7TH INTERNATIONAL CONGRESS ON CONTROVERSIES IN RHEUMATOLOGY & AUTOIMMUNITY

CORRA Autoimmunity Network Member

O001 / #159

FREE COMMUNICATIONS 01: LAB AND BIOMARKERS
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DIFFERENTIATED MONOCYTES EXPRESS THE PDC MARKERS BDCA-2, CD123 AND ILT7

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Background and Aims: Plasmacytoid dendritic cells (pDCs) were previously thought to be the major source of type I interferon in SLE. BDCA-2 appears to be exclusively expressed on pDCs in fresh blood and has been investigated as a therapeutic target. However, we showed that pDCs lose their immunogenic functions prior to onset of SLE[PMID: 33262343]. Here, we aimed to characterise pDC marker expression on myeloid lineage cells.

Methods: Following density gradient separation, PBMCs were cultured in RPMI. At 0 and 24h, cells were stained for CD3, CD19, CD14, CD16, CD11c, HLA-DR, CD123, BDCA-2, BDCA-4 and ILT7 and analysed by flow cytometry. We next performed an in vitro M1 macrophage differentiation. Monocytes were purified by negative selection and cultured with GM-CSF for 5 days. On day 6, IFN-γ and LPS were added and cells analysed by flow cytometry.

Results: For PBMCs, at 0 hours, apart from pDCs, no monocyte subset or myeloid DCs expressed BDCA-2, BDCA-4, CD123 or ILT7. However, at 24h, each of these markers was expressed by at least one myeloid subset, predominantly by classical and intermediate monocytes. M1 macrophages (CD14+HLA-DR+CD80+CD206+) expressed all four pDC markers.

Conclusions: BDCA-2, CD123 and ILT7 are not specific to pDCs and are also expressed on monocyte subsets upon differentiation. Since monocyte subsets are key responder cells to IFN-I, with pathogenic roles in SLE, the efficacy of therapies targeting these markers may be explained by their effects on other myeloid cells and not pDCs. This is important for the safety of these therapies as well as their potential indications beyond the IFN-I mediated diseases.

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C-X-C MOTIF CHEMOKINE 13 (CXCL13) AS POTENTIAL DIAGNOSTIC BIOMARKER IN SERONEGATIVE ARTHRITIS

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Background and Aims: A major challenge in the field of chronic seronegative arthritis [e.g., negative for anti-citrullinated peptides autoantibodies (ACPA) and/or rheumatoid factors (RF)] is the research of potentially new circulating diagnostic and prognostic biomarkers. C-X-C motif chemokine 13 (CXCL13) is a promising molecule for this purpose, because of its association with active synovitis (Bechman et al. BMC Rheumatology 2020) and a poor prognosis in rheumatoid arthritis (RA) (Bugatti et al. Rheumatology 2014). We aimed to analyse CXCL13 serum levels in patients with peripheral psoriatic arthritis (PsA) in comparison to RA.

Methods: Cross sectional analysis of 81 patients with peripheral PsA [male/female=44/37; median age (25°-75°percentile)=54(46-62) years; 28-joint Disease Activity Score-C Reactive Protein (CRP-DAS28)=1.9 (1.6-2.5); active psoriasis=43%; Disease Activity in Psoriatic Arthritis (DAPSA) score=8(3-14)] and 143 RA [male/female=30/113; age=62(50-70) years; seropositive=67%; CRP-DAS28=2.1(1.5-2.8)] was performed. 100 sex and age-matched healthy controls (HC) were enrolled. CXCL13 levels were assessed using commercial ELISA test (R&D).

Results: CXCL13 levels (pg/mL) were higher in all subgroups [PsA:50.9(34.5-80.2), $p<0.01$; RA:77.2(52.9-107.7), $p<0.01$; RA/ACPA+:77.7(55.9-110.7), $p<0.01$; RA/ACPA-:69.5 (49.3-104), $p<0.01$] than in HC [22.3 (17.7-33.8)]. No significant differences were found among RA patients according with their seropositivity ($p=0.378$). CXCL13 was lower in PsA than in RA [vs ACPA+ RA, $p<0.01$; vs ACPA- RA, $p=0.012$] and positively correlated with CRP ($r=0.30$;$p=0.008$) but not with DAPSA score in PsA patients.

Conclusions: These results confirm the biomarker value of CXCL13 in the field of chronic arthritis. Higher levels in seronegative RA than in PsA suggest its potential value in the differential diagnosis of these two subsets.

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CHARACTERIZATION OF EXTRACELLULAR VESICLES SURFACE LYMPHOCYTES MARKERS AND MICRORNA CARGO IN PATIENTS AFFECTED WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background and Aims: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune disorders. Extracellular vesicles (EVs) are cell-derived nanoparticles involved in intercellular signaling convoying their cargo that act in autoimmune pathogenesis. The study aims to characterize circulating EVs surface markers and microRNA cargo investigating their potential role as biomarkers in IIM.

Methods: EVs were isolated from platelet-free plasma of IIM patients and healthy donors (HDs) through size exclusion chromatography and ultrafiltration. EVs were quantified by nanoparticles tracking analysis (NTA), immune-characterized by imaging-flow cytometry (IFC), and EVs-microRNA cargo investigated through Next-Generation Sequencing (NGS).

Results: NTA measurements reported higher mean EVs concentration in IIM patients (n=58) than in HDs (n=60) (1.75x10^10 ± 1.35x10^10 SD [EVs/mL] vs. 1.34x10^10 ± 7.35x10^9; p=0.0461). IFC characterization showed a prevalence of CD3-CD19+ EVs both in IIM (n=26) and HDs (n=25) (7.38x10^7 ± 3.67x10^7 vs. 6.20x10^7 ± 3.85x10^7, respectively) compared to CD3+ (2.64x10^6 ± 1.38x10^6 vs. 2.35x10^6 ± 1.78x10^6) (p<0.0001). NGS analysis detected 10 EVs-microRNA with different expression profile between IIM (n=21) and HDs (n=21). Hsa-miR-451a (p=0.0010), hsa-miR-15a-5p (p=0.0086), hsa-miR-486-5p (p=0.0012), hsa-miR-222-3p (p=0.0098), hsa-miR-32-5p (p=0.0038), hsa-miR-185-5p (p=0.0217) were up-regulated in IIM than HDs. Hsa-let-7b-5p (p=0.0046), hsa-let-7a-5p (p=0.0032), hsa-let-7e-5p (p=0.014), hsa-let-7f-5p (p=0.0123) were down-regulated in IIM.

Conclusions: The prevalence of B lymphocytes markers on circulating EVs surface might indicate their cell origin. Moreover, the increased EVs concentration in IIM than HDs and the dysregulated EVs-microRNA cargo expression suggest that EVs could potentially have a role in IIM, representing promising disease biomarkers.

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SEROLOGICAL AND CELLULAR BIOMARKERS PREDICTIVE OF RESPONSE TO TWO DIFFERENT JAK INHIBITORS (FILGOTINIB, UPADACITINIB) IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background and Aims: Objective of the study was to evaluate whether there are different biomarkers predicting response to two different Jak inhibitors with different selectivity (FIL,UPA) in patients with rheumatoid arthritis

Methods: We enrolled 52 RA patients with 48 females, 5 males. 33 patients were on therapeutic treatment with UPA15 mg / day, 19 with FIL 200 mg / day. Clinimetry with DAS28, CDAI, TJC, SJC, VAS, HAQ, and serological parameters ESR, CRP, APCA, RF, MRP (Myeloid Related Protein),classical pathway, MBL, complement alternative, TNF, IL-6, lymphocyte subpopulations CD3, CD4, CD8, CD19, CD56 , haematological parameters with ratio neutrophils / lymphocytes (N/L), monocytes / lymphocytes (M/L) and platelets / lymphocytes (P/L) were also evaluated at baseline, 12 and 24 weeks.

Results: Significant improvement were obtained for the following clinical and laboratory parameters: DAS28, CDAI, TJC, SJC, HAQ, VAS, ESR, CRP. Significant differences in the two patient groups were: FIL P/L 176.53 vs 153.59 p = 0.049 and IL-6 p = 0.0039 For the UPA MRP group 5.72 vs 2.05 mcg / ml p = 0.029 and IL-6 p = 0.032. Differences in the UPA group were present for lymphocytes CD56 NK 259 vs 216 cells/mcl p = 0.044

Conclusions: our preliminary results show a different behavior of FIL and UPA on some parameters in patients with RA. While FIL demonstrates a reduction in IL-6 levels and P/L ratio, UPA demonstrates a reduction in IL-6 and MRP values. The reduction in the UPA group of CD56 / NK cells demonstrates the different selectivity on the IL-15 pathway.

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FUNCTIONAL DIFFERENCE OF T HELPER CELLS BETWEEN HEALTH AND RHEUMATOID ARTHRITIS PATIENTS: INDUCED PD1/PDL1 MOLECULAR INTERACTION

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Background and Aims: The Programmed cell death protein 1 (PD1) and its ligand (PDL1) are expressed on various subsets of cells including T and B cells and were successfully targeted for cancer immunotherapy. However, the role of these molecules in autoimmune diseases is vaguely known so far. In this study, we aimed to evaluate the regulation efficiency of PD1/PDL1 interaction in healthy and Rheumatoid Arthritis (RA) patients.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from healthy and RA patients. T and B cells were negatively enriched by magnetic-activated cell sorting. Effector/memory helper T (Th) cells were sorted based on CD4 positivity and the differential expression of CD25 and CD127 using FACS aria III. T and B cells were stimulated by anti-CD3/CD28, and CpG/anti-CD40, respectively. The regulatory effects were assessed by monitoring cell proliferation and intracellular cytokines IFN-γ, TNF-α, and IL-21 using Flow cytometry.

Results: Effector/memory Th cells from healthy individuals showed an increased expression of activation markers CD25 and PD1 compared to RA patients upon stimulation. However, Th cell proliferation did not differ between healthy and RA patients either in monocultures or in co-cultures with PDL1+ Breg cells. The intracellular cytokines, IFN-γ, and IL-21 production were higher in RA compared to healthy sample monocultures, while TNF-α production was similar. Interestingly, PDL1+ Bregs downregulated all cytokines by approximately 50 % in both healthy and RA samples.

Conclusions: PD1/PDL1 cross-linking might not affect helper T cell proliferation, however, downregulates IFN-γ and IL-21 production, indicating that the disease progression can be manipulated by inducing PDL1+Breg cells in RA patients.

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NOVEL BIOMARKERS FOR SERONEGATIVE EARLY RHEUMATOID ARTHRITIS

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Background and Aims: With a prevalence of approximately 1%, rheumatoid arthritis (RA) is one of the most frequent autoimmune disorders. Treatment at early stages can significantly slow down disease progression or even prevent irreversible damages. However, an early diagnosis is often challenging. Up to 50% of early RA patients are negative for the standard serological markers rheumatoid factor (RF) or anti-cyclic citrullinated peptide (CCP) antibodies. A more comprehensive analysis of antigenic proteins and their underlying epitopes can provide the necessary information for innovative serological tests with higher sensitivity for early diagnosis of RA.

Methods: To identify novel biomarkers, we applied high-density peptide microarrays displaying large numbers of autoantigens/antigen candidates converted into >100.000 overlapping peptides including all citrullinated and carbamylated variants. Using this highly diverse library, we screened sera from different disease and control cohorts and identified various epitopes with a higher prevalence in previously seronegative early-stage patients.

Results: Bioinformatic analysis combined with machine learning resulted in a peptide biomarker combination, which allowed the diagnosis of early seronegative RA vs. healthy controls with an accuracy of 87% and early seropositive RA vs. healthy controls with an accuracy of 94%, respectively. The validation of the marker set using well-characterized patient samples (n=1027) by Aptiva particle-based multi-analyte technology (Werfen) revealed highly significant peptides for discriminating RA vs. controls. Random forest modeling demonstrated a sensitivity and specificity of 80 and 90%, respectively.

Conclusions: Hence, the novel marker set has the potential to improve the early diagnosis of RA.

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ANTIBODIES AGAINST ADVANCED GLYCATION END-PRODUCTS AND MALONDIALDEHYDE ACETALDEHYDE ADDUCTS IDENTIFY NEW SUBGROUP OF SERONEGATIVE ARTHRITIS PATIENTS WITH DISTINCT CLINICAL PHENOTYPES AND HLA CLASS II ASSOCIATION.

