**Disclosures**: None declared

**Disclosure of Interests**: None declared

**DOI**: 10.1136/annrheumdis-2020-eular.4923

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**1. This study, developed within the Innovative Medicines Initiative Joint Undertaking project PRECISESADS framework, aimed at identifying inflammatory and oxidative stress determinants involved in the enhanced CV-risk present in SLE patients and to analyze the relevance of the sustained positivity for anti-dsDNA on the establishment of their atherothrombotic status.**

**Methods**: One hundred and twenty-four SLE consecutive patients (not including patients with associated antiphospholipid syndrome), belonging to the PRECISESADS project, were evaluated for the presence of CVD and its association 150 per 100 000 [1]. Methotrexa (MTX) administered at the dose 10-15mg/m² is currently recommended as the first-line treatment in most of JIA subtypes [2]. Despite its widespread use in rheumatology, the mechanism of MTX immunomodulatory action remains incompletely understood [3]. Free adenosine is one of the particles possibly associated with the action of MTX, acting via three types of adenosine receptor: ADORA2A, ADORA2B, and ADORA3 [4].

**Objectives**: The aim of our study was to determine the association between single nucleotide polymorphisms in ADORA2A (rs2236624, rs2298383) and ADORA3 (rs33933) receptors gene and the disease activity and presence of MTX therapy side effects in patients with JIA.

**Methods**: One hundred children with JIA of all subtypes treated with MTX were recruited to the study. Demographic and clinical parameters were collected at the baseline of MTX therapy and on a control visit 4–6 months (median 5.09 months) after starting MTX. The clinical parameters included inflammatory markers values, number of joints with active arthritis, number of joints with restricted range of movement, physician’s global assessment of disease activity, parent/patient global assessment of overall well-being, functional ability (measured by the Childhood Health Assessment Questionnaire – CHAQ) and the value of Juvenile Idiopathic Arthritis Disease Activity Score 71 (JADAS 71). Presence of MTX side effects was evaluated on the control visit. SNP genotyping was performed using genomic DNA isolated from peripheral blood samples.

**Results**: Both polymorphic variants of ADORA2A (rs2236624, rs2298383 - CC/CT) were significantly associated with 3.5 times higher odds of gastrointestinal side effects occurrence (OR: 3.52, 95%CI: 1.12-11.03, p=0.03 and OR: 3.49, 95%CI: 0.89-13.66 p=0.07) after adjustment to age, sex, dose and route of MTX administration. In addition, children with the ADORA3 rs33933 polymorphic variant (CT/CC) after six months of MTX treatment had significantly lower number of joints with active arthritis (0.0 vs 1.0, p=0.04), lower JADAS 71 score (3.0 vs 5.1, p=0.16) and lower value of CRP (0.6 vs 2.4, p=0.02).

**Conclusion**: Although future studies are needed to verify our findings, polymorphisms in ADORA2A and ADORA3 genes may become the determinants of MTX treatment efficacy and gastrointestinal toxicity in children with JIA.

**References**:  


**Disclosure of Interests**: None declared

**DOI**: 10.1136/annrheumdis-2020-eular.4772

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**FRI0453**

**COMPARATIVE GENE PROFILE IN MONOCYTES FROM CHILDHOOD- AND ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: CLUES TO DIFFERENT SYSTEMIC INVOLVEMENT**

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**Background**: OBJECTIVE: To understand the differences in gene expression in monocytes from children and adults with Systemic Lupus Erythematosus (SLE) compared to healthy controls.

**Methods**: Whole blood samples were collected from 24 patients with SLE being followed at the Autoimmune Rheumatic Diseases Complex of the Reina Sofia Hospital (University of Cordoba, Spain) and 24 healthy controls. RNA from monocytes was isolated and gene expression was measured using the Human immune profile array (BD Biosciences). Quality of the RNA was assessed (RNA integrity number, RIN>7) and the expression of 460 genes in monocytes was measured. Results were compared using the t-test.

**Results**: We found 74 genes with different expression in monocytes from patients with SLE compared to healthy controls. In children with SLE we found a significantly lower expression of the genes involved in the complement system and the innate immune response (e.g., C5, C6, C7, C9, FcgammaRIb1, TLR2, TLR4, TLR6, TLR9). In adults with SLE we found a significantly higher expression of the genes involved in the adaptive immune response (e.g., CD8a, CD19, CD40, CD86, IL10, TNF). These findings are consistent with the different clinical manifestations observed in children and adults with SLE.

