keywords: Autoimmunity, Complement System, Connective Tissue Diseases

O016 / #191

FREE COMMUNICATIONS 03: OPEN ISSUES AND NOVELTIES IN ARD
03-07-2025 2:10 PM - 3:10 PM

PRESERVATION OF IMMUNE TOLERANCE WITH CANCER IMMUNOTHERAPY

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Background and Aims: Immune checkpoint inhibitor (ICI) therapy for cancer exacerbates autoimmune conditions including psoriasis. Successful immunotherapy using anti-PD-1 antibody requires crosstalk between the interleukin-12 isoform (IL-12p40) and interferon-gamma (IFN-γ). However, the severity of psoriasis is reduced upon exposure to anti-IL-12p40 antibody. We have recently reported a novel peptide, designated IK14004, that inhibits IL-12p40/IFN-γ production by human immune cells. The aim of our study was to compare the effects of this peptide on psoriasis and Lewis lung cancer (LLC) in murine models.

Methods: IK14004 was administered intraperitoneally to C57BL/6 mice exposed to Imiquimod (IMQ) to induce psoriasis. Evaluation of peptide effects was based on the Psoriasis Area and Severity Index (PASI) and histopathological criteria which included assessment of epidermal hyperplasia and dermal infiltration by CD45-expressing immune cells. The latter was compared with the inflammatory response within the tumour microenvironment (TME) of peptide-exposed LLC allografts.

Results: IK14004 inhibited IMQ-induced psoriatic skin pathology which was associated with a marked reduction in the dermal inflammatory cell infiltrate. Administration of IK14004 to mice bearing LLC allografts inhibited tumour growth by 40% associated with a significantly greater proportion of CD45-expressing immune cells within the TME of peptide-treated mice compared with vehicle-treated animals.

Conclusions: We propose a model of cancer immunotherapy that may not compromise immune tolerance, i.e., exacerbate autoimmune pathologies. In this model, IL-12p70 is

uncoupled from IL-12p40/IFN-γ production, T regulatory (Treg) cells remain functional and cytotoxic lymphocytes are activated. Co-delivery of IK14004 with ICIs may serve to reduce autoimmune responses.

Keywords: Peptide, Autoimmunity, cancer Checkpoint inhibitors

O017 / #566

FREE COMMUNICATIONS 03: OPEN ISSUES AND NOVELTIES IN ARD
03-07-2025 2:10 PM - 3:10 PM

THE ROLE OF ANTI-G PROTEIN-COUPLED RECEPTORS ANTIBODIES IN THE ASSESSMENT OF SYSTEMIC SCLEROSIS-PRIMARY HEART INVOLVEMENT

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Background and Aims: Primary heart involvement (pHI) is a major complication of systemic sclerosis (SSc). Echocardiography, through the assessment of coronary flow velocity reserve (CFR), has been used to identify coronary microvascular dysfunction (CMD) in SSc. Autoantibodies targeting G-coupled protein receptors (GPCRs) – particularly, anti-endothelin type A and anti-angiotensin type 1 receptors (ETAR and AT1R) antibodies – have been associated with the microvascular SSc manifestations. Our study aims to evaluate the association between these antibodies and CMD.

Methods: Patients fulfilling the 2013 ACR/EULAR classification criteria for SSc were enrolled; patients with coronary artery disease or other cardiomyopathies were excluded. Serum levels of anti-ETAR and anti-AT1R antibodies were determined by ELISA; the seropositive threshold was provided by the manufacturer (>10 U/ml). Echocardiography with CFR assessment was performed on all patients: CFR ≤2.5 was considered marker of CMD.

Results: Thirty-five patients were enrolled. The median disease duration was 1 year, the majority of patients had diffuse cutaneous SSc (58%) and positive anti-topoisomerase I antibodies (50%). pHI was diagnosed in 20% patients, while CMD in 73%. Diffuse cutaneous SSc was associated to higher anti-GPCRs titers (p=0.05), without significant associations with organ involvements. Positive anti-ETAR and anti-AT1R were associated with significantly lower CFR values, and anti-GPCRs titers inversely correlated with CFR values on echo (rho =-0.41, p=0.03 and rho=-0.37, p=0.05, respectively). A longer disease duration (from Raynaud's phenomenon) was associated with higher anti-GPCRs titers (p=0.04 and p=0.02 respectively).

Conclusions: Anti-GPCRs antibodies appear to be associated with CMD is SSc and their determination may be useful in the early assessment of SSc-pHI.

Keywords: systemic sclerosis, heart involvement, functional autoantibodies

O018 / #484

FREE COMMUNICATIONS 04: APS AND PREGNANCY IN RHEUMATOLOGICAL DISEASES
03-07-2025 5:50 PM - 6:50 PM

EVALUATION OF THE ASSOCIATION BETWEEN CONVENTIONAL ANTIPHOSPHOLIPID ANTIBODIES AND MARKERS OF ENDOTHELIAL CELL ACTIVATION AND OXIDATIVE STRESS IN A HEALTHY POPULATION

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Background and Aims: Antiphospholipid syndrome (APS) is characterized by the occurrence of vascular thrombosis and/or pregnancy morbidity associated with persistent positivity for antiphospholipid antibodies (aPL). Besides APS, aPL might be present in various clinical settings such as infections, malignancies, drugs. aPL can also be present in healthy individuals. However, the role of aPL in healthy individuals remains poorly studied, as does their potential pathogenic effect.

Methods: Healthy individuals were propectively recruited. For each healthy subject, we collected demographic data (age, sex) as well as cardiovascular risk factors (hypertension, smoking, dyslipidemia, diabetes, obesity). All healthy individuals underwent screening of ACL, ab2GPI, and lupus anticoagulant (LA). We measured VCAM-1, ICAM-1, E-selectin, MCP-1, TBARs, vitamins A and E in healthy subjects with higher levels of ACL and/or ab2GPI and/or LA, and in aPL-negative subjects matched for age, sex, and cardiovascular risk factors.

Results: We included 1223 healthy individuals. The median age at inclusion was 42 [18-83] years, with a female-to-male ratio (F/M) of 1.13. No « triple positive aPL profile » was found. We compared the levels of various markers studied between 31 aPL-positive and 61 matched aPL-negative subjects. The levels of ICAM-1 and E-selectin were significantly higher in aPL-positive subjects compared to matched aPL-negative subjects (E-selectin, p=0.0008; ICAM-1, p=0.004).

Conclusions: The higher serum concentrations of soluble adhesion molecules ICAM-1 and E-selectin in healthy individuals with higher aPL levels reflect probably aPL-induced endothelial cell activation. Further studies will be needed to determine whether an increase in these markers of endothelial cell activation is predictive of thrombosis in asymptomatic aPL carriers.

Keywords: antiphospholipid antibodies, healthy population, endothelial cell activation

O019 / #326

FREE COMMUNICATIONS 04: APS AND PREGNANCY IN RHEUMATOLOGICAL DISEASES
03-07-2025 5:50 PM - 6:50 PM

QUADRUPLE ANTIPHOSPHOLIPID ANTIBODIES POSITIVITY IS ASSOCIATED WITH ACCRUAL DAMAGE IN ANTIPHOSPHOLIPID SYNDROME SUBSETS

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Background and Aims: Antibodies against phosphatidylserine/prothrombin (aPS/PT) have received significant attention in diagnosing APS, particularly thrombotic APS, emphasizing the potential utility in identifying individuals at higher risk for thrombotic events. Here, we evaluate the association of aPS/PT antibodies with damage accrual in APS.

Methods: We conducted an exploratory cross-sectional study. We included 143 patients fulfilling the ACR/EULAR 2023 APS classification criteria. Immunoglobulin (Ig)G/IgM aPS/PT, IgG/IgM anticardiolipin (aCL), and IgG/IgM anti- β2 glycoprotein I (anti- β2 GPI) antibodies were detected using ELISA assay and lupus anticoagulant (LA) with a series of coagulation tests.

Results: IgG aPS/PT, but not IgM aPS/PT was associated with both arterial and venous thrombosis events (p=0.036) concerning arterial or venous thrombosis alone (42.9% vs 34.9% vs 22.2%). There was no difference between IgG/IgM aPS/PT and obstetric APS subsets. IgG and IgM aPS/PT were significantly associated with the microvascular domain (p=0.01 and p= 0.005, respectively), while IgG aPS/PT was associated with valvulopathy (p= 0.022). Both triple aPL positivity (IgG/IgM aCL+IgG/IgM anti- β2 GPI +LA) and quadruple aPL positivity (IgG/IgM aCL+IgG/IgM anti- β2 GPI +LA) were associated with accrual damage (p=0.035 and p= 0.003, respectively). However, at the multivariate logistic regression, only quadruple aPL showed a 4-fold risk of accrual damage in APS patients (OR 4.2, 95%IC 1.1-16.4, p=0.038).

Conclusions: Both IgG and IgM aPS/PT were associated with more severe APS subsets, such as the presence of arterial and venous thrombosis, as well as the microvascular and valvulopathy domains. Moreover, quadruple aPL positivity was associated with accrual damage, suggesting their utility in risk stratification in APS patients.

Keywords: antiphospholipid antibodies, lupus anticoagulant, anti-prothrombin antibodies

O020 / #391

FREE COMMUNICATIONS 04: APS AND PREGNANCY IN RHEUMATOLOGICAL DISEASES
03-07-2025 5:50 PM - 6:50 PM

INSIGHTS INTO PEDIATRIC ANTIPHOSPHOLIPID SYNDROME: RESULTS FROM A MULTICENTER TURKISH STUDY

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Background and Aims: Pediatric antiphospholipid syndrome (APS) presents differently from its adult counterpart. This study aimed to describe the frequency of thrombotic and non-thrombotic clinical manifestations, laboratory findings, treatment approaches, and prognosis in pediatric APS patients.