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Background and Aims: In rheumatoid arthritis (RA) around two-thirds of patients are autoantibody-positive for rheumatoid factor, anti-citrullinated protein antibodies (ACPA) and/or anti-carbamylated protein antibodies (anti-CarP). The remaining seronegative subgroup of RA is clinically heterogeneous and thus far, biomarkers predicting the disease course in these patients are lacking. Therefore, we analysed the value of new autoantibodies in RA directed against malondialdehyde acetaldehyde adducts (MAA) and advanced glycation end-products (AGE).

Methods: In sera of 648 RA patients and 538 non-RA arthritis patients from the Leiden Early Arthritis Clinic anti-MAA and anti-AGE IgG antibody levels were measured using ELISA. Associations between genetic risk factors, acute phase reactants, radiological joint damage and anti-PTM positivity were investigated using regression and correlation analyses.

Results: Anti-AGE and anti-MAA were most prevalent in RA (44.6% and 46.1% respectively) but were also present in non-RA arthritis patients (32.9% and 30.3% respectively). Within seronegative RA patients the presence of anti-AGE and anti-MAA antibodies is associated with HLA-DRB1*03 (OR=1.98, p=0.003, and 2.37, p<0.001, respectively). HLA-DRB1*03 associates with anti-AGE in non-RA patients (OR=2.34, p<0.001) independent of anti-MAA. Presence of anti-MAA antibodies associated significantly with markers of inflammation, ESR and CRP, in both groups independent of anti-AGE. Interestingly, the presence of both anti-AGE and anti-MAA antibodies associated with radiologic progression in seronegative RA patients.

Conclusions: Anti-AGE and anti-MAA are present in around 50% of RA patients and 30% of non-RA patients, and although not specific for RA they associate with HLA risk factors and clinical outcomes especially in RF-, ACPA- and anti-CarP-negative patients.

O008 / #463

FREE COMMUNICATIONS 02: RA AND INFLAMMATORY ARTHRITIDES
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REAL-WORLD EXPERIENCE WITH FILGOTINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: EFFICACY AND SAFETY IN A MONOCENTRIC PROSPECTIVE STUDY.

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Background and Aims: The JAK-1 inhibitor filgotinib has been recently licensed for Rheumatoid Arthritis (RA), thus real-world evidence is lacking. Our aim was to assess efficacy and safety of filgotinib in a real-world setting.

Methods: In this prospective monocentric study, we included all patients with RA (ACR/EULAR 2010 criteria) regularly followed-up (every 2-6 months), undergoing therapy with filgotinib (reimbursed in our Region since September 2021). Data were captured in the Regional Biologic Registry between 09/2021 and 10/2022. Disease activity was measured by DAS28-CRP, CDAI, and SDAI; concomitant cDMARDs and glucocorticoid therapy, and all adverse events (AE) experienced during filgotinib treatment were recorded

Results: We enrolled 42 RA patients, 4 (9.5%) b/tsDMARD naïve, 9 (21.4%) monotherapy, mean±SD follow-up 7.5±4.5 months (Table1). Twenty-three patients (54.8%) had ≥6month follow-up: mean±SD DAS28-CRP, CDAI, and SDAI significantly decreased from baseline (Table2). Fifteen (65.2%) and one (4.3%) patients achieved DAS28-CRP remission and LDA at 6 months, respectively. Patients with failure to >2 classes of bDMARDs (18) or those failing a JAK-i (6) prior to filgotinib initiation showed a response similar to that observed in other patients. Overall, 17 patients (40.5%) experienced ≥1 AE, of whom 2 (4.8 %) were SAE (1 ILD progression, 1 death). 5/42 patients discontinued Filgotinib: 2 due to primary inefficacy (4.8%), 3 for AE/SAE (7.1%). Within the first 6 months of treatment, no change in mean glucocorticoid dose was observed.

Table 1.

Total n = 42	
Age, y	61.6 ± 9.9
Caucasian n(%)	38 (90.4)
Sex – female n(%)	38 (90.4)
BMI	23.9 ± 3.1
Charlson	3.33 ± 1.7
Symptoms duration, y	18.2 ± 10.9
Erosions n(%)	29 (69)
Extra-articular disease n(%)	13 (30.95)
Lung n(%)	4 (9.5)
Rheumatoid nodules n(%)	2 (4.8)
Peripheral neuropathy n(%)	1 (2.4)
Eye disease n(%)	4 (9.5)
Cardiovascular n(%)	1 (2.4)
RF+/ACPA+ n(%)	30 (71.4) / 25 (59.5)
Naive to b/tsDMARDs n(%)	4 (9.5)
Multi-failure n(%)	18 (42.9)
Previous JAK-i n(%)	6 (14.3)
Monotherapy n(%)	9 (21.4)
Follow up, m	7.5 ± 4.5
≥6 months n(%)	23 (54.8)

Multifailure: patients who failed >2 classes of bDMARDs prior to Filgotinib therapy

Table 2

Total n=23	Baseline	6 months	p-value
CDAI, mean±SD	24.54±11.7	9.09±6.3	.013
SDAI, mean±SD	34.9±15.8	13.73±10.8	.012
DAS28-CRP, mean±SD	3.51 ± 1.17	2.23 ± 0.9	.001
Multifailure	3.8 ± 1.1	2.2 ± 1.3	.001
Non-multifailure	3.4 ± 1.2	2.6 ± 1	.008

Multifailure: patients who failed >2 classes of bDMARDs prior to Filgotinib therapy

Conclusions: Real-world treatment with filgotinib was associated with clinical improvement and low AE rate. Multi-failure RA patients and those failing a previous JAK-i benefited from Filgotinib therapy.

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FREE COMMUNICATIONS 02: RA AND INFLAMMATORY ARTHRITIDES
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CLINICAL AND HISTOLOGICAL FEATURES OF RESIDUAL PAIN IN REMISSION RHEUMATOID ARTHRITIS PATIENTS.

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Background and Aims: Remission in rheumatoid arthritis (RA) is the optimal goal but,even when it is reached,the “residual pain” can persist.The aims of this study were (i) to characterize the size and perception of residual pain and (ii) to evaluate the synovitis impact on residual pain in remission RA patients.

Methods: One hundred twenty-seven RA patients,of which 68 in clinical and ultrasound remission (REM-RA) and 29 in high disease activity (HDA-RA),were enrolled in the study.Thirty fibromyalgia patients were enrolled as control group (FIBRO).Upon enrolled,demographic,clinical,ultrasound features and PROs (RAID,FACIT,GHQ and VAS-pain questionnaires) were collected.RA patients underwent biopsy of the synovial membrane of the knee in order to assess the degree of synovitis,according to the Krenn Score (KSS).

Results: Considering the RA group,DAS28-CRP inversely correlated with FACIT (R2=-0.506,p<0.0001) while total GHQ score (R2=0.407;p<0.0001) and VAS-pain (R2=0.402,p<0.0001) are directly correlated to DAS28-CRP.Moreover a GHQ higher score was found in 26% of REM-RA patients compared to 52% (p=0.004) and 77% (p<0.0001) of HDA-RA and FIBRO groups respectively while the REM-RA patients had lower VAS-pain values (20) compared to HDA-RA (50;p<0.0333) and FIBRO (70;p<0.0001).Moreover REM-RA patients presented lower RAID scores (3.34) than HDA-RA (5.56;p=0.0003) and FIBRO patients (7.63;p<0.0001).Finally,the presence of subclinical synovitis (KSS≥2) in REM-RA patients (50%) was not associated with a VAS-pain higher score.

Conclusions: Remission status in RA is associated with a better psycho-physical state but,despite that,there is the persistence of a certain degree of residual pain,regardless of the subclinical synovitis degree,suggesting different underlying biological mechanisms in residual pain in RA remission status.

O010 / #431

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ASSOCIATION OF ADIPOKINES AND PRO-INFLAMMATORY CYTOKINES WITH SUBCLINICAL MYOCARDIAL DYSFUNCTION IN PSORIATIC ARTHRITIS

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Background and Aims: Subclinical myocardial dysfunction is frequent in inflammatory rheumatic diseases. We explored the potential association of adipokines and pro-inflammatory cytokines with subclinical myocardial dysfunction of patients with active psoriatic arthritis (PsA).

Methods: Fifty-five PsA patients without cardiovascular risk factors and 25 controls underwent standard and speckle tracking echocardiography with GLS calculated. Standard anthropometric data, disease specific data and DAPSA scores were recorded. Patients with DAPSA score <15 were defined as mild while patients with DAPSA score >15 were defined as moderate to severe. Standard biochemistry, serum adipokines levels (adiponectin, resistin, leptin) and pro-inflammatory cytokines (TNFα, IL-17, BLC and MIG) were analysed.

Results: Median age was 53.0 (46.0 - 61.0), median PsA duration 6.0 (4.0 – 13.0) years and median DAPSA score 25.5 (13.0 – 41.5). Lower GLS, TAPSE and LVEF were found in moderate to severe PsA compared to mild disease and controls. PsA patients with GLS≤20 had higher BMI, DAPSA score and uric acid levels, and lower adiponectin levels. Although PsA patients with GLS≤20 had higher IL-17 levels, it was not statistically significant (P=0.056). When analysis included healthy controls and assessed differences between subjects with GLS>20 and GLS≤20, the difference in IL-17 became statistically significant, 0.17 pg/mL (0.06-0.32) vs. 0.43 pg/mL (0.23-0.65), P=0.017.

Conclusions: Moderate to severe PsA patients without cardiovascular risk have more frequently reduced myocardial function. PsA patients with impaired myocardial function might have lower adiponectin and higher IL-17 levels compared to PsA patients with normal myocardial function and healthy controls.

O011 / #474

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DIFFICULT-TO-TREAT PSORIATIC ARTHRITIS: ANALYSIS OF A SINGLE-CENTER COHORT FROM NORTHERN ITALY

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Background and Aims: Biologic disease modifying anti-rheumatic drugs (bDMARDs) have dramatically improved the outcome of patients affected by chronic inflammatory arthritis. However, a satisfactory disease control is not achieved in a proportion of patients. While a "difficult-to-treat" (D2T) definition has been validated in rheumatoid arthritis (RA), it was only recently suggested for psoriatic arthritis (PsA) (Perrotta FM et al, Rheumatol Ther 2021). Based on this definition, we aimed to assess prevalence and characteristics of D2T-PsA in our cohort.

Methods: We conducted a single-center, cross-sectional study: consecutive, adult PsA patients receiving bDMARDs at a tertiary care, dedicated outpatient clinic were enrolled. Demographic, clinical, and clinimetric data, and the Health Assessment Questionnaire (HAQ) were gathered. Comparison between D2T and non-D2T patients was performed with univariate analysis.

Results: Among 269 PsA patients, only 8 (3%) fulfilled D2T definition. In bivariate analysis, D2T patients presented higher rate of osteoarthritis (62.5% vs 24.9%; *p=0.03*), fibromyalgia (62.5% vs 14.94%; *p<0.004*), and therapy with steroids (50% vs 12.1%; *p=0.008*). Furthermore, D2T patients presented significantly higher patient global assessment (PGA 0-10) (7.5 vs 2.00; *p<0.001*) and VAS pain 0-10 (8.00 vs 2.00; *p<0.001*). Among non-D2T patients, 24 were in moderate disease activity (9.19%). Due to the unbalance between the groups numerosity, multivariate analysis was not feasible.

Conclusions: Only few patients satisfied the PsA-D2T definition in our cohort; application of a RA-like D2T definition to a heterogeneous disease as PsA should be discussed more broadly in the future.

O012 / #417

FREE COMMUNICATIONS 02: RA AND INFLAMMATORY ARTHRITIDES
16-03-2023 3:00 PM - 4:00 PM

STEROID-SPARING POTENTIAL OF JANUS KINASES INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A COHORT STUDY.