**Disclosures**: None declared

**DOI**: 10.1136/annrheumdis-2020-eular.6492
with positivity for anti-dsDNA antibodies. A second cohort of 62 SLE patients was included, of which endothelial dysfunction, lipid profile, the presence of atheroma plaques (identified by a pathologic increase in the carotid intima media thickness -CIMT), and the frequencies of anti-dsDNA positivity for 7 years, were evaluated. Serum inflammatory and oxidative stress biomolecules, and NETosis-derived bioproducts were further evaluated by multiplex assay and specific commercial kits, respectively. Besides, miRNomes were identified using next-generation sequencing. Clinical significance of the biomolecules analyzed was explored by correlation/association studies with immunological and CV-risk features.

**Results:** A significant relationship among the incidence of CVD (i.e, coronary artery disease or cardiac involvement) and the positivity for anti-dsDNA antibodies was recognized in the first SLE cohort. Accordingly, in the second SLE cohort, significantly impaired micro-vascular endothelial function (identified by reduction of hyperemia post occlusion area), increased arteriogenic index and pathologic increase in the CIMT were assessed in patients positive for anti-dsDNA in relation to anti-dsDNA negative patients. Around a 65% of SLE patients displayed a sustained positivity for anti-dsDNA antibodies for more than 7 years. These patients showed a distinctive and specific molecular profile compared with patients that had remained negative for anti-dsDNA, including increased inflammatory profile (IL1B, IL2, IL6, IL17, EOTAXIN, GFG, GMCSF, IFNγ, IP10, RANTES, TNF), enhanced oxidative status (lipoperoxides), and higher NETosis (nucleosomes, elastase). Levels of those biomolecules were closely interconnected and associated to their regulatory miRNAs, which accordingly exhibited differential expression in SLE anti-dsDNA(+) vs anti-dsDNA(-) patients. Finally, the frequency for positivity of anti-dsDNA significantly correlated both with markers of endothelial dysfunction and with the presence of atheroma plaques in SLE patients, pointing at the direct involvement of anti-dsDNA-Ab in the development of these processes.

**Conclusion:** 1: Positivity for anti-dsDNA antibodies confers a specific inflammatory/oxidative profile linked to an enhanced CV-risk in SLE patients. 2. Moreover, the sustained positivity for anti-dsDNA antibodies fosters the establishment of an atherothrombotic status in these autoimmune patients.

**Acknowledgments:** Supported by the EU/EFPIA –IMI-JU PRECISESADS (n° 115965) and ISCIII (PI18/0837 and RIER RD16/00102015), Co-funded with RIER.

**Disclosure of Interests:** Inmaculada Concepción Aranda-Valero: None declared, Alejandra M. Patiño-Trives: None declared, Roldán Molina Rosa: None declared, María A Aguirre: None declared, Pérez Sánchez Laura: None declared, Carlos Pérez Sánchez: None declared, María Luque-Tevar: None declared, Iván Arias de la Rosa: None declared, María del Carmen Abalos-Aguilera: None declared, Desiree Ruiz-Vilchez: None declared, Mario Espinosa: None declared, Nuria Barbarroja Puerto Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE and Pfizer, Speakers bureau: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene, , Charity Lopez-Pedraza Grant/research support from: ROCHE and Pfizer. doi: 10.1136/annrheumdis-2020-eular.4923

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**FR4054 UNDER DETECTION OF INTERSTITIAL LUNG DISEASE IN JUVENILE SYSTEMIC SCLEROSIS (JSSC) UTILIZING PULMONARY FUNCTION TESTS. RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT**


Background: Juvenile systemic sclerosis (JSSc) is an orphan disease with a prevalence in around 3 in a million children. Pulmonary involvement in JSSC can be detected early in the inception cohort. Traditional methods in JSSc pulmonary function testing (PFT) with FVC and DLCO are used for screening and computed tomography (HRCT) was more reserved for those with abnormal PFTs. More recently, it has become apparent that PFTs might not be sensitive enough for detecting ILD in children.

**Objectives:** Using a prospective international juvenile systemic scleroderma cohort (JSSC(J)) [2], to determine if pulmonary screening with FVC and DLCO is sufficient enough to assess the presence of interstitial lung disease in comparison to CT evaluation.

**Methods:** The international juvenile systemic scleroderma cohort database was queried for available patients with recorded PFT parameters and HRCT performed to determine sensitivity of PFTs detecting disease process.

**Results:** Of 129 patients in the JSSC, 67 patients had both CT imaging and an FVC reading from PFTs for direct comparison. DLCO readings were also captured but not in as many patients with tandem HRCT (n = 55 DCLO and HRCT scan). Therefore, initial analyses focused on the sensitivity, specificity and accuracy of the FVC value from the PFTs to capture the diagnosis of interstitial lung disease as determined by HRCT.