Methods: This retrospective study included 65 pediatric APS patients from 15 centers in Turkey, diagnosed according to the updated Sapporo or 2023 ACR-EULAR criteria. Data on demographics, clinical presentations, laboratory findings, treatment, and outcomes were collected from medical records.

Results: Of 65 pediatric APS patients, 51 (78.5%) were female, with a median diagnosis age of 13.1 years. Fifteen (23.1%) had primary APS, and 50 (76.9%) had an underlying autoimmune disease. Thrombotic events included venous (55.3%), arterial (24.6%), small-vessel (10.7%), and mixed thrombosis (6.1%). Catastrophic APS occurred in 4.6%. Non-thrombotic manifestations included hematologic disorders (64.6%), neurologic (28.2%), and cardiac valve disease (9.2%). Laboratory findings showed the presence of aCLs in 52(80%), anti-β2GPI in 36(55%), and LA in 40 patients(61.5%). ll patients with venous thrombosis received long-term anticoagulation therapy. Among patients with arterial thrombosis,12% received no treatment,44% received antiaggregation therapy, 44% received anticoagulation therapy with or without concomitant antiaggregation therapy. Immunosuppressive drugs were used in 76.9%, including glucocorticoids (100%), rituximab (9.2%), CYC (26.2%), and MMF (10.8%). Recurrent thrombosis occurred in 6.1%, with two deaths due to thrombotic events.

Conclusions: Despite its rarity in children, APS can manifest severely and lead to significant morbidity and mortality. While classification criteria have been primarily designed for adults, there is a clear indication for the future development of pediatric-specific criteria.

Keywords: Antiphospholipid Syndrome, Pediatric Antiphospholipid Syndrome, Thrombosis

O021 / #279

FREE COMMUNICATIONS 04: APS AND PREGNANCY IN RHEUMATOLOGICAL DISEASES
03-07-2025 5:50 PM - 6:50 PM

MATERNAL AND FETAL OUTCOMES IN LATIN AMERICAN SLE PREGNANCIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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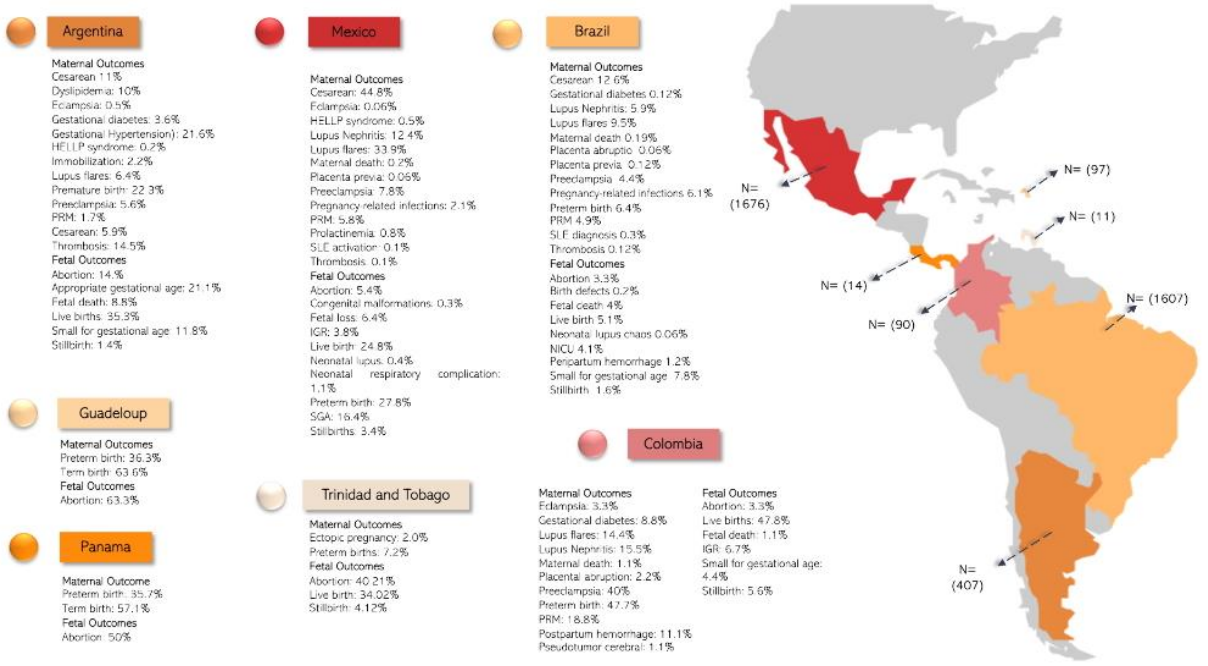
Background and Aims: Systemic Lupus Erythematosus (SLE) predominantly affects women, particularly during their reproductive years, leading to increased risks during pregnancy. Latina women develop SLE at younger ages, increasing their susceptibility to pregnancy complications such as preeclampsia, preterm birth, and fetal growth restriction. This study aims to systematically review maternal and fetal outcomes in pregnant Latina women with SLE and to conduct a meta-analysis to assess specific risks associated with the disease.

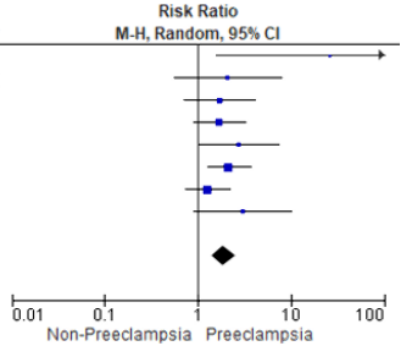
Methods: A systematic review following PRISMA guidelines was performed using databases including PubMed and SciELO, covering studies on SLE and pregnancy in Latin America up to December 2022. Eligible studies included case reports, cohort studies, and clinical trials involving pregnant women with SLE. Meta-analysis focused on key outcomes, including preeclampsia and lupus nephritis, with relative risk (RR) calculations.

Results: Forty-four studies involving 2190 pregnancies were included. High rates of preeclampsia (11-52%), preterm birth (18.6-70.8%), and fetal loss were reported (Image 1). Meta-analysis showed that lupus nephritis nearly doubled the risk of preeclampsia (RR = 1.89, 95% CI: 1.40-2.55) compared to women without nephritis (Figure 1).



Study or Subgroup	Lupus Nephritis Events	Lupus Nephritis Total	Non-Lupus Nephritis Events	Non-Lupus Nephritis Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Surita 2007	9	32	0	44	1.1%	25.91 [1.56, 429.54]	2007
Cavallasca 2008	3	16	5	56	5.0%	2.10 [0.56, 7.85]	2008
Saavedra 2012	8	35	8	60	10.6%	1.71 [0.71, 4.16]	2012
Costa Rodriguez 2019	18	66	13	81	19.1%	1.70 [0.90, 3.21]	2019
Ocampo-Ramirez 2019	6	13	5	30	8.6%	2.77 [1.03, 7.47]	2019
Saavedra 2020 *	15	51	31	226	25.3%	2.14 [1.25, 3.67]	2020
Erazo-Martinez 2021 *	8	13	17	35	24.4%	1.27 [0.73, 2.19]	2021
Otaduy 2022	12	69	3	52	5.9%	3.01 [0.90, 10.14]	2022
Total (95% CI)		**295**		**584**	**100.0%**	**1.89 [1.40, 2.55]**	
Total events	79		82				

Heterogeneity: Tau² = 0.02; Chi² = 7.75, df = 7 (P = 0.36); I² = 10%
Test for overall effect: Z = 4.13 (P < 0.0001)



Conclusions: Latina women with SLE face a heightened risk of adverse pregnancy outcomes, particularly preeclampsia and preterm birth. Lupus nephritis and disease activity are key risk factors, underscoring the need for tailored care and early intervention to improve maternal and fetal outcomes in this population.

Keywords: systemic lupus erythematosus, Pregnancy Complications, Latin America

O022 / #475

FREE COMMUNICATIONS 04: APS AND PREGNANCY IN RHEUMATOLOGICAL DISEASES
03-07-2025 5:50 PM - 6:50 PM

EFFECTS OF MULTIDISCIPLINARY FOLLOW-UP ON CLINICAL STABILITY AND PREGNANCY COMPLICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE ANALYSIS OF 74 PREGNANCIES

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Background and Aims: Rheumatoid arthritis (RA) is one of the most prevalent chronic diseases among women of reproductive age. Recently, the number of pregnancies in RA patients has increased, partly due to improved chances of achieving lasting remission. About half of these patients experience clinical improvement during pregnancy, the other half are at risk of disease flares, leading to higher complication rates. This study aims to evaluate whether close monitoring by a multidisciplinary team of rheumatologists and gynecologists can prevent disease exacerbations and improve pregnancy outcomes.