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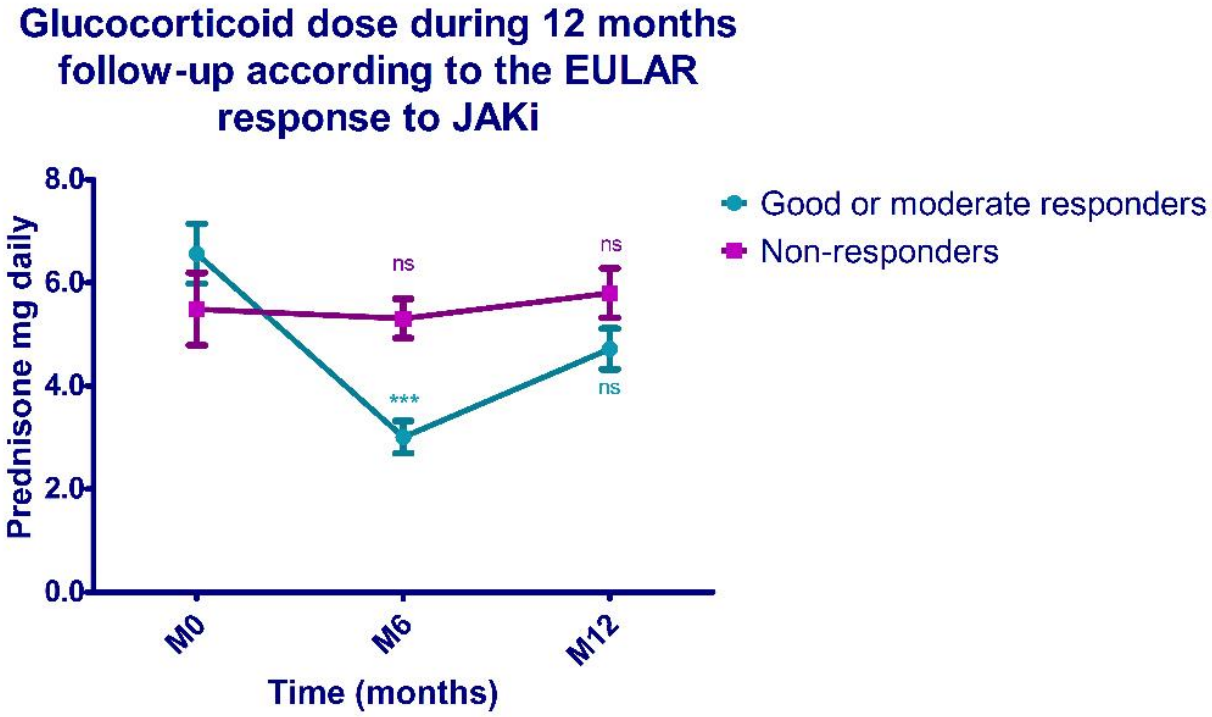
Background and Aims: Whether glucocorticoids (GC) may affect the efficacy and safety of Janus kinases inhibitors (JAKi) is unknown.

Methods: We evaluated the use of GC in a cohort of patients with rheumatoid arthritis (RA) who started treatment with JAKi between 03/2018 and 10/2021. The primary outcome was the EULAR response (moderate/good) after 6 months; secondary outcomes were EULAR response at 12 months and drug discontinuation. Patients who discontinued JAKi were imputed as non-responders for efficacy outcomes. We expressed the associations between outcomes and covariates as odds ratio (OR) and 95% confidence interval (CI).

Results: We included 149 patients (mean age 59 years, RA duration 16 years; females 89%) treated with JAKi (tofacitinib 34%, baricitinib 43%, upadacitinib 16%, filgotinib 7%). 66% of patients took GC (mean 4.5 mg/d), decreasing to 48% after 6 months. GC dose was transiently reduced in responders (56%) at 6 months (-1.8 mg/d, $p<0.001$; Figure), but it was neither associated with response nor drug retention at 12 months; 6% of patients restarted GC between 6 and 12 months. In multiple logistic regression, GC use had no association with the response at 6 months, which was significantly related to the male sex (OR 2.9;1.6-5.3), no extra-articular disease (OR 2.6;1.7-4.0) and no rheumatoid factor (OR 1.7;1.2-2.4). 20% of patients discontinued JAKi within 6 months (59% adverse events, 41% inefficacy), and 26% within 12 months (31% adverse events, 69% inefficacy), regardless of GC

use.



ANCOVA for repeated-measures. Bullet points and squares represent the estimated marginal means for the interaction between EULAR response and time, and error bars the standard error of the mean. Star-shaped marks represent p-values for pairwise comparisons between M0 and M6 or M0 and M12. *** = p<0.001; ns, non-significant

Conclusions: JAKi allowed a slight decrease in GC use. The efficacy and safety of JAKi were independent of GC use.

O013 / #408

FREE COMMUNICATIONS 03: PEARLS IN AUTOIMMUNITY
17-03-2023 11:50 AM - 12:50 PM

BIOMARKERS OF LEAKY GUT IN PATIENTS WITH HASHIMOTO'S THYROIDITIS ISOLATED OR FRAMED IN POLYAUTOIMMUNITY

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Background and Aims: Objective An increased permeability of Intestinal barrier (IB), known as "leaky gut", has been demonstrated in patients with intestinal disorders and in patients with autoimmune diseases involving organs far from the intestine, as in patients with Hashimoto's thyroiditis (HT). The indirect measure of IB permeability in patients with HT, even in a polyautoimmunity context, represents the aim of our study.

Methods: Methods The study group encompassed 93 patients bearing HT (median age=48 years); 33 of them associated another non-endocrine autoimmune disorder (HT+POLY) [13 gastric atrophy (HT+GA), 13 vitiligo (HT+V) and 7 celiac disease (HT+CD)]. The evaluation of gut permeability was performed by dosing serum zonulin and LPS. The serum of patients was stored at -20°until the samples were analyzed by ELISA kits.

Results: Result Zonulin and LPS were higher in patients HT+POLY than in patients with isolated HT ($p<0.0001$ and 0.0004, respectively). The highest concentrations of zonulin as compared to HT may be observed in HT+CD ($p<0.0001$), followed by HT+GA ($p<0.01$). On the contrary, the highest concentration of LPS as compared to HT may be observed in HT+V ($p<0.01$), followed by HT+GA ($p<0.05$). In the whole sample and in patients with isolated HT, zonulin and LPS concentrations significantly correlated ($p<0.0001$;$r=0.4431$ and $r=0.4409$, respectively), a correlation lost in patients with HT+POLY.

Conclusions: Conclusions Increased levels of zonulin and LPS in patients with polyautoimmunity, as compared with HT patients, suggest an increased permeability and a more severe systemic inflammatory state even when the additional disease does not involve directly the gastrointestinal tract.

O014 / #457

FREE COMMUNICATIONS 03: PEARLS IN AUTOIMMUNITY
17-03-2023 11:50 AM - 12:50 PM

A NOVEL LIPIDIC PEPTIDE THAT MODULATES IMMUNE RESPONSES POTENTIALLY RELEVANT TO SUPPRESSION OF AUTOIMMUNITY

Michael Agrez[1], Justyna Rzepecka[2], Darryl Turner[2], Gavin Knox[2], Christopher Chandler[3], Christopher Howard[4], Nicholas Fletcher[5], Kristofer Thurecht[5], Stephen Parker[6], Hayley Gooding[2], Laura Gallagher[2]
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Background and Aims: Immunosuppressive CD4+ T regulatory (Treg) cells prevent autoimmunity and functional T cell-dendritic cell (DC) interactions contribute to reciprocal stimulation leading to DC maturation that results in T cell production of interleukin-2 (IL-2) required to sustain Tregs. However, autoreactive T cells are activated by agonistic cytokines such as interferon-gamma (IFN-γ) and interleukin-12p40 (IL-12p40) that positively regulate one another. Importantly, IL-12p40 inhibits IL-12p70 activity including Treg cell function and activation of IL-12p40 is regulated by calcium-dependent signalling in DCs that involves the Src family kinase member, c-Src. We have previously reported that a 10 mer peptide, RSKAKNPLYR, inhibits c-Src activity and the aim of the present study was to examine its effect on T cell-DC interactions when conjugated to a branched lipid unit comprising dodecanoic acid residues to facilitate stability and cell entry of the 10 mer component.

Methods: The conjugated peptide, designated IK14004, was made using solid phase peptide synthesis with Fmoc protected building blocks and product structures were confirmed by mass spectroscopy and amino acid analysis. Cell-based studies (enzyme-linked immunoassays and flow cytometry) were performed on immune cells isolated from healthy volunteers and kinase profiling was performed using non-cell-based assays.

Results: IK14004 enhances production of IL-2/IL-12p70 by T cells and expands the Treg cell population while destabilising DCs and inhibiting production of IL-12p40 and IFN-γ consistent with inhibition of c-Src activity and the calcium-dependent signalling pathway.

Conclusions: This small molecule inhibitor offers an opportunity to gain further insight into the complexity of T cell-DC interactions relevant to autoimmunity.

O015 / #273

FREE COMMUNICATIONS 03: PEARLS IN AUTOIMMUNITY
17-03-2023 11:50 AM - 12:50 PM

B-CELL SUBSETS IN PERIPHERAL BLOOD ACROSS DISEASE PHASES OF PSORIATIC DISEASE AND THEIR CORRELATION WITH SYNOVIAL TISSUE FEATURES

Dario Bruno[1], Barbara Tolusso[2], Clara Di Mario[3], Simone Perniola[1], Domenico Somma[4], Luca Petricca[5], Andrea Chiricozzi[6], Maria Rita Gigante[5], Alessandra D'Amore[6], Mariola Kurowska-Stolarska[4], Elisa Gremese[2], Stefano Alivernini[7]
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Background and Aims: To examine the frequencies of peripheral blood(PB) B-cell subsets across different PsA disease phases, evaluating their correlation with synovial tissue (ST) inflammation.

Methods: 150 patients fulfilling the CASPAR criteria(81 naive to therapy,45 c- and/or b-DMARDs resistant and 24 in clinical and US sustained remission, respectively) underwent US-guided ST biopsy and PB withdrawal.22 patients with psoriasis (PsO) and arthralgia were included as comparison group.All ST FFPE specimens were stained with H&E and classified by a pathologist using a H&E based semiquantitative score (KSS).Frequencies of PB B-cell subpopulations were determined by FACS using the CD27/IgD classification as follows: naïve B-cells,IgM memory,switched memory, late memory,plasmablasts and plasmacells.

Results: KSS was significantly different across disease phases.Specifically,KSS was contingent on disease phase being lower in remission compared to naive ($p=0.02$) and resistant PsA ($p<0.001$),while there was no difference between remission PsA and at risk PsO group.ST of c- and/or b-DMARDs resistant PsA was enriched of plasmacells than remission ($p=0.03$).Considering B-cell subpopulations,PB of c- and/or b-DMARDs resistant PsA was enriched of plasmablasts and plasmacells compared to PsO at risk ($p=0.01$ and $p=0.001$,respectively).Conversely,c- and/or b-DMARDs resistant PsA showed,at PB level, lower rates of switched memory and naïve B-cells compared to PsO at risk ($p= 0.02$ and $p=0.039$,respectively).Finally, stratifying PsA based on KSS category, remission PsA with persistent high grade synovitis($KSS \geq 5$) showed lower rates of PB plasmablasts than remission PsA with low grade residual synovial inflammation($p=0.045$).

Conclusions: Disease state across PsA course significantly impacts PB B-cell subsets distribution mirroring ST residual inflammation at the time of sustained disease remission.

O016 / #486

FREE COMMUNICATIONS 03: PEARLS IN AUTOIMMUNITY
17-03-2023 11:50 AM - 12:50 PM

CALPROTECTIN, A ROBUST AND SENSITIVE MARKER OF INFLAMMATION IN RA PATIENTS

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Background and Aims: Calprotectin (S100A8/S100A9, MRP8/MRP14) in plasma has been shown to be more sensitive than Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein (CRP) in reflecting inflammatory activity in patients with rheumatoid arthritis (RA). The aim of this study was to explore the robustness of the laboratory examination and the correlation with clinical examinations of inflammation.