Overall, 49% of the patients had ILD determined by HRCT, with 60% of patients having normal FVC (>80%) with positive HRCT findings, and 24% of patients having normal DCLO (>80%) with positive HRCT findings. Fourteen percent (n = 3/21) of patients with both FVC and DLCO values within the normal range had a positive HRCT finding.

**Conclusion:** The sensitivity of the FVC in the JSSC cohort in detecting ILD was only 39%. Relying on PFTs alone for screening for ILD in juvenile systemic sclerosis would have missed the detection of ILD in almost 2/3 of the sample cohort, supporting the use of HRCT for detection of ILD in children with SSC. In addition, the cut off utilized, of less than 80% of predicted FVC or DLCO could be too low for pediatric patients to exclude beginning ILD. This pilot data needs confirmation in a larger patient population.

Supported by the “Joachim Herz Stiftung”

**Disclosure of Interests:** Ivan Foeldvari Consultant of: Novartis, Bernd Hinrichs. None declared, Kathryn Tokor: None declared, María Jose Santos Speakers bureau: Novartis and Pfizer, Ozgur Kasapcopur: None declared, Amra Adrovic: None declared, Valida Stanevicha: None declared, Flavió R. Sztabnok: None declared, Maria T. Terrier: None declared, Ana Paula Sakamoto: None declared, Ekaterina Alexeeva Grant/research support from: Roche, Pfizer, Centocor, Novartis, Speakers bureau: Roche, Novartis, Pfizer, Jordi Anton Grant/research support from: grants from Pfizer, abbvie, Novartis, Sobi, Gebro, Roche, Novim-mune, Sanofi, Lilly, Amgen, Grant/research support from: Pfizer, abbvie, Novartis, Sobi. Gebro, Roche, Novimnune, Sobi, Lilly, Amgen, Consultant of: Novartis, Sobi. Pfizer, abbvie, Consultant of: Novartis, Sobi, Pfizer, Sobi, Gebro, Speakers bureau: abbvie, Pfizer, Roche, Novartis, Sobi, Gebro, Speakers bureau: abbvie, Pfizer, Roche, Novartis, Sobi, Gebro, Maria Katsikas: None declared, Vanessa Smith Grant/research support from: The affiliated company received grants from Research Foundation - Flanders (FWO), Belgian Fund for Scientific Research in Rheumatic diseases (FWRO), Boehringer Ingelheim Pharma GmbH & Co and Janssen-Cilag NV, Consultant of: Boehringer-Ingelheim Pharma GmbH & Co, Speakers bureau: Actelion Pharmaceuticals Ltd, Boehringer-Ingelheim Pharma GmbH & Co and UCB Biopharma Spri, Rolando CIMAZ: None declared, Mikhail Kostik: None declared, Simone Appenzeller: None declared, Mahesh Janarthanan: None declared, Monika Molt: None declared, Dana Nemcova: None declared, Dineke Schonenberg: None declared, Cristina Battaglotti: None declared, Lillemor Berntsson Consultant of: paid by Abbvie as a consultant, Speakers bureau: paid by Abbvie for giving speeches about JIA, Blanca Bica: None declared, Juenger Brunner Grant/research support from: Pfizer, Novartis, Consultant of: Pfizer, Novartis, Abbvie, Roche, BMS, Speakers bureau: Pfizer, Novartis, Abbvie, Roche, Pfizer, Roche, Novartis, Sobi, Gebro, Maria Katsikas: None declared, Vanessa Smith Grant/research support from: AbbVie, Chugai, Merck Sharp & Doehme, Novartis, Pfizer, Roche, Speakers bureau: Abbvie, Bayer, Chugai, Merck Sharp & Doehme, Novartis, Roche, Draganara Lazarevic: None declared, Kirsten Minden Consultant of: GlaxoSmithKline, Sanofi, Speakers bureau: Roche, Susan Nielsen: None declared. Farzana Nuruzzaman: None declared, Anjali Patwardhan: None declared, Yosef Uziel: None declared, Nicola Helmus: None declared. doi: 10.1136/annrheumdis-2020-eular.17788

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**FR4055 IS THERE AN INCREASE IN THE FREQUENCY OF INFECTIOUS DISEASES IN THE FAMILIES OF PATIENTS WITH FMF?**

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**Background:** Familial Mediterranean Fever (FMF) is the most common periodic fever syndrome in childhood with an autosomal recessive inheritance pattern and is characterized by unprovoked fever attacks, serositis episodes. The causative gene of the disease is MEFV that encodes pyrin protein. The pyrin protein takes a role in pathways related to inflammation, and mutations of it lead to increased inflammation. It is already shown that frequencies of some certain diseases like PAN, HSP increase in patients with FMF. Nevertheless,