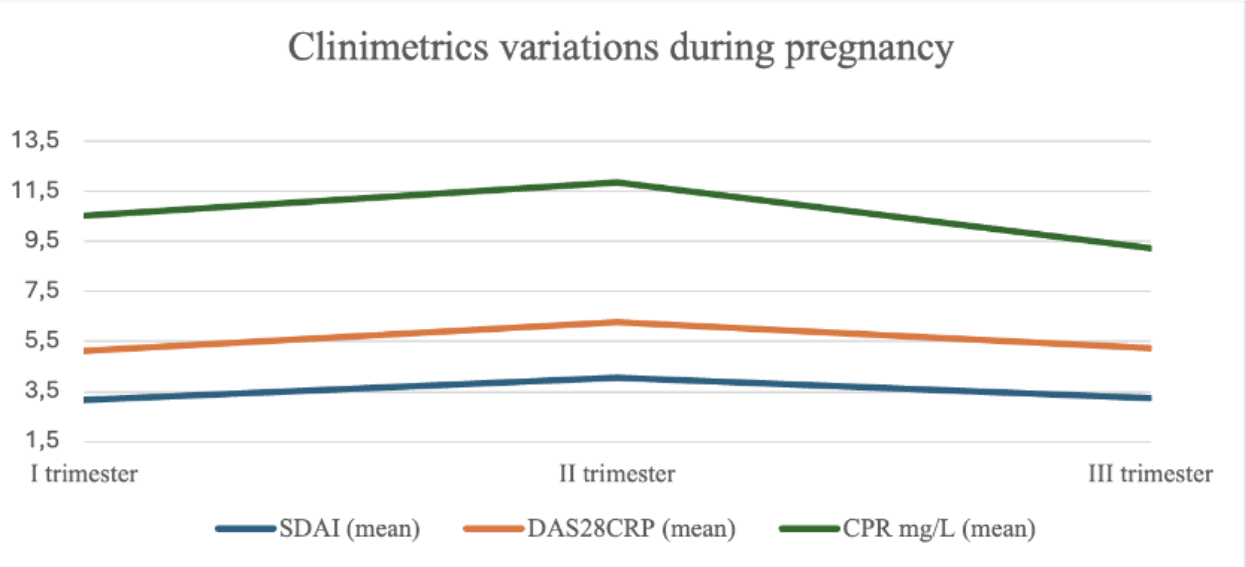
Methods: We retrospectively analyzed 74 pregnancies of 67 RA patients followed every four weeks in a multidisciplinary clinic. Demographic, clinical, biochemical, and treatment data were collected at the first visit, while clinical metrics were assessed using SDAI, DAS28-PCR scores, and CRP levels at each visit. Flares were defined as an SDAI increase of at least 4.7 points.

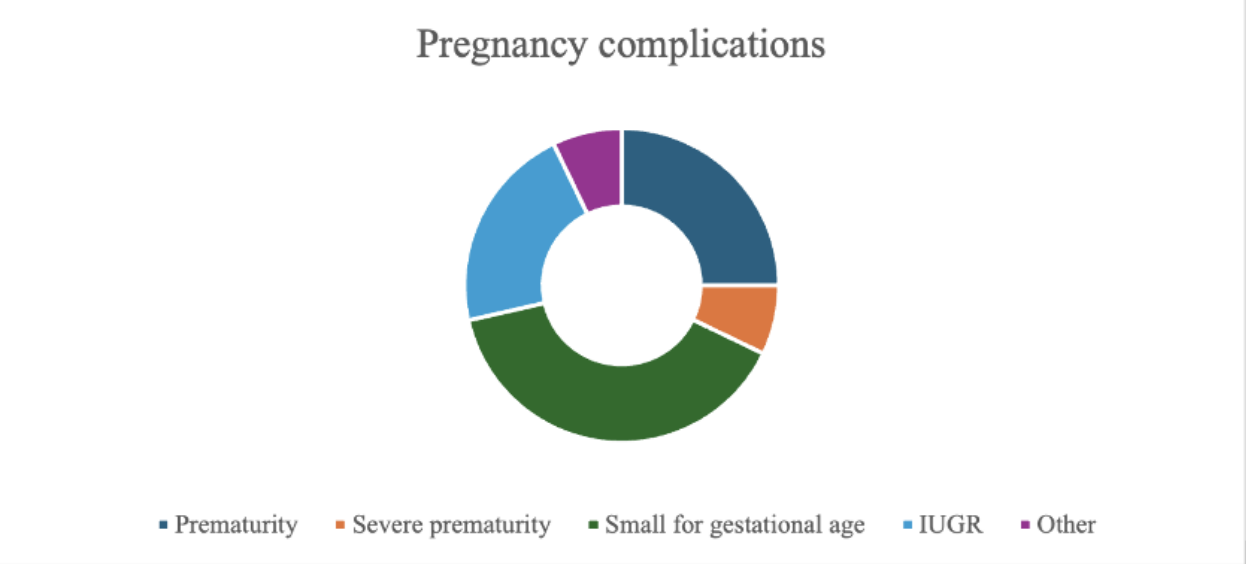
Results: Demographic characteristics are shown in Table 1. Disease flares occurred in 17.57% of pregnancies. Additionally, in 7 pregnancies, joint involvement occurred that, although it did not meet the criteria for a flare, required a modification in therapy. Pregnancy complications occurred in 21.62% of cases; no complications were reported in patients whose therapy was modified to prevent disease flares. Treatment with bDMARDs during pregnancy was identified as a protective factor against flares (p=0.05). Finally, there was a significant reduction in SDAI between the second and third trimesters (p=0.01).

Conclusions: Our study suggests that close follow-up by a multidisciplinary team can promptly address even minor clinical changes, preventing disease flares and reducing obstetric complications.

	Total	Patients who had a flare (N=13)	Patients who did not have a flare (N=61)	P value
Age at conception (years, mean ± SD)	34.9 ± 4.3	35.2 ± 4	34.8 ± 4.4	0.7
Disease duration at conception (years, mean ± SD)	8.64 ±5.9	9.6 ± 7.5	8.43 ± 5.4	0.1
RF (%)	28.38%	7.7%	32.73%	**0.09**
Anti-CCP (%)	33.78%	15.38%	37.70%	0.2
aPL (%)	4.05%	4.92%	0%	0.5
BMI >30 (%)	6.76%	15.38%	4.92%	0.2
Previous pregnancy complications (%)	1.35%	0%	1.64%	1
Remission (SDAI < 3.3, %)	75.68%	76.92%	75.41%	0.9
csDMARDs (HCQ, SSZ)	71.62%	70%	72.22%	0.8
GCs (%)	40.54%	46.15%	39.34%	0.7
bDMARDs (CTZ, ADA, ETN) (%)	16.22%	5%	20.37%	**0.05**
Pregnancy complications (%)	21.62%	15.38%	22.95%	0.7
Prematurity <37 w	9.46%	7.69%	13.11%	0.5
Prematurity <34 w	2.70%	0%	3.28%	0.5
IUGR	14.86%	15.38%	14.75%	0.9
Other	9.46%	7.69%	3.28%	0.9
Characteristics of patients in the first trimester				
SDAI (mean ±SD)	3.17 ± 4.05	2.99 ± 2.79	3.24 ± 4.44	0.1
DAS28CRP (mean ±SD)	1.96 ± 0.76	1.91 ± 0.59	1.97 ± 0.82	0.4
CRP (mean ±SD)	0.54 ± 0.75	0.41 ± 0.52	0.59 ± 0.81	**0.02**
Characteristics of patients in the second trimester				
SDAI (mean ±SD)	4.06 ± 4.06	7.65 ± 4.9	2.68 ± 2.64	**0.02**
DAS28CRP (mean ±SD)	2.21 ± 0.84	2.64 ± 0.96	1.75 ± 0.49	**<0.001**
CRP (mean ±SD)	0.56 ± 0.66	0.65 ± 0.63	0.31 ± 0.22	0.4
Characteristics of patients in the third trimester				
SDAI (mean ±SD)	3.24 ± 3.56	6.29 ± 5.06	2.02 ± 1.68	**<0.001**
DAS28CRP (mean ±SD)	2.01 ± 0.77	2.64 ± 0.96	1.76 ± 0.49	**<0.001**
CRP (mean ±SD)	0.40 ± 0.41	0.65 ± 0.64	0.31 ± 0.22	**<0.001**

Table 1





Keywords: Rheumatoid Arthritis, pregnancy, flare

O023 / #473

FREE COMMUNICATIONS 04: APS AND PREGNANCY IN RHEUMATOLOGICAL DISEASES
03-07-2025 5:50 PM - 6:50 PM

PREGNANCY RESULTS IN OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (OAPS) AND OBSTETRIC MORBIDITY ASSOCIATED WITH ANTIPHOSPHOLIPID SYNDROME (OMAPS).

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Background and Aims: Antiphospholipid syndrome (APS) is associated with adverse obstetric outcomes. Many patients do not fulfil classification criteria and they are called then OMAPS (obstetric morbidity associated to antiphospholipid syndrome). This study aims to evaluate the obstetric results in pregnancies with antiphospholipid antibodies, focusing on the obstetric antiphospholipid syndrome (OAPS) and OMAPS subgroups.

Methods: A retrospective analysis was conducted on data from pregnancies with antiphospholipid antibodies followed up at the UEAS (Unidad de Enfermedades Autoinmunes Sistémicas) del Hospital Universitario Miguel Servet de Zaragoza. Only pregnant women with antiphospholipid antibodies sometime positive were included. Chi-squared tests were performed to evaluate the differences in newborn survival across treatment variables, including low dose aspirin (LDA), low molecular weight heparin (LMWH), hidroxychloroquine (HCQ), and low dose prednisone.

Results: 506 pregnancies were included in the study with a median mother age of 35.5 ± 4.7 years. Live birth rate observed was 67.6% in OAPS and 70.5% in OMAPS subgroups with no significant differences between them. In the OMAPS subgroup, the live birth rate increased from 28.6% to 76.1% with LMWH treatment and from 13% to 62.8% in the OAPS subgroup. According to LDA treatment, live birth rates increased from 25 to 59% in OAPS subgroup and from 42.9% to 73.4% in OMAPS subgroup (all with $p < 0.001$).