Methods: Plasma samples from early (n=220, mean disease duration 7.2 months) and established RA (n=177, mean disease duration 10.0 years) patients were analyzed for calprotectin levels at baseline and after 1, 2, 3, 6 and 12 months by use of either Enzyme-linked immunosorbent assay (ELISA, Calpro AS) or fluoroenzyme immunoassay (FEIA, measured on EliA platform). Clinical measures as number of swollen joints and examiner's global score (EGA) by use of visual analogue scale (VAS) (score 0-100) were included as well as Ultrasound performed by an experienced sonographer.

Results: The two Calprotectin methods showed high correlation (Spearman correlation 0.91 and 0.96 for early respective established RA). When comparing number of patients in remission having normal calprotectin levels compared to normal CRP levels, there was a higher percentage of agreement for Calprotectin compared to CRP, 93-96% vs 71-85% depending on timepoint and remission criteria.

Conclusions: Calprotectin has been shown to be a better marker of inflammation than the commonly used inflammatory markers and may therefore be widely included in clinical laboratories. The present study supports the robustness of the analyses, showing similar calprotectin measures across different analytical methods and better correlation with remission than CRP in RA patients.

O017 / #462

FREE COMMUNICATIONS 03: PEARLS IN AUTOIMMUNITY
17-03-2023 11:50 AM - 12:50 PM

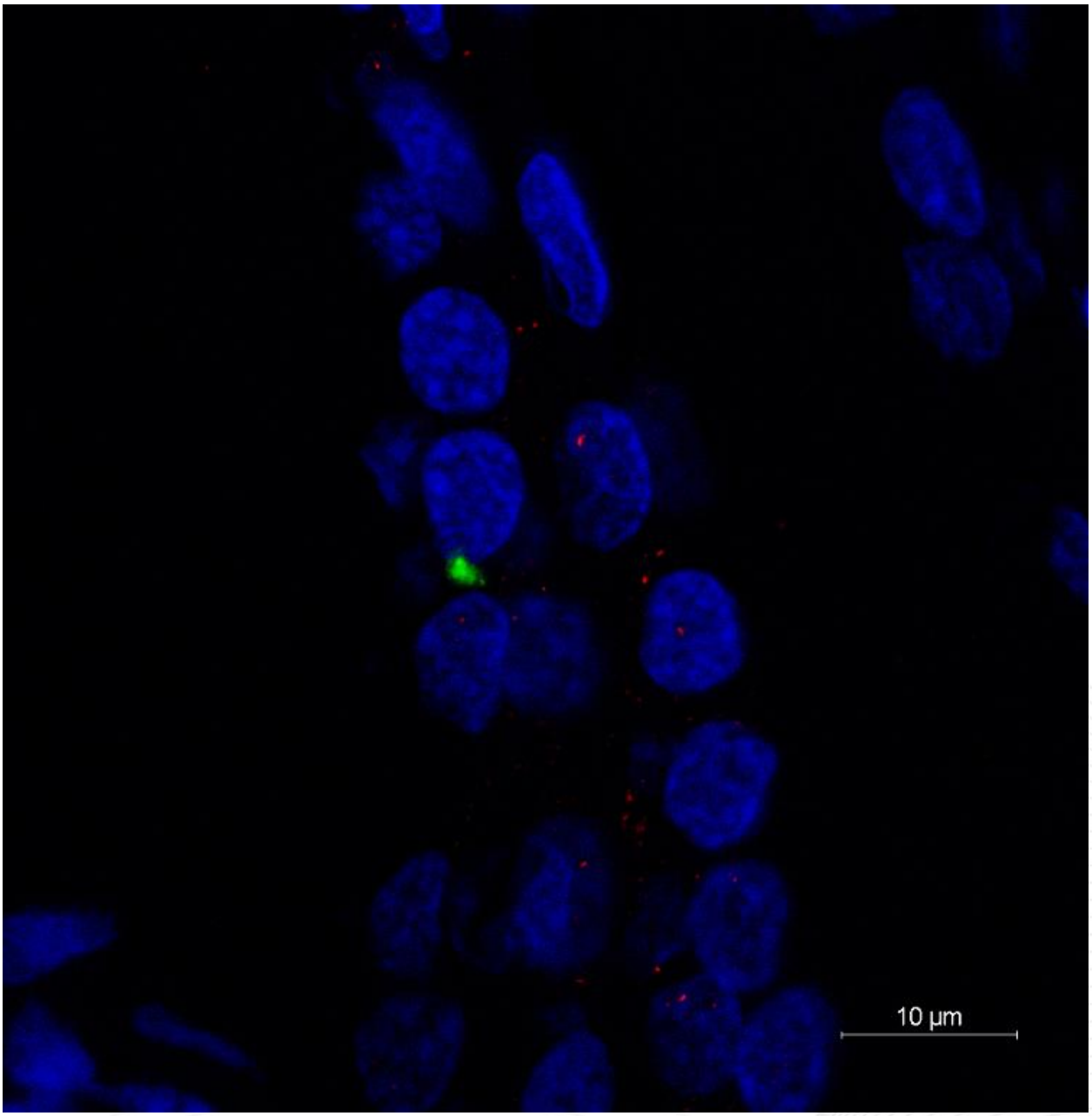
HHV-6 ENCODED GPCRS U12 AND U51 AND THYROID AUTOIMMUNITY

Liba Sokolovska[1], Maksims Citjakovs[1], Modra Murovska[2], Alina Sultanova[1]
[1]Riga Stradins Unviersity, Institute Of Microbiology And Virology, Riga, Latvia, [2]Rīga Stradiņš University, Institute Of Microbiology And Virology, Riga, Latvia

Background and Aims: Studies have linked HHV-6 with thyroid autoimmunity, yet the exact mechanisms of HHV-6 involvement remain unclear. We propose that two poorly studied HHV-6 proteins – U12 and U51, may contribute to autoimmunity. They are homologous to chemokine receptors (G-protein coupled receptors), can be expressed on cell surfaces, and can influence viral replication. By conducting molecular and immunological investigations we aim to elucidate the potential role of U12/U51 in thyroid autoimmunity.

Methods: Thyroid tissue and plasma samples from 54 AIT patients (harboring HHV-6 in the thyroid) were investigated. RNA was isolated from thyroid tissues, used for cDNA synthesis, and nPCR to detect U12, U51 mRNA. FFPE thyroid tissues were microscoped to visualize U12/U51. U12 and U51 antibodies were detected with the Luminex system

Results: 44% of thyroid tissues harbored U12/U51 mRNA. Thyroid tissues with mRNA harbored significantly higher viral loads (1998 vs 238 viral copies/10^6 cells, $p<0,0001$). Nearly all AIT patients were shown to harbor U12/U51 antibodies, regardless of mRNA presence. Microscopy revealed the colocalization of HHV-6 and U12/U51 in the thyroid.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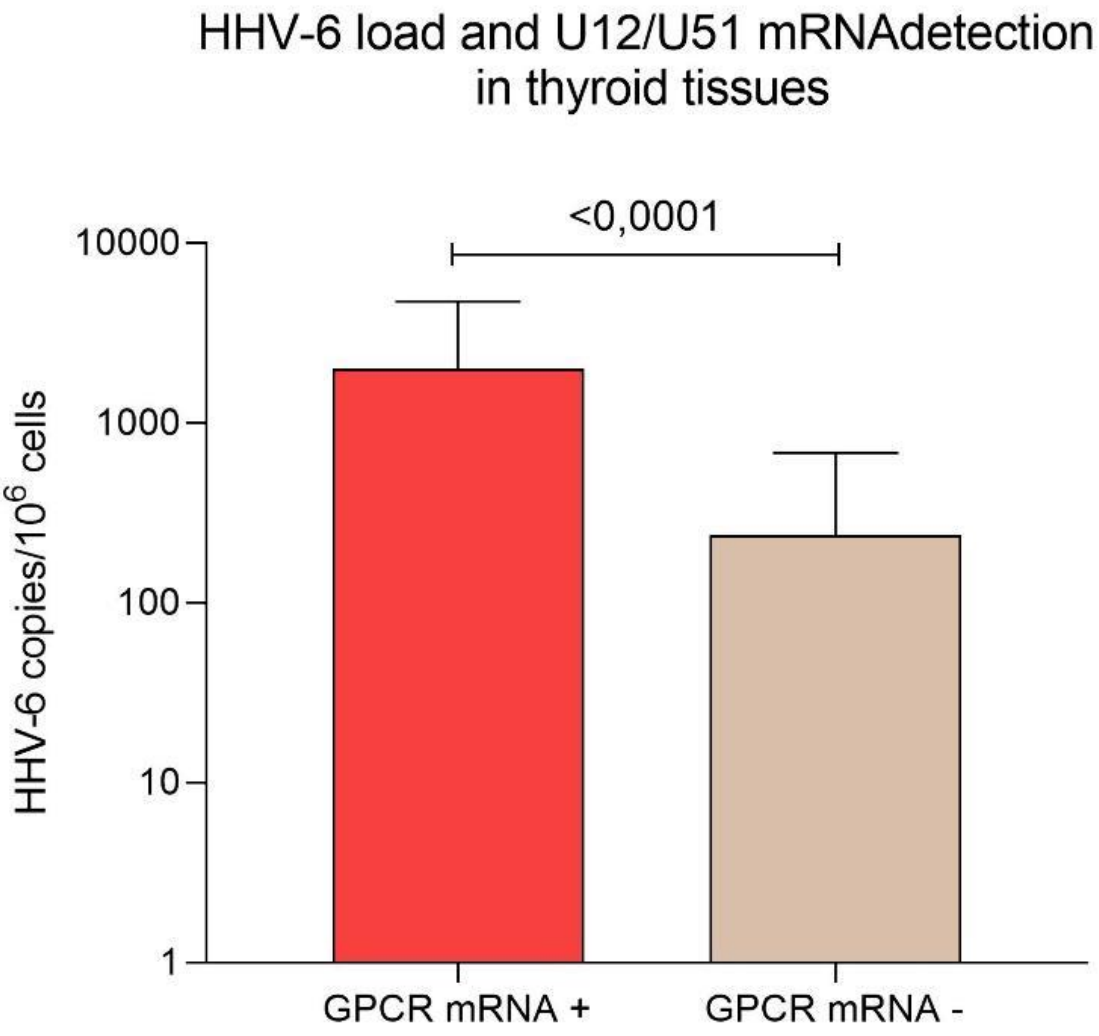

Conclusions: The combination of the presence of U12/U51 mRNA and viral protein-specific antibodies with the visualization of both HHV-6 and its GPCRs in the thyroid suggests that both could be involved in autoimmunity development/exacerbation. HHV-6 and U12/U51 could enhance thyroid cell destruction, autoantigen release, and inflammation through viral replication enhancement or through direct antibody binding and subsequent immune response against U12/U51 **Acknowledgments**. EU Horizon 2020 project “Reducing networking gaps between RSU and internationally leading counterparts in viral infection-induced autoimmunity research (VirA)” (No952376)

O018 / #120

FREE COMMUNICATIONS 03: PEARLS IN AUTOIMMUNITY
17-03-2023 11:50 AM - 12:50 PM

BLOCKING OF THE LEUKOCYTE TRANSMIGRATION AS A THERAPEUTIC TARGET FOR THE DEVELOPMENT OF NOVEL ANTI AUTOIMMUNE DISEASES DRUG CANDIDATES

Arie Lev Gruzman
Bar-Ilan University, Chemistry, Ramat-Gan, Israel

Background and Aims: Leukocyte transendothelial migration is one of the most important steps in launching an inflammatory immune response. However, overstimulated of disregulated mode of the leukocyte transmigration from blood to the tissus can lead to devastating autoimmune diseases. Based on previously reported trioxotetrahydropyrimidin integrin inhibitors and in silico calculations, we designed several molecules with a modified barbituric acid scaffold and tested them in vitro.

Methods: In silico calculations and modeling, organic synthesis, analytical chemistry (NMR and Mass spectroscopy), leukocyte transmigration flow assay, adhesion molecules activity assay kits, six mouse inflammatory/autoimmune diseases models (Nonalcoholic fat liver, IBD, arthritis, acute respiratory syndrome, brain form of lupus and multiple sclerosis), toxicity studies, structure-activity relationship study, blood biochemistry, histochemistry and target validation study.