Conclusions: LMWH and LDA treatments are crucial for improving newborn survival in pregnancies affected by antiphospholipid antibodies, in both OAPS and OMAPS subgroups.

Keywords: OAPS, OMAPS, Pregnancy results

O024 / #274

FREE COMMUNICATIONS 05: VASCULITIS, SLE AND SJöGREN'S SYNDROME
03-08-2025 10:30 AM - 11:30 AM

COMPARATIVE EFFICACY OF MEPOLIZUMAB 100 MG, MEPOLIZUMAB 300 MG AND BENRALIZUMAB 30 MG IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: A MONOCENTRIC RETROSPECTIVE OBSERVATIONAL STUDY

Federica Davanzo, Roberto Padoan, Luca Iorio, Marta Codirenzi, Eleonora Fiorin, Andrea Doria
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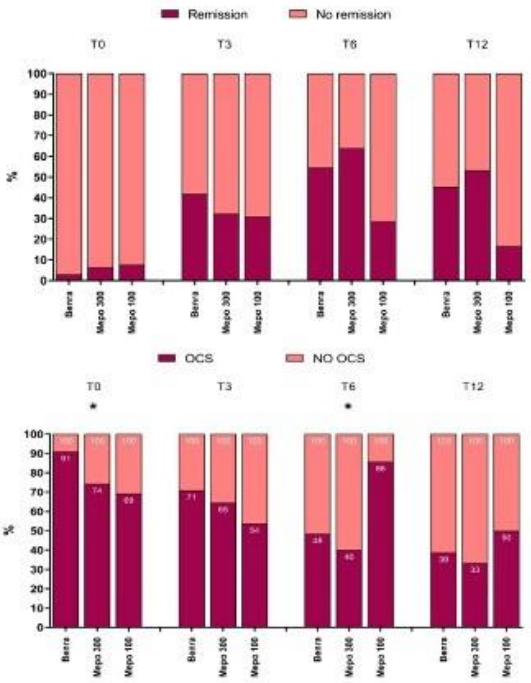
Background and Aims: Monoclonal antibodies targeting IL-5 (mepolizumab) and IL-5α receptor (benralizumab) have shown to be effective in the treatment of EGPA. The aim of this study was to assess and compare the effectiveness of mepolizumab and benralizumab in a monocentric cohort of EGPA patients.

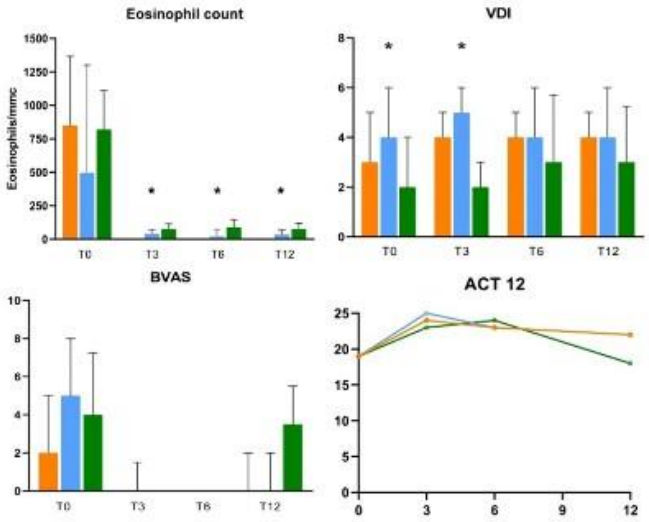
Methods: We included EGPA patients treated with benralizumab 30 mg/8weeks, mepolizumab 100 mg/4weeks or mepolizumab 300 mg/4weeks for 12 months and compared according to clinical, functional and biological data. Remission was defined as BVAS of 0 and prednisone dose ≤4 mg/day.

Results: 61 patients (female 50.8%, age 52 [41-59] years) were exposed to 77 treatment lines (n=33 benralizumab, n=31 mepolizumab300mg, n=13 mepolizumab100mg). Remission rates increased over time, with mepolizumab100mg showing the numerically lowest rate at 12 months, benralizumab: 45%; mepolizumab300mg 53%, 17% mepolizumab100mg; p=0.124). At 12 months BVAS significantly decreased in benralizumab (p<0.001) and mepolizumab300mg (p=0.022). Eosinophil counts reduced at 3 months and throughout follow-up, with benralizumab as the most depleting agent (p<0.001). Prednisone intake reduced significantly for mepolizumab300mg and benralizumab (prednisone discontinuation at 6 months; mepolizumab300mg:56%; benralizumab:46%). Mepolizumab300mg led to shorter time to prednisone discontinuation (log-rank p=0.006) and to higher retention rate at 24 months (log-rank p=0.271). 53.8% of mepolizumab100mg patients switched to other biologics. The main reason for

discontinuation was persistent ENT symptoms in the benralizumab group (p=0.001).

	Benralizumab 30 mg/8w (n = 33)	Mepolizumab 300 mg/4w (n = 31)	Mepolizumab 100 mg/4w (n = 13)	p-value
Male, n (%)	17 (51.5)	16 (51.6)	7 (53.8)	0.989
Age, y, median (IQR)	56 (47-62)	58 (51-62)	46 (39-58)	0.259
Disease duration (m), median (IQR)	31 (16-94)	26 (5-103)	16 (0-105)	0.660
Disease duration < 6 months, n (%)	6 (18.2)	10 (32.3)	6 (46.2)	0.141
BVAS, median (IQR)	0 (0-4)	0 (0-6)	0 (0-2)	0.948
VDI, median (IQR)	3 (2-5)	4 (3-6)	2 (0-4)	**0.010**
Eosinophils/mmc, median (IQR)	850 (515-1368)	496 (95-1300)	810 (200-1110)	0.302
ANCA-MPO positivity, n (%)	2 (6.1)	7 (22.6)	1 (9.1)	0.112
CRP mg/L, median (IQR)	2.9 (1.5-3.8)	2.9 (0.9-4.6)	3.2 (1.3-6.9)	0.846
FEV1, %, median (IQR)	82 (65-95.5)	94 (69-108)	78 (73.5-88.5)	0.392
FeNO, ppb, median (IQR)	44.00 (21.30-61.73)	29.78 (19.48-48.5)	53.5 (33.72-63.91)	0.577
ACT, median (IQR)	19 (15.5-22.5)	19 (18-25)	19 (15-22)	0.554
Active manifestations at biologics initiation, n (%)				
General symptoms	6 (18.2)	7 (22.6)	1 (7.7)	0.505
Pulmonary infiltration	2 (6.1)	3 (9.7)	0 (0)	0.475
Severe asthma	29 (87.9)	15 (48.4)	12 (92.3)	**0.0004**
ENT involvement	22 (66.7)	20 (64.5)	9 (64.3)	0.953
Sinusitis	17 (51.5)	19 (61.3)	8 (61.5)	0.688
Cutaneous involvement	2 (6.1)	2 (6.5)	1 (7.7)	0.979
Cardiac involvement	0 (0)	2 (6.5)	1 (7.1)	0.304
Gastrointestinal involvement	0 (0)	2 (6.5)	0 (0)	0.218
Renal involvement	0 (0)	1 (3.2)	0 (0)	0.471
Peripheral neuropathy	5 (15.2)	10 (32.3)	2 (15.4)	0.210
Treatments at the time of biologics initiation, n (%)				
Patients on OCS, n (%)	30 (90.9)	23 (74.2)	9 (69.2)	0.128
OCS, mg/day, median (IQR)	7.5 (5-12.5)	5 (0.62-12.5)	5 (0-10)	0.291
Patients on OCS ≥ 7.5 mg/day, n (%)	18 (54.5)	4 (30.8)	13 (41.9)	0.303
Immunosuppressant, n (%)	6 (7.8)	11 (35.5)	4 (5.2)	0.285
Previous anti-IL-5/Rα biologic, n (%)	8 (24.2)	9 (29.0)	0 (0)	0.229





	Benralizumab 30 mg/8w	Mepolizumab 300 mg/4w	Mepolizumab 100 mg/4w	P value
Discontinuation, n, %	13 (39.4)	3 (9.7)	7 (53.8)	< 0.001
Reason for treatment discontinuation:				
Primary failure, n %	2 (15.8)	1 (33.3)	2 (28.6)	0.390
Secondary failure, n%	10 (76.9)	2 (66.7)	5 (71.4)	0.684
Uncontrolled ENT	**10 (100)**	**0 (0)**	**3 (60)**	**0.001**
Uncontrolled asthma	**2 (20)**	**2 (100)**	**4 (80)**	**0.007**
Vasculitis flare, n %	1 (7.7)	0 (0)	0 (0)	0.370
Other, n %	1 (7.7)	0 (0)	0 (0)	0.370
Adverse events, n %	0 (0)	0 (0)	0 (0)	-
Remission, n %	0 (0)	0 (0)	0 (0)	-
Shift to other biologics, n (%)	**12 (36.4)**	**3 (9.7)**	**7 (53.8)**	**0.001**
Benralizumab, n (%)	-	3 (9.7)	4 (30.8)	0.081
Mepolizumab 100, n (%)	0 (0)	0 (0)	-	0.298
Mepolizumab 300, n (%)	7 (21.2)	-	3 (23.1)	0.890
Dupilumab, n (%)	5 (15.1)	0 (0)	0 (0)	0.028

Benralizumab 30 mg/8w Mepolizumab 100 mg/4w Mepolizumab 300 mg/4w

Conclusions: Benralizumab and Mepolizumab300mg exhibited a significant steroid-sparing effect, with mepolizumab 300 mg demonstrating superior drug survival. Benralizumab seems to be the most effective eosinophil depleting agent. Persistent ENT symptoms were the main reason for treatment discontinuation, particularly in benralizumab-treated patients.