Results: One of the molecules: **GT-73**, completely blocked leukocyte transendothelial migration, without any toxic effects on immune or endothelial cells (IC_{50}=2.4 µM). In vivo, **GT-73** exhibited significant therapeutic effects in all tested in vivo models. A detailed acute and chronic toxicity profile of the lead compound in vivo did not reveal any toxic effects. **GT-73** was active in pharmacological relevant doses (10-30 mg/kg) and in several routes of administration. Most important that **GT-73** was active orally. The mechanism of **GT-73** action was validated (reversible covalent inhibition of active dimer form of PECAM-1). The critical for the activity functional groups were also determined: tert-butyl and methyl ester.

Conclusions: GT-73 might therefore provide a unique starting point for designing a novel class of leukocyte transmigration blocking agents with broad therapeutic applications in inflammatory and auto-immune pathologies.

O019 / #243

FREE COMMUNICATIONS 04: APS AND OTHER CTDS
17-03-2023 11:50 AM - 12:50 PM

PREDICTORS OF DISEASE ACTIVITY PERSISTENCE AND DAMAGE IN A MONOCENTRIC SYSTEMIC SCLEROSIS COHORT

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Background and Aims: In systemic sclerosis, the concepts of “disease activity” and “damage” have recently been defined. We aimed to identify predictors of persistence of disease activity and damage accrual in a large SSc cohort.

Methods: 173 SSc patients (ACR/EULAR 2013 criteria) from Padua Hospital were enrolled. Clinical/serological findings, disease activity (EUSTAR-AI), and damage (Medsger Severity Scale and SCTC Damage Index) indices were evaluated at baseline and at each follow-up visit. We defined disease activity persistence as EUSTAR AI ≥ 2.5 for more than 50% of follow-up and moderate-severe damage as SCTC-DI > 6.

Results: 173 SSc patients (88% females) were followed up for a median time of 3,5 years; 23 (13.2%) showed persistent disease activity over time. Diffuse cutaneous subset, cardiac involvement, higher ESR values, lower TLC values, and higher values of damage scores at baseline were associated with persistent disease activity; ACA-positive patients were more frequently persistently inactive. ESR values (OR 1.04, 95%CI 1.01-1.07) and MSS score (OR 1.75, CI 1.29-2.37) were independent predictors of activity persistence. Patients with moderate-severe damage at the end of follow-up (16, 9%) had more frequently telangiectasia, ILD and persistent activity over time, as well as lower DLCO and TLC values at baseline; telangiectasia (OR 4.7, CI 1.18-18.5) and TLC values (OR 0.95, CI 0.92-0.98) were the only independent predictors of moderate-severe damage at the end of follow-up.

Conclusions: Identifying predictors of disease activity persistence and damage accrual at baseline may help identify at-risk patients who require prompter treatment and give additional prognostic information.

O020 / #395

FREE COMMUNICATIONS 04: APS AND OTHER CTDS
17-03-2023 11:50 AM - 12:50 PM

DIFFERENTIAL EXPRESSION OF TYPE I INTERFERON SIGNATURE AMONG ANTIPHOSPHOLIPID ANTIBODIES POSITIVE PATIENTS

Irene Cecchi[1], Massimo Radin[1], Alice Barinotti[1], Silvia G Foddai[1], Elena Rubini[1], Ana Suárez[2], Dario Roccatello[1], Savino Sciascia[1], Javier Rodríguez-Carrio[2]
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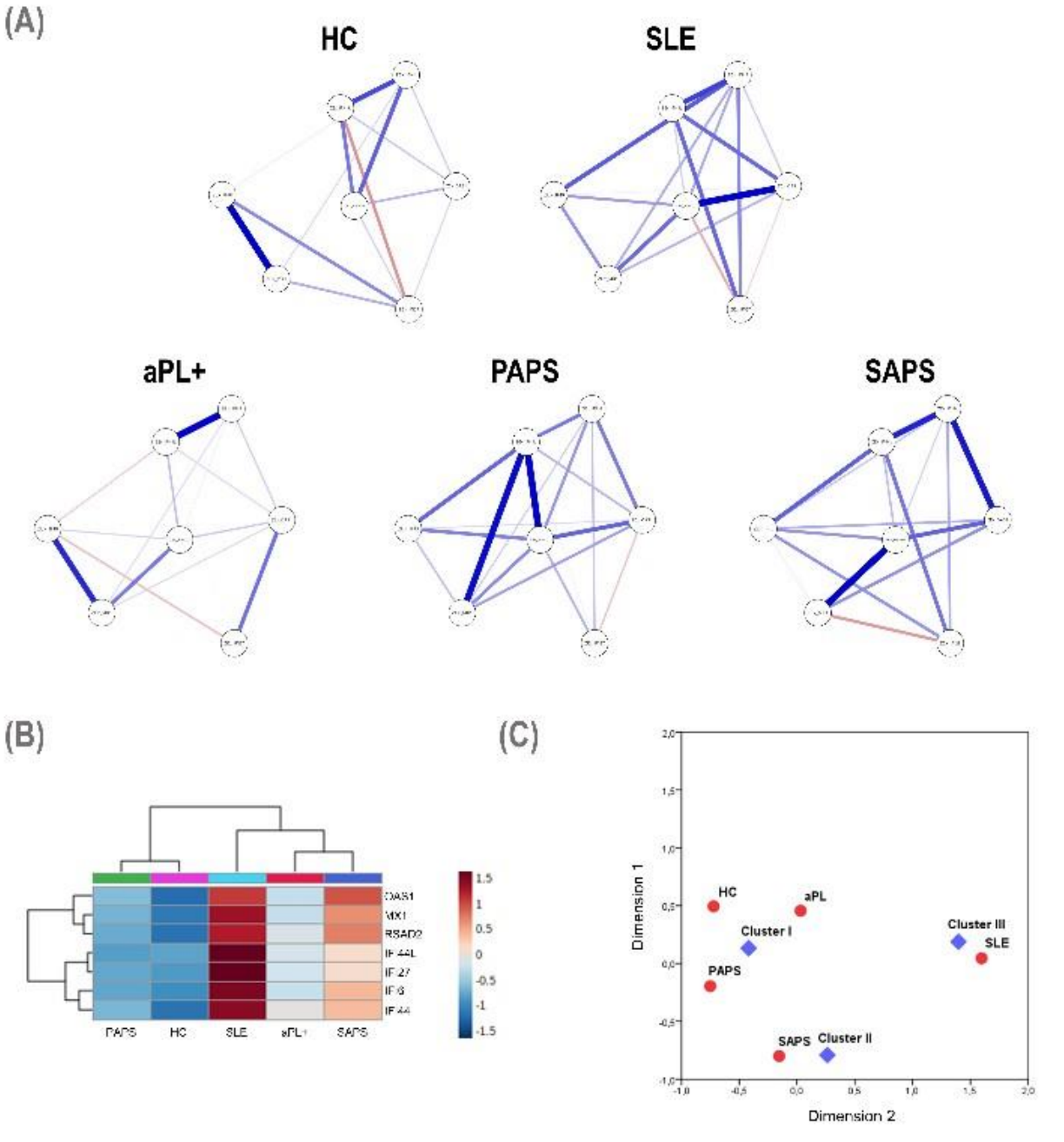
Background and Aims: The role of Interferon (IFN) activation in antiphospholipid antibodies (aPL) positive patients is unclear. This study aimed to evaluate the expression of IFN stimulated genes (ISG) among different aPL positive subjects.

Methods: 112 patients were enrolled (31 PAPS, 25 SAPS, 27 SLE patients without aPL, 29 aPL carriers, and 19 HCs). Gene expression was evaluated for IFI6, IFI44, IFI44L, MX1,IFI27, OAS1, RSAD2. Gene expression was averaged into a IFN score. Differences were measured by Kruskal-Wallis tests and associations among genes were studied by cluster and correspondence analyses. Correlations among genes were plotted by network analyses.

Results: An overall activation of ISG was noted across APS subsets, with differences among genes. Some ISG were upregulated in the aPL+ group versus HC, other ISG were only increased in SLE (IFI6), between SLE and SAPS (MX1), between PAPS and SAPS (IFI27, OAS1). The IFN score revealed differences in the IFN pathway activation, being elevated in aPL carriers/PAPS versus HCs (both $p<0.050$) and increasing in SAPS ($p<0.010$) and SLE ($p<0.001$). Network analyses revealed qualitative differences: weaker structures in HCs and aPL carriers, compared to stronger and higher-degree networks in SAPS and SLE groups; the influence of each node was different across groups. Unsupervised cluster analysis identified 3 clusters based on ISG patterns, correlating with clinical status. IFN score and ISG correlate with thrombotic recurrences (all

rho>0.400).



Conclusions: An overall IFN pathway activation has been observed in aPL positive patients and across all APS subsets. Qualitative and quantitative differences across the APS spectrum can be identified.

O021 / #275

FREE COMMUNICATIONS 04: APS AND OTHER CTDS
17-03-2023 11:50 AM - 12:50 PM

INCREASED CONCENTRATIONS OF ENDOTHELIAL-DERIVED AND ICAM-1-POSITIVE SMALL EXTRACELLULAR VESICLES ARE FOUND IN THE PLASMA OF PATIENTS WITH THROMBOTIC ANTIPHOSPHOLIPID SYNDROME.

Ula Štok[1,2], Aleš Ambrožič[1], Saša Čučnik[1,2], Polona Žigon[1,3]
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Background and Aims: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by thrombosis and/or obstetric complications in the presence of antiphospholipid antibodies (aPL). The binding of aPL to the cell surface triggers its activation, which also leads to the release of extracellular vesicles. Research on extracellular vesicles in APS has mainly focused on medium or large vesicles, whereas research on small extracellular vesicles (sEVs) is limited. The aim of our study was to investigate different subtypes of sEVs in plasma from patients with thrombotic APS and healthy controls.

Methods: The size and plasma concentration of sEVs were determined by immunophenotypic analysis of sEVs on an ExoView® platform.

Results: We were able to detect the presence of sEVs as the measured particles were positive for the transmembrane protein tetraspanins and were smaller than 200 nm in size. The size of sEVs was comparable in patients and healthy controls, whereas we observed a trend toward an increase in the total number of sEVs in patients with thrombotic APS. The frequency of endothelial cell-derived sEVs (CD144+) was increased in APS, whereas no differences were observed in the frequency of monocyte-derived sEVs (CD14+) in patients with thrombotic APS compared with healthy controls. In the APS group, we also detected an increased number of sEVs positive for the adhesion molecule ICAM-1, a known marker of endothelial cell and monocyte activation.

Conclusions: The results of increased levels of endothelial (CD144+) and ICAM-1-positive sEVs suggest cell activation in APS, even in the absence of an acute thrombotic event.

O022 / #287

FREE COMMUNICATIONS 04: APS AND OTHER CTDS
17-03-2023 11:50 AM - 12:50 PM

PROGRESSIVE ILD IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A MULTICENTRE STUDY

Elisabetta Zanatta[1], Elisabetta Cocconcelli[2], Chiara Giraudo[3], Giacomo Emmi[4], Luca Quartuccio[5], Yannick Allanore[6], Paolo Spagnolo[2], Elisabetta Balestro[2], Andrea Doria[1], Luca Iaccarino[1]
[1]Rheumatology Unit. University of Padova, Department Of Medicine, Dimed, Padova, Italy, [2]Respiratory Disease Unit, Department Of Cardiac, Thoracic, Vascular Sciences And Public Health, Padova, Italy, [3]Unit of Advanced Clinical and Translational Imaging, University of Padova, Department Of Medicine (dimed), Padova, Italy, [4]University of Firenze, Department Of Experimental And Clinical Medicine, Firenze, Italy, [5]University of Udine, Rheumatology Clinic, Department Of Medicine, Udine, Italy, [6]Hôpital Cochin, APHP, Université Paris Descartes, Service De Rhumatologie, Paris, France

Background and Aims: Interstitial lung disease (ILD) is a frequent organ involvement in idiopathic inflammatory myopathies (IIMs). Some patients with ILD may develop a progressive fibrosing phenotype despite treatment. The occurence of progressive IIMs-ILD and the associated phenotype remain to be determined. We aimed to investigate the prevalence, clinical/serological, and functional/radiological characteristics of patients with progressive IIMs-ILD.