Keywords: EGPA, Vasculitis, Mepolizumab

O025 / #26

FREE COMMUNICATIONS 05: VASCULITIS, SLE AND SJöGREN'S SYNDROME
03-08-2025 10:30 AM - 11:30 AM

BIOLOGICAL TREATMENT MAY BE FIRST STEROID-SPARING OPTION IN A SUBGROUP OF TAKAYASU ARTERITIS PATIENTS

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Background and Aims: Background: There is no data regarding in which patients biologic immunosuppressive (bIS) treatment should be chosen in Takayasu's arteritis (TAK)**.** We aimed to assess the characteristics of TAK patients needed biologic treatment during follow-up.

Methods: Patients fullfilling the ACR 1990 criteria for TAK and who received conventional ISs (cISs) or bISs were included in this retrospective multicentre study. Data were collected from patient files.

Results: We included 329 patients (F/M: 284/45) in the study. The number of the patients who received bISs was 113 (34%)(89 TNF inhibitors, 24 tocilizumab) and who received only cISs was 216 (66%) during follow-up. Mean age was 43.0±13.5 years, mean follow-up duration was 78.7± 65.8 months. Patients who received bISs were younger than patients who received cISs (36.8±11.3 vs 46.2±13.2 years, $p<0.01$) at last visit assessment. The frequency of constitutional symptoms at baseline visit was higher in bISs group (85% vs 66%, $p<0.01$). Baseline erythrocyte sedimentation rate (bISs vs cISs: 66.7±33.5 vs 45.0±29.1 mm/h, $p<0.01$) and CRP (19 (0.3-280) vs 12.5 (0.2-286) mg/L, $p= 0.002$) were higher in patients receiving bISs. Number of relapses were higher in patients who needed bISs.

Conclusions: In this study, TAK patients with biologic treatment need during follow-up had more frequent constitutional symptoms and higher acute phase reactants with a higher relapse rate compared to patients receiving cIS treatment. Our results may suggest that in young TAK patients with prominent acute phase reactants and constitutional symptoms at diagnosis, biologic treatment may be used as first sparing option.

O026 / #476

FREE COMMUNICATIONS 05: VASCULITIS, SLE AND SJöGREN'S SYNDROME
03-08-2025 10:30 AM - 11:30 AM

BENRALIZUMAB VS MEPOLIZUMAB: A EUROPEAN REAL-LIFE RETROSPECTIVE MULTICENTRE STUDY

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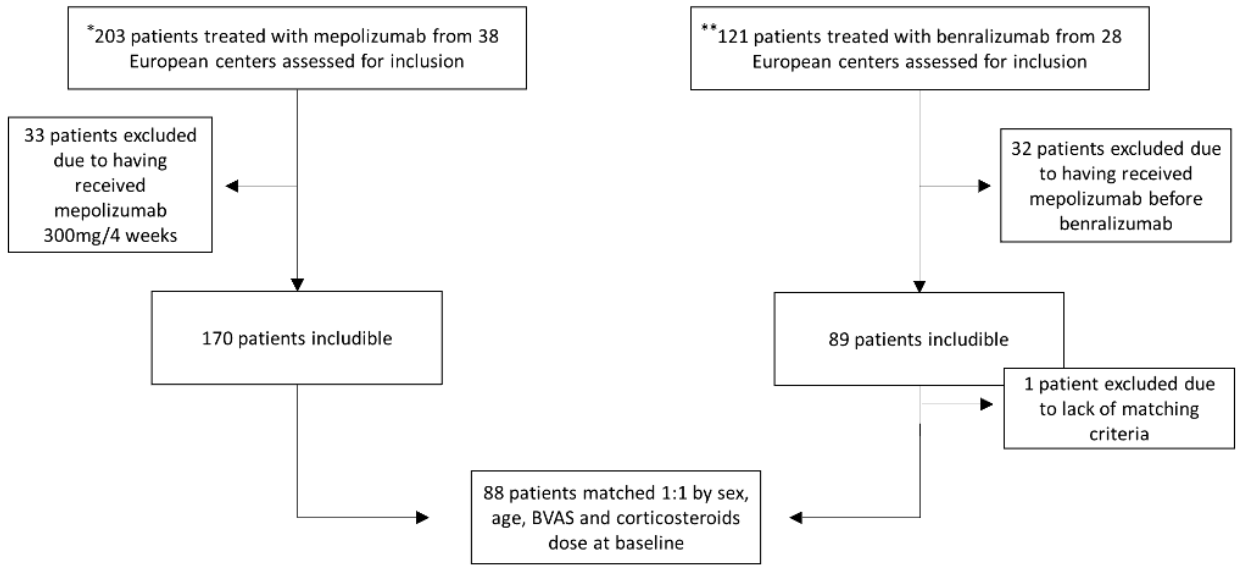
Background and Aims: Interleukin 5 (IL-5) inhibitors are currently used for treating eosinophilic granulomatosis with polyangiitis (EGPA). This study aims at comparing the effectiveness and safety of mepolizumab and benralizumab in a European cohort of EGPA patients.

Methods: A retrospective observational cohort study was conducted on patients treated with mepolizumab or benralizumab at the asthma dose. Patients were matched 1:1 by sex, age, Birmingham Vasculitis Activity Score [BVAS] and oral corticosteroids [OCS] dosage at the initiation of therapy (T0), and data were then compared after 3, 6, and 12 months (T3-12). Complete response [CR] was defined as MIRRA trial. Safety outcomes were compared over a 12-month follow-

up. **(Fig.1)**

Study flow chart



* Bettiol et al. *Arthritis Rheumatol (Hoboken, NJ)* 2022
** Bettiol et al. *Lancet Rheumatol* (2023)

Results: 88 patients were matched for each group [57% females, median age 54 years (IQR 45-60)]. Baseline characteristics at T0 is reported in **Fig. 2**. 45.4% of patients in the mepolizumab group and 51.1% in the benralizumab group achieved CR or partial response (PR) at T3, with CR rates increasing during follow-up for both treatments. However, at T12, a higher CR rate was found in the benralizumab group (48.1% vs 32.4%, p=0.005). Concerning safety profile, 11 patients (12.5%) and 15 (17.0%) reported adverse events during mepolizumab and benralizumab treatment, respectively. Most events were mild (only one on mepolizumab and 2 on benralizumab requiring hospitalization (**Fig.3)**. Finally, 9 patients discontinued mepolizumab and 16 benralizumab (p= 0.130).

	Patients on mepolizumab treatment (n=88)	Patients on benralizumab treatment (n=88)	p-value*
General features			
Female, sex at T0	50 (57.0%)	50 (57.0%)	Matching variable
Age at therapy beginning, years	54 (IQR 45-60)	54 (IQR 44-60)	Matching variable
BVAS, median (IQR)	4 (IQR 2-7)	3 (IQR 2-8)	Matching variable
Daily OCS dose, median (IQR)	10 (IQR 7.5-12.5)	10 (IQR 7-13)	Matching variable
FEV 1, median (IQR)	75 (IQR 62-83)	81 (IQR 65-91)	0.106
Age at diagnosis, years	48 (39-55)	45 (36.53)	0.235
Disease duration, median (IQR)	5 (IQR 2-11)	5 (IQR 2-12)	0.222
ANCA positivity	14/86 (16%)	17/78 (22%)	0.186
Eosinophil count	700 (280-1037.5)	540 (207.5-1080)	0.498

	T3	T6	T12	Overall
N patients experiencing at least one adverse event (AE)				
Mepolizumab	5/86[#] (5.8%)	4/82 (4.9%)	2/66 (3.0%)	11
Benralizumab	7/82[#] (8.5%)	5/76 (6.6%)	4/64 (6.25%)	16
AE requiring hospitalization				
Mepolizumab	0	0	1	1
Benralizumab	2	0	0	2
N patients discontinuing therapy				
Mepolizumab	3/84[#] (3.6%)	3/76 (3.9%)	3/68 (4.4%)	9
Benralizumab	3/87[#] (3.4%)	5/83 (6%)	8/72 (11.1%)	16

Conclusions: Mepolizumab and benralizumab at the dosage approved for eosinophilic asthma showed a comparable overall effectiveness in controlling systemic and respiratory manifestations in EGPA, with a good safety profile.

Keywords: EGPA, Mepolizumab, benralizumab

O027 / #450

FREE COMMUNICATIONS 05: VASCULITIS, SLE AND SJöGREN'S SYNDROME
03-08-2025 10:30 AM - 11:30 AM

NOVEL AUTOANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS: IGG AND IGA ISOTYPES OF ANTI-LIN28A AND ANTI-IRF5 AS INDICATORS OF DISEASE ACTIVITY

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Background and Aims: To identify novel autoantibodies that reflect global and organ-specific disease activity in systemic lupus erythematosus (SLE).

Methods: Serum samples were screened for IgG and IgA seroreactivity against 1609 protein autoantigens using an immunome microarray (Sengenics). We determined differentially abundant antibodies (daAbs) in SLE patients versus healthy controls within a discovery (n=196 versus n=110) and an independent validation cohort (n=30 versus n=83) from the European PRECISESADS project (NTC02890121). Validated daAbs were analysed in relation to global and organ-specific disease activity using linear and logistic regression, along with daAb and pathway enrichment analysis.