Methods: We collected clinical, serological and functional/radiological data of 125 IIMs-ILD patients at diagnosis and follow-up. The prevalent radiological pattern at diagnostic high-resolution CT scans (ground-glass opacities, GGO; fibrotic changes, FC; consolidation, C) was evaluated by expert radiologists. Progression was defined in presence of at least two of these characteristics at one-year follow-up: decline in forced vital capacity (FVC)% pred.≥ 5%, worsening of HRCT or worsening of clinical symptoms.

Results: In 78/125 (62%, 55 females) IIMs-ILD patients, functional and radiological data were available after one-year follow-up. The predominant HRCT pattern was GGO (n=39; 50%), followed by FC (n=22, 28%) and C (n=17, 22%). At one-year follow-up, 14 (18%) patients had developed progressive ILD, whereas 65 (82%) were stable. Demographics, functional data and radiological pattern at ILD diagnosis did not differ between progressors vs. stable IIMs-ILD patients, as well as treatment with glucocorticoids and immunosuppressants. Anti-MDA5 autoantibodies [OR 6.10, 95%CI(1.30–28.4)], heliotropic rash [8.00(1.55–41.23)], and xerostomia [8.19 (1.84 – 36.36)] were progression-associated factors at univariate but not at multivariate analysis.

Conclusions: Progressive ILD occurred in one fifth of our IIMs-ILD cohort. Our results suggest that all patients with IIMs-ILD should be monitored to detect progression, independently of IIMs- and ILD-specific features.

O023 / #371

FREE COMMUNICATIONS 04: APS AND OTHER CTDS
17-03-2023 11:50 AM - 12:50 PM

PAEDIATRIC ANTIPHOSPHOLIPID SYNDROME: THE ESTIMATED PREVALENCE IN PIEDMONT AND AOSTA VALLEY AND AN UPDATED SYSTEMATIC REVIEW OF THE LITERATURE

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Background and Aims: Antiphospholipid syndrome (APS) is a rare thromboinflammatory disease characterized by the persistence of circulating antiphospholipid antibodies (aPL) in association with thrombotic events. In order to better characterize the paediatric involvement of the disease, we reviewed the experience in the Northwest Italy and we performed a systematic review to update the evidence of the last ten years.

Methods: We conducted a registry-study collecting data from the Piedmont and Aosta Valley Rare Disease Registry including paediatric patients diagnosed with APS in the last ten years. In concomitance, a detailed literature search was performed *a priori* to identify articles describing clinical and laboratory characteristics of paediatric APS in the last ten years.

Results: A total of 17 patients (mean age 15.1 ±2.8, 76% female) developed APS in the paediatric age in the Northwest of Italy. In 29% of cases SLE was a concomitant diagnosis. Deep vein thrombosis was the most frequent manifestation (28%) followed by Catastrophic APS (CAPS) (6%). The estimated prevalence of pediatric APS in Piedmont and Aosta Valley Region is 2.5/100.000 people whereas the estimated annual incidence is 0.2/100.000 inhabitants. The systematic review included six articles with a total of 386 pediatric patients (65% females, 50% with SLE as concomitant diagnosis). Rate of venous and arterial thrombosis were 57% and 35% respectively. “Extra-criteria manifestations” included mostly hematological and neurological involvement. Almost one quarter of patients (19%) reported recurrent events and 13% manifested a CAPS.

Conclusions: Clinical manifestations of paediatric APS seem to be more severe and with a high prevalence of non-criteria manifestations.

O024 / #499

FREE COMMUNICATIONS 04: APS AND OTHER CTDS
17-03-2023 11:50 AM - 12:50 PM

EFFICACY OF RITUXIMAB IN INFLAMMATORY MYOPATHIES. EXPERIENCE ON 27 PATIENTS FROM A PROSPECTIVE MONOCENTRIC COHORT

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Background and Aims: The aim of the present study is to demonstrate the efficacy of Rituximab (RTX) for the treatment of inflammatory myopathies. We also considered the effectiveness of a low-dose RTX as a remission-maintenance therapy.

Methods: From a monocentric cohort of patients with inflammatory myopathies, we achieved all patients who have been treated with RTX (2 infusions of 1 gram, week 0-2). We considered low-dose RTX as a single dose of 1g every 6 months. The response to RTX was considered based on physician judgement (complete, partial, no-response).

Results: Twenty-seven patients were included. Most patients (74%) were treated with RTX for muscular involvement, 18.5% for arthritis, 16% for ILD and 11% for skin manifestations. Anti-Jo1 autoantibodies were found in 11 patients (40%), anti-SSA in 7 (26%), anti-SRP in 5 (18.5%), anti-PM/Scl 75 in 2 (7%), anti-Mi2 in 1 (4%), PL7 in 1 (4%), anti-TIF1-γ in 1 (4%), anti Ku in 1 (4%) and anti Sp100 in 1 (4%). Concomitant therapies included oral glucocorticoid (n=24), methotrexate (n=15), mycophenolate mofetil (n=10), IVIG therapy (n=3), azathioprine (n=2), hydroxychloroquine (n=2), leflunomide (n=1) and tacrolimus (n=1). We observed complete response to RTX in 70% of patients, partial response in 18.5%, no-response in 7%. Five patients were treated with a low dose maintenance therapy after having achieved remission with standard dose. All of them maintained a complete response to RTX.

Conclusions: In our cohort, RTX was effective in 88.5% patients and the low-dose was efficacious as a maintenance therapy in all cases.

O025 / #261

FREE COMMUNICATIONS 05: OPEN ISSUES AND NOVELTIES IN ARD
17-03-2023 4:45 PM - 5:45 PM

EFFICACY OF ULTRA-LOW DOSE RITUXIMAB FOR REMISSION MAINTENANCE IN ANCA-ASSOCIATED VASCULITIS

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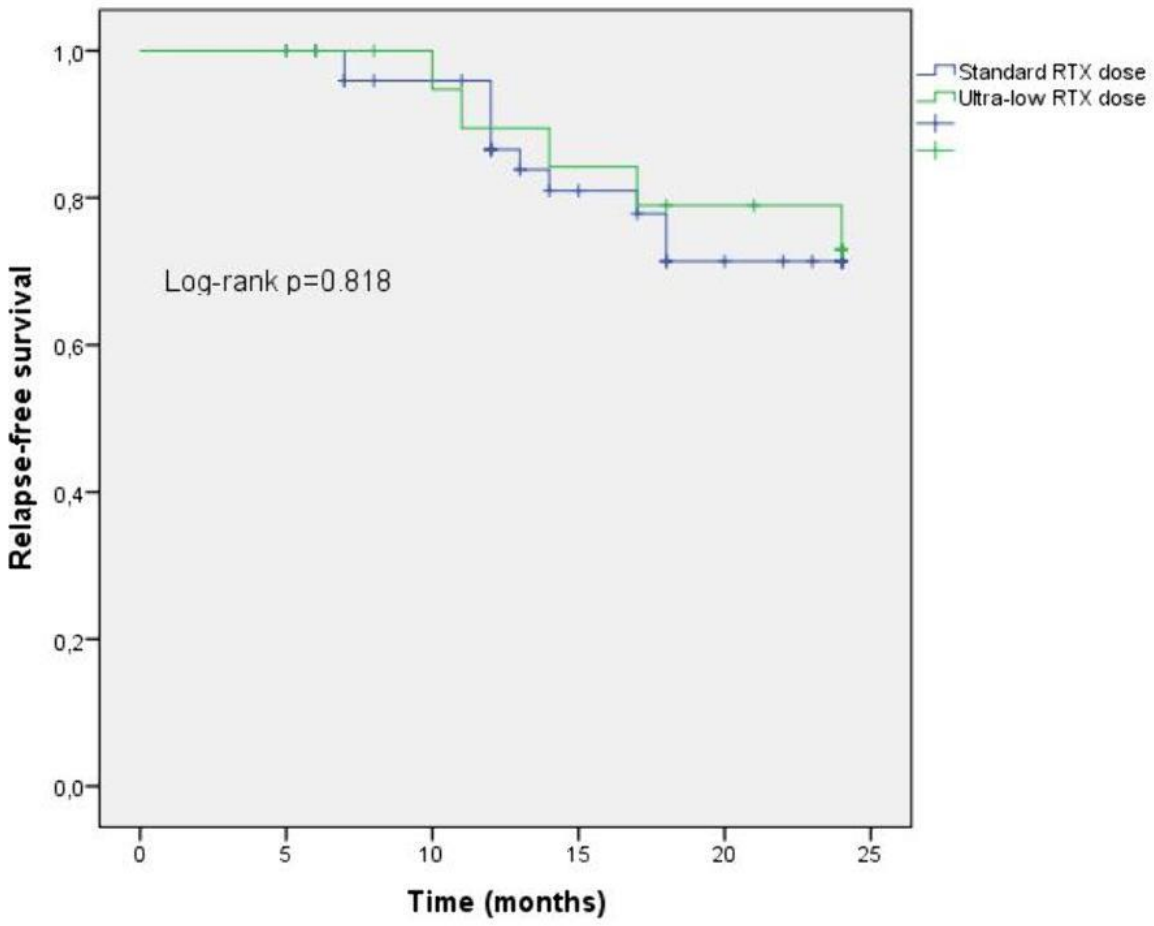
Background and Aims: Rituximab (RTX) achieved high remission-induction and sustained maintenance rates in patients with ANCA-associated vasculitis (AAV). However, RTX is expensive and may potentially lead to serious side effects. Defining the best maintenance regimen in AAV is still an unmet need

Methods: Consecutive AAV patients (classified as GPA and MPA) who successfully achieved disease remission (BVASv3=0) with conventional RTX regimen were included. Patients received at least three maintenance RTX infusions with either 1000 mg or 500 mg, twice per year (standard low dose) or once per year (ultra-low dose). The patients were compared after 18 months

Results: A total of 83 AAV patients (51±16 years, 49.4% female, 95.2% ANCA positive, 65.8% anti-PR3, 61 GPA, 22 MPA) achieved complete disease remission with conventional induction regimen. After 7 [6-9] months, 29.9% patients started maintenance treatment with ultra-low dose RTX, while 70.1% with standard low dose, for 18 months. No significant differences at baseline were noted. At the end of observation period, relapse-free survival was comparable between the two group (22.7% vs 21.2%, log-rank p=0.818). No differences were noted in ANCA negative rate (p=0.262), B-cells depletion rate (p=0.725), serum IgG (p=0.367), VDI (4 [1-5] vs 2 [1-4], p=0.098). Although not significant, patients treated with ultra-low dose had lower severe infection rate (10.5% vs 26.8%, p=0.154), lower severe hypogammaglobulinaemia (31.8% vs 36.5%, p=0.697) and less deaths (4.5% vs 5.8%,

p=0.831).



Conclusions: Reduced RTX exposurewas not associated with an impaired efficacy in maintenance therapy in AAV patients. Remission maintenance with ultra-low dose RTX is a safe and more cost-effective option

O026 / #130

FREE COMMUNICATIONS 05: OPEN ISSUES AND NOVELTIES IN ARD
17-03-2023 4:45 PM - 5:45 PM

DIFFERENCES IN CLINICAL PROFILE BETWEEN EARLY-ONSET AND LATE-ONSET TAKAYASU ARTERITIS

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Background and Aims: Takayasu's arteritis (TAK) is widely thought to affect predominantly young Asian women. However, little is known regarding the clinical profile of late-onset TAK. This study investigated the clinical profile of patients with TAK with a focus on late-onset TAK.

Methods: We retrospectively enrolled patients with TAK who were hospitalized in Fuwai Hospital between January 2010 and December 2019. Demographic, clinical characteristics, vascular involvement, and biochemical findings were compared between those with early-onset TAK (<40 years) and with late-onset TAK (>=40 years).