Results: We identified 89 IgG and 66 IgA validated daAbs in SLE patients versus healthy controls. IgG and IgA anti-IRF5 were associated with a Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score of ≥10 (adjusted odds ratio [OR_{adj}]: 1.69; 95% confidence interval [CI]: 1.09–2.63; p=0.020 and OR_{adj}: 1.64; 95% CI: 1.04–2.61; p=0.034). IgG (OR_{adj}: 0.53; 95% CI: 0.38–0.75; p<0.001) and IgA (OR_{adj}: 0.47; 95% CI: 0.30–0.73; p=0.001) anti-LIN28A were negatively associated with Lupus Low Disease Activity State (LLDAS). IgG anti-LIN28A was negatively associated with Definition of Remission in SLE (DORIS) remission (OR_{adj}: 0.52; 95% CI: 0.32–0.85; p=0.009). Several IgG and IgA daAbs and enriched pathways based on autoantigen specificities were shared across organ

manifestations. Half of the active SLE patients had positive levels of IgG anti-LIN28A across most organ manifestations.

Conclusions: Novel IgG and IgA autoantibodies, including anti-IRF5 and anti-LIN28A, were associated with SLE disease activity and highly abundant across organ manifestations.

Keywords: Biomarkers, SLE, AUTOANTIBODIES

O028 / #423

FREE COMMUNICATIONS 05: VASCULITIS, SLE AND SJöGREN'S SYNDROME
03-08-2025 10:30 AM - 11:30 AM

MANAGEMENT OF SJOGREN'S DISEASE IN REAL-LIFE: INSIGHTS FROM AN ITALIAN COHORT.

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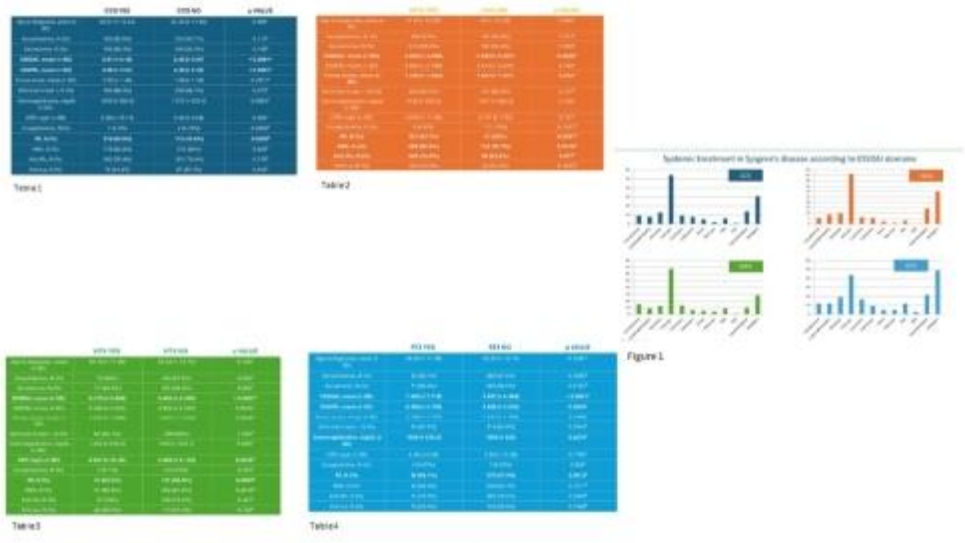
Background and Aims: Primary Sjögren's disease (SD) is a systemic autoimmune disorder characterized by a lymphocytic infiltrate affecting exocrine glands, resulting in gland dysfunction and sicca symptoms. Presently, no specific treatment is available for SD, and the diagnostic delay is typically at least 3 years after the onset of symptoms. Our study aimed to evaluate current treatments of SD patients a in an Italian multicohort from tertiary rheumatologic centers.

Methods: A multi-centre, cross-sectional, observational study has been conducted on the 474 consecutive SD patients. Chi2 test was used for analysis of contingency tables, while Mann– Whitney test was used to compare ranks. The whole statistical analysis was performed using R software. p- values <0.05 were considered as significant.



Results:

HCQ was the most commonly prescribed drug, followed by CCS, MTX, and RTX. HCQ, CCS, and MTX were used for articular manifestations, while RTX was reserved for hematological and biological involvement, lymph nodes and glandular swelling, as well as specific organ-related involvement (Fig.1). CCS-treated patients had higher ESSDAI, higher ESSPRI, and

RF positivity (Table 1). HCQ-treated patients had higher ESSDAI, lower focus score, and a positivity for RF, ANA, and anti-Ro antibodies (Table 2). MTX-treated patients had higher ESSDAI, elevated CRP, and positivity for RF (Table 3). RTX-treated patients exhibited higher ESSDAI, higher ESSPRI, and elevated gammaglobulin levels (Table 4).

Conclusions: Our study provides a 'real-life' picture of treatments available for SD in real-life analyzing the various baseline factors related to the patients and/or the disease that could contribute to the use of different drugs.

Keywords: treatment, sjogre's disease, real life

O029 / #573

FREE COMMUNICATIONS 05: VASCULITIS, SLE AND SJöGREN'S SYNDROME
03-08-2025 10:30 AM - 11:30 AM

RISK FACTORS FOR NEW-ONSET AUTOIMMUNE DISEASES IN LONG COVID PATIENTS: A REAL-WORLD COHORT

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Background and Aims: Long COVID is estimated to affect 400 million people worldwide, with a strong autoimmune component suspected in its pathogenesis. In a general practice-based prospective cohort, we aimed to identify risk factors for new-onset autoimmune disease among Long COVID patients.

Methods: Clinical and demographic data were available for 111 patients with Long COVID, diagnosed according to WHO criteria. ICPC codes were used to identify pre-existing and incident autoimmune diseases (standardized national electronic health records). Human Phenotype Ontology (HPO) was used for classification. COOP-charts were used to quantify patient-reported quality of life (QoL). Risk factors were identified by multivariable logistic regression, prediction was tested with ROC curve analysis.

Results: Out of 111 Long COVID patients, 16 had pre-existing autoimmune disease (rheumatoid arthritis, type I diabetes, psoriasis, IBD and others). During >220 person-years of follow-up, 22 incident cases of autoimmune disease were observed, of which 12 (55%) were IBD, and 4 (18%) anti-phospholipid syndrome. Patients with new-onset autoimmunity were more frequently female, unvaccinated and had experienced less acute COVID-19 episodes. Among patient-reported QoL data at baseline, COOP-change score was significantly higher for subsequent incident cases (p=0.044). Female sex (OR 4.42 [1.12-22.13]) , vaccination status (OR 0.092 [0.0078-0.60]) and COOP-change (OR 2.42 [1.15-5.81]) were independent risk factors for new-onset autoimmune disease in multivariable logistic regression. Together, these risk factors significantly predicted new-onset autoimmune disease (AUROC 0.79 [0.67-0.92], p=0.0002).

Conclusions: In a real-world prospective cohort, female sex and worse COOP-change QoL score are independent negative predictors of new-onset autoimmune disease in Long COVID, while SARS-CoV-2 vaccination is protective.

Keywords: COVID-19, risk factors, new-onset

O030 / #197

FREE COMMUNICATIONS 06: PEARLS IN AUTOIMMUNITY
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DEVELOPMENT OF A PAN-DISEASE ANTIGEN PANEL FOR AUTOIMMUNE DISEASES

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Background and Aims: Autoantibodies serve as important biomarkers for diagnosing autoimmune diseases. However, current clinical assays for their detection often face challenges, such as uncertainty about the specific autoantigen or a narrow focus on well-known autoantigens,which typically results in low sensitivity and specificity. To address these limitations we have developed a multiplex antigen bead-array that enables the parallel detection of both known and novel autoantibodies. Ultimately, we aim to improve the classification and serological characterization of autoimmune diseases.

Methods: We performed proteome-wide autoantibody screenings on plasma samples from 446 patients with vasculitis, 83 patients with systemic sclerosis, as well as healthy and inflammatory controls. These screenings utilized custom antigen-arrays featuring 42,000 protein fragments (representing 17,000 unique proteins) and 2,000 full-length secreted proteins from the Human Protein Atlas. The Samples were sourced from well-characterised cohorts through collaborations with expert clinicians.

Results: In ANCA-vasculitis, we identified new candidate biomarkers associated with subgroups of patients with specific clinical features and relapse. The screening of patients with systemic sclerosis revealed novel candidate biomarkers for both the diagnosis and

subclassification of patients with skin and lung fibrosis. Moreover, we generated a bead-array for accurate and parallel detection of autoantibodies targeting the well-known autoantigens Scl70/TOPO-1, TRIM21/Ro52/SSA, CENPs, MPO and PR3.

Conclusions: Our multiplex antigen-array effectively detected well-known clinically relevant autoantibodies. Combining clinical expertise with our high-throughput approach enabled the discovery of novel candidate biomarkers, which could improve patient diagnosis and subclassification. These findings underscore the potential of multiplex autoantibody assays for enhancing diagnostic precision across a range of autoimmune conditions.

Keyword: autoantibodies, protein arrays, multi-disease serology, biomarkers, autoimmunity

O031 / #204

FREE COMMUNICATIONS 06: PEARLS IN AUTOIMMUNITY
03-08-2025 1:55 PM - 2:55 PM

PROFILING THE BLOOD PROTEOME IN AUTOIMMUNE DISEASE USING PROXIMITY EXTENSION ASSAY

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Background and Aims: Autoimmune diseases are heterogeneous diseases characterized by dysregulation of the immune system. They often result in chronic inflammation and damage to overall health. Due to the complex nature of these diseases, they are frequently difficult to diagnose and present with comorbidities which increase mortality risk. There is a pressing need for the discovery of novel biomarkers to facilitate early diagnosis, stratification and treatment evaluation of patients within these disease populations.