Results: One hundred and forty-two (20.2%) of 704 patients with TAK were aged >=40 years when they experienced their earliest TAK-related symptoms. Late-onset TAK patients experienced more cardiac symptoms, were more likely to have cardiovascular risk factors and coronary artery involvement, and were less likely to have neurologic symptoms than those with early-onset TAK. Late-onset TAK patients had a lower estimated glomerular filtration rate (96.64 [84.60–106.98] vs. 110.37 [94.58–122.61]; p<0.001) and higher blood urea nitrogen (5.43 [4.39–7.05] vs. 4.97 [4.10–6.15]; p=0.002). Late-onset TAK patients tended to have more inflammatory biomarker activity, including a higher frequency of elevated erythrocyte sedimentation rate (44.3% vs. 25.9%; p<0.001) and higher levels of C-reactive protein (4.47 [2.25–11.80] vs. 3.35 [1.82–8.65]; p=0.013) and high-sensitivity C-reactive protein (4.01 [1.12–10.72] vs. 2.12 [0.88–7.97]; p=0.009).

Conclusions: Patients with late-onset TAK are more likely to have cardiac symptoms, cardiovascular risk factors, and coronary artery involvement, less likely to have neurologic symptoms, and tend to have more inflammatory activity and renal impairment than those with early-onset TAK.

O027 / #47

FREE COMMUNICATIONS 05: OPEN ISSUES AND NOVELTIES IN ARD
17-03-2023 4:45 PM - 5:45 PM

PHASE II CLINICAL TRIAL TO ASSESS THE SAFETY AND EFFICACY OF INTERLEUKIN-6 RECEPTOR BLOCKER IN COMBINATION WITH IPILIMUMAB AND NIVOLUMAB FOR METASTATIC MELANOMA

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Background and Aims: Management of immune-related adverse events (irAEs) is challenging as using corticosteroids as first-line therapy can lead to significant morbidity. Our preliminary results suggested a role for interleukin-6/Th17 pathway in both irAEs and immunotherapy resistance. Therefore, we evaluated the safety and efficacy of tocilizumab plus combination immune checkpoint inhibitors (ipilimumab/nivolumab) in previously untreated metastatic melanoma patients.

Methods: Phase II, open-label, single center study (NCT04940299). Participants (n=35) receive subcutaneous tocilizumab 162 mg weekly or bi-weekly for up to 12 weeks as approved for rheumatoid arthritis plus ipilimumab/nivolumab per the standard dosing for melanoma. Objectives: 1) assess grade 3 or higher irAEs; 2) estimate objective response rate (ORR) by RECIST 1.1 and overall survival; and 3) explore biomarkers of toxicity and tumor response/resistance. Safety assessments continue for up to 2 years in participants who discontinue therapy for any reason.

Results: To date, 25 participants have been enrolled; duration of treatment ranged from 6 to 41 weeks. Eleven patients (44%) had grade III/IV irAEs: colitis (20%), hepatitis (16%), pancreatitis (8%), and polymyalgia rheumatica-like and type I diabetes (4% each). Median time to irAE onset was 8.3 weeks (2.7-17.3) and irAEs led to study discontinuation in 4%. There have been no treatment-related deaths. The ORR was 60% including 44% in patients with elevated LDH and disease control rate (CR+PR+SD) was 75%.

Conclusions: Our preliminary data showed a numerically lower rate of grade III/IV irAEs compared to similarly designed ipilimumab/nivolumab melanoma trials without negative impact on efficacy. Ongoing immune analysis will be presented to help further interpret these results.

O028 / #223

FREE COMMUNICATIONS 05: OPEN ISSUES AND NOVELTIES IN ARD
17-03-2023 4:45 PM - 5:45 PM

CHARACTERIZATION OF CIRCULATING MICROVESICLES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM) REVEALS RELATIONSHIP WITH IIM PHENOTYPE AND TREATMENT RESPONSE

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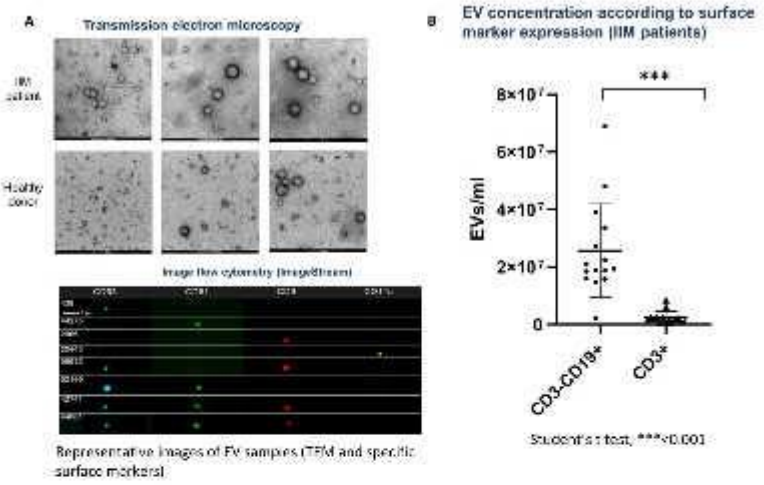
Background and Aims: Few biomarkers are currently available for monitoring of idiopathic inflammatory myopathies (IIM). Extracellular vesicles (mEVs) are small lipid-bilayer particles involved in modulation of immune response. We aim to investigate correlates between plasma mEVs and clinical and laboratory features of IIM.

Methods: Adult IIM patients (EULAR 2017) and age-/sex-matched healthy controls (HD) were included. mEVs were isolated through size exclusion chromatography and ultra-filtration. Particles morphology, concentration and surface marker characterization were assessed via transmission electron microscopy, nanoparticle tracking analysis and imaging flow cytometry respectively. Data were cross-sectionally analyzed; parametric Student-t test and one-way ANOVA with Bonferroni correction or non-parametric tests were used.

Results: We included 45 IIM patients (F:M 2:1; mean age±SD 59.2±13.5y) and 45 HD. The specific IIM diagnosis was identified. 39 (86.7%) patients were receiving glucocorticoids and/or immunosuppressants at the time of blood sampling. Immunophenotyping revealed a significantly increased proportion of CD19+ mEVs, indicating a likely B cell origin.
IIM patients displayed significantly increased mEV concentrations compared to HD (mean±SD [mEVs/mL], $1.95x10^{10}$±$1.47x10^{10}$ vs. $1.45x10^{10}$ ± $7.82x10^{9}$, p=0.025). mEVs concentrations were significantly higher in treatment-naïve patients and decreased upon treatment. Patients with IIM onset ≤6 months displayed higher circulating levels of mEVs ($3.20x10^{10}$±$2.42x10^{10}$ vs. $1.80x10^{10}$±$1.80x10^{10}$, p=0.042), as did seropositive patients against seronegative ($2.09x10^{10}$±$1.63x10^{10}$ vs. $1.49x10^{10}$±$0.43x10^{10}$, p=0.063). Cancer associated myositis patients

displayed the highest levels of circulating



EV, extracellular vesicles; IIM, idiopathic inflammatory myopathies CAM, cancer associated myositis; DM, dermatomyositis; PM, polymyositis; Asys, anti-synthetase syndrome; IBM, inclusion body myositis; HD, healthy donors; TEM, transmission electron microscopy

mEVs.

Conclusions: Circulating, B cell-derived mEVs are significantly increased in IIM, especially in recent-onset, seropositive, treatment-naïve disease. Our findings reinforce the potential role of mEVs as biomarkers for early diagnosis, treatment response and disease monitoring in IIM.

O029 / #332

FREE COMMUNICATIONS 05: OPEN ISSUES AND NOVELTIES IN ARD
17-03-2023 4:45 PM - 5:45 PM

MACHINE LEARNING ANALYSIS AS A NEW TOOL FOR ASSESSING OUTCOME IN A COHORT OF 107 PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background and Aims: To assess the long-term outcome in inflammatory idiopathic myopathies (IIM) patients using Artificial intelligence (AI) and focusing on clinical and laboratory features and treatment. IIM are a group of rare heterogeneous diseases classified into dermatomyositis (DM), inclusion body myositis (IBM), anti-synthase syndrome (ASS), immune-mediated necrotizing myopathy (IMNM), overlap syndromes. The clinical course can be highly variable with systemic involvement of different organs and patients can have a rapidly progressive, remitting, or periodic relapsing course. Machine learning (ML) allows to analyze great information and evaluating decision-making processes, deep learning (DL) analyzes data through neural networks and learns from them. Both processes are increasingly used in medical research.

Methods: We evaluate the long-term outcome of 107 patients affected by IIM. All patients had a diagnosis based on Bohan and Peter criteria or EULAR/ACR criteria for IIM and had at least a 2-year follow-up period. We considered different parameters, including clinical manifestations and organ involvement, number and type of treatments, serum creatine kinase levels, muscle strength (MMT8 score), disease activity (MITAX score), disability (HAQ-DI score), disease damage (MDI score), and physician and patient global assessment (PGA).

Results: The database collects data that will be analyzed, applying, with R, supervised ML algorithms such as lasso, ridge, elastic net, classification, and regression trees (CART) and random forest to find the factors that best predict disease outcome.

Conclusions: The use of artificial intelligence (AI) algorithms will allow us to identify the parameters that best correlate with the disease outcome in IIM.

O030 / #151

FREE COMMUNICATIONS 05: OPEN ISSUES AND NOVELTIES IN ARD
17-03-2023 4:45 PM - 5:45 PM

NON HCV-RELATED MIXED CRYOGLOBULINEMIC VASCULITIS WITH BIOPSY-PROVEN RENAL INVOLVEMENT: THE EFFECTS OF RITUXIMAB

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Background and Aims: Remarkable results in severe HCV-related cryoglobulinemic vasculitis have been obtained with Rituximab (RTX). Details of the clinical characteristics and effective treatment of non HCV-related cryogloulinemic syndromes are presently lacking. This abstract reports on a prospective single-Center open study aimed at evaluating the clinical presentation and effects of RTX administered alone in patients (pts) with severe non HCV-related cryoglobulinemic syndrome

Methods: We analyzed all pts with a previous diagnosis of non HCV-related cryoglobulinemia and biopsy-proven renal involvement. Inclusion criteria for the study were the presence of cryoglobulins on at least 2 determinations and the absence of HCV infection. They were all treated with 4 once-weekly doses of RTX (375 mg/m^2) plus two more doses, administered 1 and 2 months later (improved protocol)

Results: All 11 pts presented with biopsy-proven renal involvement, 4/11 with leukocytoclastic vasculitis, and 8 with involvement of the peripheral nervous system. Mean cryocrit was 2.5%. 4/11 pts had symptomatic sicca complex. After 6 months we observed a remarkable improvement in the necrotizing skin ulcers and a substantial amelioration of the electrophysiological parameters of motor and sensory peripheral neuropathy. Improvement in both renal function (from 2.8 to 1.4 mg/dl, $p<0.001$) and proteinuria (from 4.2 to 0.4 g/24 hours, $p<0.001$) was found in 10/11 pts. Good renal response was confirmed at the end of follow-up (38.4 months).

Conclusions: In our cohort the administration of 4 once-weekly infusions of RTX followed by 2 more infusions after 1 and 2 months proved to be effective in the management of these rare pts.

O031 / #500

FREE COMMUNICATIONS 06: SYSTEMIC LUPUS ERYTHEMATOSUS
18-03-2023 10:05 AM - 11:05 AM

BELIMUMAB AND ANTIMALARIAL AGENTS PREVENT RENAL FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM FOUR RANDOMISED CLINICAL TRIALS

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Background and Aims: We aimed to determine the effect of the use of antimalarial agents (AMA) and different doses and pharmaceutical forms of belimumab on preventing renal flares in patients with active systemic lupus erythematosus (SLE).

Methods: We pooled data from the BLISS-52, BLISS-76, BLISS-SC and BLISS-Northeast Asia (NEA) clinical trials of belimumab (N=3225), that included seropositive, active SLE patients with no active severe lupus nephritis (LN). Participants were allocated to receive intravenous (IV) belimumab 1 mg/kg (N=559), IV belimumab 10 mg/kg (N=1033), subcutaneous (SC) belimumab 200 mg (N=556) or placebo (N=1077) in addition to standard therapy. The outcome of the present analysis was development of renal flares, defined according to the analysis plan within the BLISS programme. The hazard of renal flare was assessed with adjusted Cox regression models.

Results: In total, 192 patients developed a renal flare after a median of 197 days. In multivariable Cox regression analysis, use of AMA was associated with a lower risk of renal flares (HR: 0.64; 95% CI: 0.54–0.96; p=0.026). Compared with placebo, the risk of renal flares was lower among patients receiving IV belimumab 1 mg/kg (HR: 0.44; 95% CI: 0.25–0.79; p=0.006) and IV belimumab 10 mg/kg (HR: 0.63; 95% CI: 0.45–0.87; p=0.005), but not SC belimumab 200 mg (HR: 0.90; 95% CI: 0.57–1.42; p=0.648).

Conclusions: Belimumab and AMA prevent against renal flares in patients with active, seropositive SLE but no ongoing severe renal involvement. The prominent effect of low-dose belimumab motivates the investigation of the efficacy of intermediate doses of belimumab.

O032 / #210

FREE COMMUNICATIONS 06: SYSTEMIC LUPUS ERYTHEMATOSUS
18-03-2023 10:05 AM - 11:05 AM

EPIDEMIOLOGY OF SLE IN THE LAST DECADE: DATA FROM A LARGE POPULATION-BASED STUDY IN NORTHEASTERN ITALY

Margherita Zen[1], Filippo Vesentini[1], Laura Salmaso[2], Claudio Barbiellini Amidei[3], Ugo Fedeli[3], Stefania Bellio[2], Mario Saia[2], Andrea Doria[1]
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Background and Aims: Updated data regarding SLE epidemiology in Europe are few, and information from Italy is scanty. We aimed at estimating the incidence and prevalence of SLE in northeastern Italy over the period 2012–2020.

Methods: A retrospective population-based study was conducted in Veneto Region (4,900,000 people) using the Population Registry, an administrative health database where all residents are recorded, which was linked with healthcare copayment exemption database and hospital discharge records. Between 2012 and 2020, SLE cases were defined by a healthcare copayment exemption for SLE (national registry code 028) or any hospital diagnosis of SLE (ICD-9-CM 710.0), whichever came first. Standardized incidence and prevalence were reported by age and gender, and trends during the follow-up were analyzed through Poisson regression models.

Results: We identified 4,283 SLE patients (85% female), with 1,092 incident cases. Across the study period, SLE standardized point prevalence significantly increased from 66.7 (95% CI 64.3-69.0) to 72.9 per 100,000 residents (70.5-75.3, annual increase 1.1%, p<0.0001). SLE incidence was 2.8 per 100,000 (95% CI 2.6-2.9), with a significant difference between females (4.5, 4.3-4.8) and males (0.9, 0.8-1.0, p<0.001), and with a 8% annual decline (p<0.0001). The highest incidence was observed in women aged 30-39 (8.40, 7.31-9.65). The female-to-male incidence rate ratio overall was 5.00 (4.25-5.87; p<0.0001), with a peak in the 30-39 age group (10.4, 6.58-16.87).

Conclusions: Over the last decade SLE prevalence has increased, while incidence has stably declined. In view of the introduction of new high-cost drugs, a clear definition of the epidemiology of SLE is crucial for all healthcare stakeholders.

O033 / #272

FREE COMMUNICATIONS 06: SYSTEMIC LUPUS ERYTHEMATOSUS
18-03-2023 10:05 AM - 11:05 AM

EVALUATION OF PREDICTIVE FACTORS OF WORSE PROGNOSIS IN LUPUS NEPHRITIS: FOCUS ON NEW PATHOGENETIC PATHWAYS

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Background and Aims: IL-17/ IL-23 axis seems to have a role in lupus nephritis (LN). The aim of this study is to evaluate the prognostic factors in a cohort of patient with LN focusing on the impact of IL-17/IL 23 axis on renal outcome

Methods: 84 patients with active LN at disease onset or at renal flare were enrolled. Clinical data were collected at baseline and at 6(T6),12(T12),24(T24) months and at the last follow-up(FU). Renal biopsies were evaluated according to ISN/RPS classification. Active interstitial infiltrate (IF) was assessed using the BANFF score. Baseline IL-17 and IL-23 serum levels were assessed in 37 patients

Results: The results of univariate and multivariate analysis for each outcome considered showed that IF>5% and antiphospholipid antibodies positivity (APL+) were associated with worse renal outcomes. IF was associated to not reaching early remission in both univariate analysis (*p<0,01)* and multivariate analysis (OR 0.12(0.04-0.37)), and to chronic damage (*p= 0,01*), no persistent remission (*p= 0,02*), proteinuria (*p <0,01*), in the univariate analysis. APL+ was associated to less early remission achievement in both univariate analysis (*p= 0,03*) and multivariate analysis (OR 0.36(0.11-1.37)) as well as to chronic damage in univariate analysis (*p= 0,04*) and multivariate analysis (OR 0.77 (0.39-15.16)). Higher IL-23 serum level was associated with persistent proteinuria (*p<0,01*) and chronic damage (*p=0.05*)

Conclusions: IF and APL+ represent in this study the strongest predictors of worse renal outcome. A higher IL-23 serum level seems to be a negative prognostic factor suggesting a possible role of IL-17/IL- 23axis as a biomarker of more aggressive LN

O034 / #274

FREE COMMUNICATIONS 06: SYSTEMIC LUPUS ERYTHEMATOSUS
18-03-2023 10:05 AM - 11:05 AM

IMMUNOPHENOTYPIC CHARACTERIZATION OF PERIPHERAL BLOOD-DERIVED B LYMPHOCYTES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DURING B-CELL TARGET THERAPY WITH ANTI-BLYS

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Background and Aims: BLyS inhibition following belimumab therapy is associated with circulating B-cell and short-lived plasmacells reduction. Aim of the study:characterize B-cell phenotype in SLE patients at baseline and after anti-BlyS treatment.

Methods: Fifty-four active SLE patients (49 females, mean age 40.6±13.2years, disease duration 12.3±9.0years, SLEDAI-2K 6.6±3.1) who received belimumab were enrolled. Phenotyping of peripheral blood B-cells (using as phenotypic markers IgD,CD38,CD27) was performed at six(T6) and twelve(T12)months by flow cytometry.

Results: In the whole cohort a reduction of $CD19^{pos}$[T0:11.1±6.1% vs T6:6.4±3.4%,p<0.01;T12:4.2±3.4%,p<0.01] and $CD19^{pos}IgD^{pos}CD27^{neg}$[T0:55.8±28.7% vs T6:34.9±22.2%,p<0.01;T12:30.0±19.4%,p=0.04] and an increase of $CD19^{pos}IgD^{neg}CD27^{pos}$[T0:21.0±20.2% vs T6:37.5±21.4%,p<0.01;T12:42.2±21.7%,p=0.02] after therapy was observed. Stratifying patients based on organ involvement, a reduction of $CD19^{pos}$[T0:10.7±4.6% vs T6:6.8±2.4%,p=0.03;T12:4.5±3.5%,p=0.03] and $CD19^{pos}IgD^{pos}CD27^{neg}$[T0:61.0±24.6% vs T6:38.9±17.5%,p<0.01;T12:36.9±16.0%,p=0.03] in patients with mild organ involvement and an increase of $CD19^{pos}IgD^{neg}CD27^{pos}$in both subgroups [(severe T0:24.1±25.0% vs T6:44.9±27.4%,p=0.01) (mild T0:18.9±18.3 vs T6:31.2±12.7%,p<0.01)] was found. Evaluating the B-cell subsets according to the treatment response, a reduction of $CD19^{pos}IgD^{pos}CD27^{neg}$ at T6 [(responders T0:55.4±29.3 vs T6:32.3±19.9,p<0.01) (no-responders T0:63.1±41.3% vs T6:41.4±33.5%,p=0.05)] and an increase of $CD19^{pos}IgD^{neg}CD27^{pos}$[(responders T0:22.4±21.2% vs T6:39.6±19.4%,p<0.01) (no-responders T0:20.6±26.1% vs T6:38.6±35.3%,p<0.05) was observed in both groups. ROC curve analysis of $IgD^{neg}CD27^{pos}$subset identified a cut-off of 9.94% [AUC(95% CIs:0.761:(0.566-0.957),p=0.023)] associated with response at T6. Moreover, having an $IgD^{neg}CD27^{pos}$rate ≥9.94% [OR:4.5(95%CIs:0.9-17.2)] and the presence of anti-dsDNA antibodies at baseline [OR:5.2(95%CIs:1.2-22.1)], identified patients who achieved early response within T6 from therapy initiation

Conclusions: Anti-BLyS therapy significantly impacts on the B-cell subpopulations in SLE in relation with the distinct organ involvement. Moreover, baseline immunological features and $IgD^{neg}CD27^{pos}$B-cell subset rate are novel putative biomarkers of response to anti-BLyS therapy in SLE.

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FREE COMMUNICATIONS 06: SYSTEMIC LUPUS ERYTHEMATOSUS
18-03-2023 10:05 AM - 11:05 AM

PREDICTORS OF CUTANEOUS RESPONSE IN SLE-PATIENTS TREATED WITH BELIMUMAB. DATA FROM A MULTICENTERED NATIONWIDE COHORT (BERLISS-SKIN)

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Background and Aims: To investigate rates and predictors of cutaneous response to belimumab in patients with systemic lupus erythematosus (SLE) skin manifestations by using CLASI.

Methods: We included patients with SLE cutaneous manifestations from the BeRLiSS cohort. The outcome was evaluated by CLASI=0 (skin remission) and CLASI20, 50, 70, defined by a decrease of at least 20%, 50% and 70% at 6, 12, 24, 36 and 48 months. Baseline predictors were evaluated by logistic regression analysis.

Results: In the analysis were included 147 patients with SLE skin manifestations. Percentages of patients achieving the different outcomes at different time points are reported in

the Figure. Low complement at baseline was associated with CLASI50 at 12-month (p=0.017) and low complement at 12 months with CLASI70 at 24-month (p=0.002). CLASI70 at 12-month was also associated with CLASI=0 at 36-months (p=0.030). There was a trend for association between number of flares in the first 24-month and CLASI=0 at 36-month (p=0.061) and CLASI50 at 24-months (p=0.086). The number of flares after the first 12 months of follow-up was positively associated with CLASI70 at 24-months (p=0.011). Smoking was a negative predictor of CLASI50 at 12 months (p=0.026) and CLASI70 at 24 months (p=0.031). CLASI damage score>0 and disease duration at baseline were negatively associated with CLASI=0 at 36 months (p=0.031, p=0.036 respectively).

Conclusions: In belimumab-treated patients with SLE-related skin manifestations, best response was found in patients with low complement and relapsing remitting pattern of disease activity. As already known, smoking is negatively associated with cutaneous response.

O036 / #313

FREE COMMUNICATIONS 06: SYSTEMIC LUPUS ERYTHEMATOSUS
18-03-2023 10:05 AM - 11:05 AM

CLINICAL ASSOCIATIONS OF TH10 AND IL-10 IN PATIENTS OF SLE

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Background and Aims: Various immune cells and cytokines are involved in the pathogenesis of SLE. Continuous immune activation results in production of large amounts of inflammatory cytokines leading to local inflammation and tissue damage. Th-10, a subset of T helper cells, known to produce IL-10 contributes in disease pathogenesis by stimulating B cells to produce antibodies. IL-10, is a pleiotropic cytokine, which exerts both anti-inflammatory and pro-inflammatory effects. Our study aimed to measure circulating Th-10 levels and serum levels of IL-10 in SLE patients and to find their correlation with the SLE disease activity index.

Methods: The study was a hospital based cross-sectional case control study with patients of SLE(n=60) and healthy controls(n=30). Detection of T helper 17 cells(Th 17) was done by measurement of combined expression of CD45, CD3, CD4 , CCR 6 and IL-17 and IL-10 using Beckman Coulter Navios using the monoclonal antibodies conjugated with different fluorescent dyes.

Results: Flowcytometric expression of Th17 was significantly(p=0.04) higher among patients 2(1.80) in comparison to controls 1.19(1.35). Statistically significant(p=0.04) increase in the expression of Th 10 cells was found among cases 1.90(7.31) when compared to controls 1.07(2.02). Similar change was observed in active and inactive cases.Expression of Th17, Th10 IL-17 and IL-10 level was significantly higher in cases of nephritis when compared to those without nephritis.

Conclusions: Study concluded the pro-inflammatory role of IL-17 and IL-10. Expression of T helper 17(Th17) cells, was a subset of CD4+ T helper cells was increased and considered to contribute to inflammation related damage through IL-17 production.