Methods: In this study, five autoimmune diseases were selected for plasma profiling as part of the Human Disease Blood Atlas program, including myositis (n=210), rheumatoid arthritis (n=84), systemic sclerosis (n=100), Sjögren's syndrome (n=99), and systemic lupus erythematosus (n=99). In total, 592 plasma samples were analysed using the Olink Explore 1536 platform, a highly sensitive and multiplexed antibody-based technology, resulting in expression data of 1163 unique proteins.

Results: Differential expression identified potential prognostic biomarkers; some of these have previously been found to be associated with autoimmune disease, and others are novel. Pathway analysis provides further insights into the underlying biological processes and molecular interactions involved in the pathogenesis of these autoimmune disorders. Many identified proteins are involved in pro-inflammatory response and have suggested immune system functions. A portion of identified proteins have strong associations with cancer as well as infectious disease.

Conclusions: In summary, this study provides a comprehensive, exploratory analysis with the aim to identify distinct protein profiles both within and across five autoimmune diseases and their subgroups.

Keywords: proteomics, Biomarkers, Autoimmune

O032 / #305

FREE COMMUNICATIONS 06: PEARLS IN AUTOIMMUNITY
03-08-2025 1:55 PM - 2:55 PM

REGULATORY AUTOANTIBODIES AND EXTRACELLULAR VESICLES DRIVE AUTOIMMUNE PATHOGENESIS

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Background and Aims: This study aims to investigate the interaction between autoantibodies and extracellular vesicles (EVs) derived from systemic sclerosis (SSc) patients, and to assess their impact on monocyte function, a key cell type in SSc pathogenesis. Specifically, the study explores whether Abs directed against the angiotensin II type-1 receptor (AT1R) directly interact with EVs and how this interaction influences the phenotype and function of monocytes.

Methods: Extracellular vesicles (EVs) were isolated from the sera of systemic sclerosis (SSc) patients and healthy controls (HC) using sequential centrifugation and polyethylene glycol precipitation. To investigate the effects on monocyte phenotype and function, peripheral blood monocytes from healthy donors were stimulated with a custom-engineered activating monoclonal AT1R antibody (AT1R mAb) either alone or in combination with EVs isolated from SSc patients or HCs.

Results: Compared to EVs from HC, those derived from SSc patients exhibited a higher expression of AT1R, promoting antibody binding. Preincubation of SSc-derived EVs with AT1RmAbs led to the activation of pro-inflammatory and differentiation of pro-fibrotic monocytes. Importantly, SSc EVs preincubated with AT1R mAbs caused a significant shift in monocyte phenotype, similar to that observed in monocytes from patients with diffuse SSc. Furthermore, monocyte migration was significantly enhanced by both AT1R mAbs and SSc-derived EVs, but not by EVs from healthy controls or by an isotype control antibody.

Conclusions: This study reveals a novel insight into autoimmune disease pathogenesis. The phenotypic shift, mirroring that seen in diffuse SSc patients, highlights the critical role of EV-AT1R antibody interactions in driving pro-inflammatory and pro-fibrotic processes.

Keywords: AUTOANTIBODIES, Extracellular Vesicles, Pathogenesis

O033 / #392

FREE COMMUNICATIONS 06: PEARLS IN AUTOIMMUNITY
03-08-2025 1:55 PM - 2:55 PM

BCMA-TARGETED BISPECIFIC T CELL-ENGAGER THERAPY OF AUTOIMMUNE DISEASE

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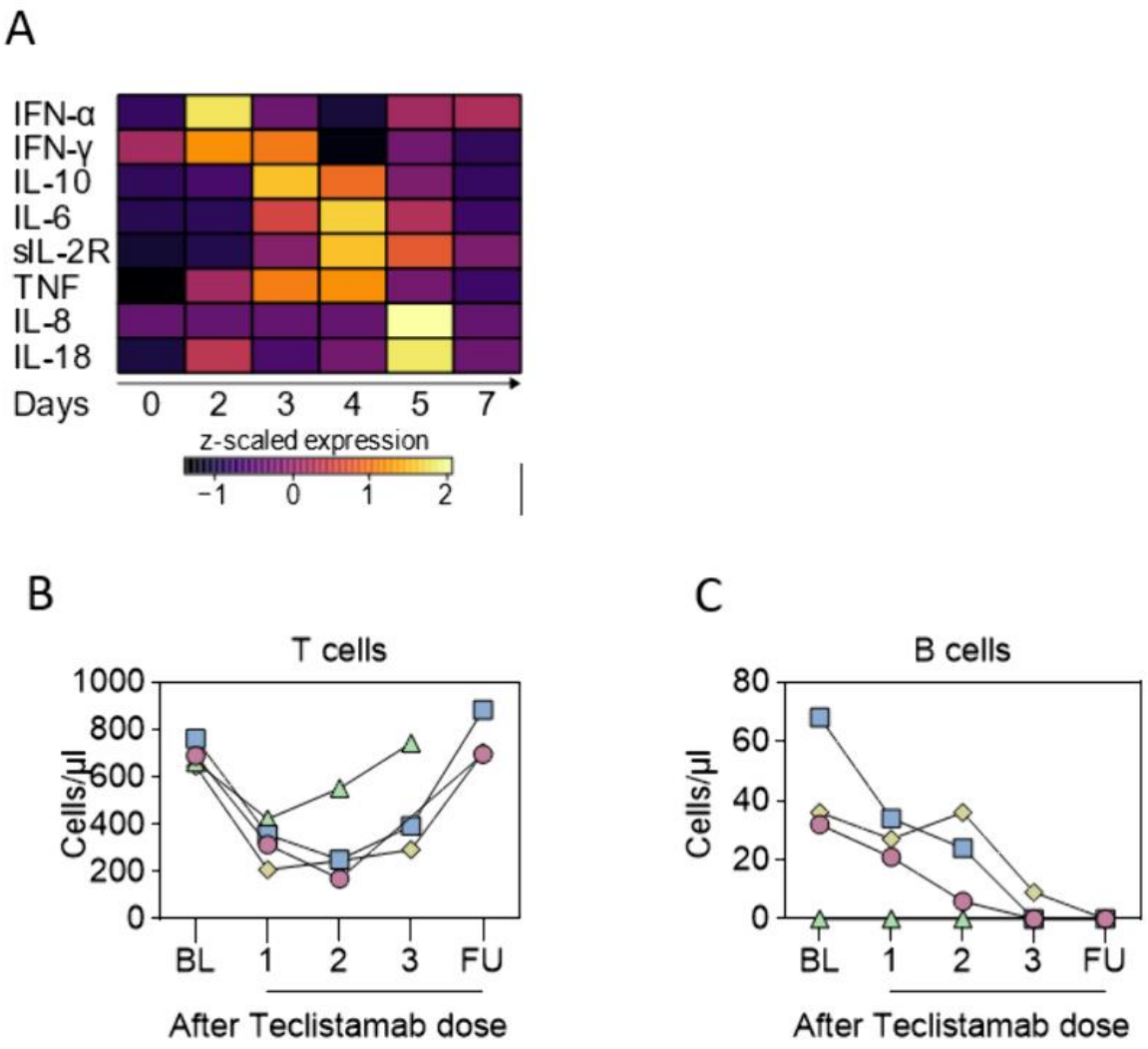
Background and Aims: Therapy with CD19-targeted chimeric antigen receptor (CAR) T-cells and bi-specific T cell engagers (BITEs) demonstrated efficacy in treatment-resistant AID. However, in some patients, disease may be anchored in long-lived plasma cells in the bone marrow expressing BCMA, not CD19. We hypothesized that the BCMAxCD3 BITE teclistamab may be a effective in severe AID even after failure of B cell depletion.

Methods: We treated 4 patients with multi-drug-resistant AID with teclistamab. Pt #1 had resistant systemic sclerosis, pt #2 Sjogren´s syndrome, pt #3 progressive MDA5+ dermatomyositis, pt #4 resistant seropositive rheumatoid arthritis. All patients had failed >5 immunosuppressants including conventional B cell depletion. Teclistamab was dosed-up in an in-patient setting: day 1 (0.06 mg/kg), day 3 (0.3 mg/kg) and day 5 (1.5 mg/kg) and repeated once (1.5 mg/kg) within one month.

Results: Teclistamab led to T cell engagement as evident by transient elevation in C-reactive protein and inflammatory cytokines. T cell engagement led to transient T cell consumption. Circulating B cells were depleted, free light chains were reduced, documenting the successful targeting of plasma cells. Immunoglobulin levels decreased. ANA, PM-Scl-75, PM-Scl-100, RF and MCV antibodies decreased, SS-A/Ro, SS-B/La and PL-7 remained stable. After 12 weeks, B cells had recovered in pt #1. High dimensional flow cytometry revealed a depletion of class-switched memory B cells and plasmablasts, which were replaced by nonclass-switched, IgD positive naïve B cells. Teclistamab significantly improved disease activity in all four

patients.



Conclusions: Our results suggest that targeting the plasma cell compartment via BCMA-targeted BITEs is safe and effective in AID.

Keyword: Plasma cells, Teclistamab, autoimmune diseases, BCMA

O034 / #253

FREE COMMUNICATIONS 06: PEARLS IN AUTOIMMUNITY
03-08-2025 1:55 PM - 2:55 PM

8CLC-DERIVED EXOSOMES MEDIATE REGULATORY T-CELL RETINOIC ACID METABOLISM THROUGH CRABP1 TO ALLEVIATE PSORIASIS

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Background and Aims: Clinical treatment of psoriasis is hindered by recurrence and long-term efficacy maintaining. Although pluripotent stem cell-derived exosomes have demonstrated excellent long-term therapeutic effects, they are limited by issues such as senescence, unclear effector molecule and mechanism.

Methods: We established an in vitro induction system that can induce pluripotent stem cells into 8C-like cells (8CLCs) with human 8-cell embryonic characteristics. These cells possess totipotency and higher genomic stability. The cell has the molecular characteristics of an extremely early embryo and is the earliest known artificial totipotent stem cell in the world. These cells possess totipotency and higher genomic stability. Stem cell-derived exosomes play an important role in physiological metabolism, cell communication, cell migration, immune response. Through GO enrichment analysis of 8CLC single-cell transcriptome data, we found that 8CLC differential genes were enriched into negatively regulating the NOTCH and NF-κB pathways. Given the characteristic that exosomes contain the contents of donor cells, we hypothesize that 8CLC-derived exosomes (8CLC-Exo) could play a beneficial role in autoimmune diseases such as psoriasis.

Results: Co-culturing T cells with 8CLC-Exo significantly reduces Th17 differentiation and promotes Treg generation. Transdermal application of 8CLC-Exo alleviates psoriatic skin lesions and increases Treg infiltration in IMQ-induced mouse model. Through comprehensive analysis of exosomal proteomics data and psoriasis patient samples RNA sequencing data, we speculate that 8CLC-Exo may promote Treg differentiation and reshape the immune homeostasis in psoriasis through the cellular retinoic acid-binding protein 1 (CRABP1)-dependent retinoic acid metabolism pathway.

Conclusions: 8CLC-derived exosomes reprogramme Treg retinoic acid metabolism through CRABP1 to alleviate psoriasis.

Keywords: Treg, Psoriasis, 8CLC-exosome

O035 / #419

FREE COMMUNICATIONS 06: PEARLS IN AUTOIMMUNITY
03-08-2025 1:55 PM - 2:55 PM

AGE-DEPENDENT INFLUENCE OF BASELINE BIOMARKER LEVELS OF NETOSIS ON ANTI-SPIKE IGG IN RECIPIENTS OF COVID-19 VACCINES

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Background and Aims: The elderly are more vulnerable to novel infections and need timely vaccinations. Immunosenescence reduces vaccine efficacy. Alum, an adjuvant, enhances NETosis and protective antibodies in murine models. We hypothesized that NETosis play a significant role in alum-containing COVID-19 vaccines.

Methods: Healthy donors(HDs) receiving ChAdOx1-S(**A**), mRNA-1273(**M**), or adjuvanted protein vaccine MVC–COV1901(**G**) vaccines at National Taiwan University Hospital(2021-2022) were recruited. NETosis biomarkers, serum citH3 and BAFF were measured serially: **naïve, Booster-Day0**, and **Booster-Day30**. Anti-S titers were assessed using AdviseDx immunoassay.

Results: A negative correlation between age and baseline citH3(r=-0.25, p=0.03, n=71, **Fig.1**) was
observed.

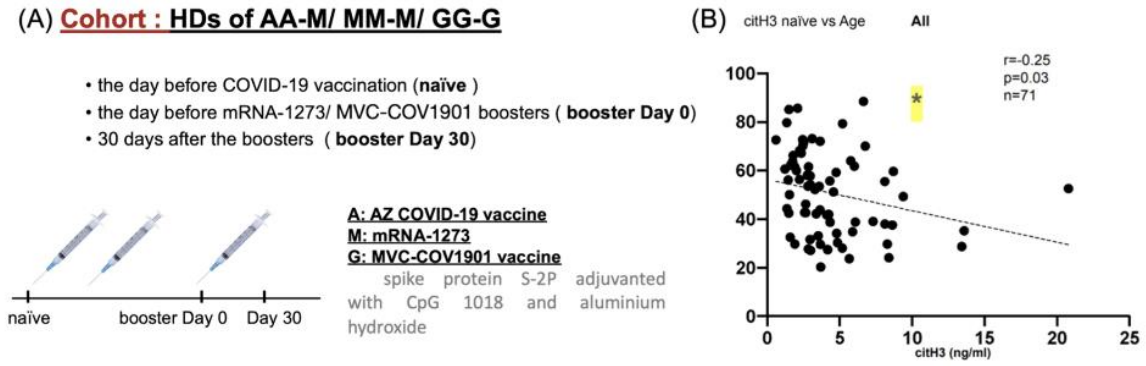

Fig. 1.

A : Timeline of blood sampling. HDs who tested negative for nucleocapsid antibodies to exclude COVID-19 were analyzed.

B : A significant negative correlation observed between baseline citH3 and age in HDs. A strong negative correlation was evident between age and baseline citH3(naïve status) for HD who was enrolled in this COVID-19 vaccine trial. (Pearson's correlation coefficient r = -0.25, p = 0.03). These HDs have undergone the first COVID-19 vaccine either with ChAdOx1-S, mRNA-1273 or MVC-COV1901.

Post-vaccination citH3 were also influenced by age(**Table.1**).

Variable	Estimate	Standard error	|t|	P value
citH3 naïve	0.1655	0.3231	0.5123	0.61
age	-0.1342	0.06274	2.139	0.04
Intercept	16.41	3.932	4.173	<0.0001

Variable	Estimate	Standard error	|t|	P value
ln(citH3 naïve)	0.3164	0.1604	1.973	0.05
ln(age)	-0.6469	0.2921	2.215	0.03
Intercept	4.073	1.215	3.352	0.001

Table. 1.

Considering baseline citH3 levels, citH3 post two doses of COVID-19 vaccination remains influenced by age. Among HDs who received two doses of the COVID-19 vaccines, serum citH3 levels were analyzed via linear regression, yielding citH3 on booster Day 0 = 16.41 + 0.17 x citH3 naïve + -0.13 * age. When applying natural logarithm transformation, the equation becomes ln(citH3 Booster Day0) = 4.10 + 0.32 * ln(citH3 naïve) + -0.65 * ln(age). Therefore, even after considering baseline citH3 levels, citH3 Day0 (i.e., post-vaccination) remains influenced by age.

In HDs who received two doses of various COVID-19 vaccines, a linear regression model indicated that citH3 on Booster-Day0 could be expressed as: citH3(Booster-Day0)=16.41+0.17*citH3(naïve)-0.13*age(p=0.04 for age, n=71). After logarithm transformation, citH3(Booster-Day0) remained significantly affected by age(p=0.03 for

ln(age)). In **GG-G**(which subgroup recieved three doses of MVC-COV1901 protein vaccine adjuvanted with alum and CpG 1018), a strong correlation was found between anti-S IgG(Booster-Day0) and baseline citH3(*r*=0.69, *p*=0.03, **Fig.2A**), which was not seen in **AA-M** and **MM-M**. Positive correlations between anti-S after two COVID-19 vaccines and baseline citH3 were noted only in MVC-COV1901 subgroup. Furthermore, temporal correlations were observed between BAFF and citH3(*r*=0.61, p<0.0001, Booster-Day30/Booster-Day0
ratio, **Fig.2B**).

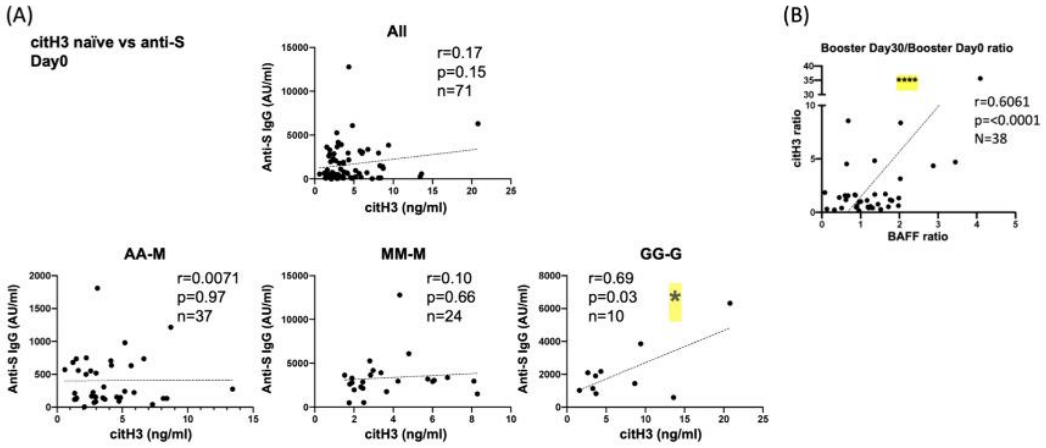

Fig. 2.

A: A correlation observed between citH3 and anti-S IgG levels in HDs who received two doses of recombinant COVID-19 vaccine. A strong positive correlation was evident between the anti-S IgG (measured on booster Day 0, with blood samples taken the day before receiving the booster shot) and baseline citH3(naïve status) for the GG-G groups (Pearson's correlation coefficient r = 0.69, p = 0.03). However, this association was not evident in the AA-M and MM-M subgroups.

B: Temporal correlations were seen between increases in BAFF and citH3. A robust positive correlation was evident between the BAFF ratio and citH3 ratio for the GG-G groups (Pearson's correlation coefficient r = 0.61, p < 0.0001, Booster Day 30/ Booster Day 0 ratio).

Conclusions: In this COVID-19 vaccine cohort, baseline NETosis biomarker were influenced by age. A positive correlation was observed between anti-S and baseline citH3 in recipients of recombinant protein vaccines, along with trends of higher NETosis formation and BAFF induction. Further studies on NETosis and vaccine efficacy are warranted.

Keywords: COVID-19 vaccines, COVID-19 vaccines, Protein vaccine, NETosis, Immunosenescence, Vaccine efficacy