Pediatric Rheumatology 2020, **18**(Suppl 2):83
https://doi.org/10.1186/s12969-020-00469-y

Pediatric Rheumatology

MEETING ABSTRACTS Open Access

Proceedings of the 26th European Paediatric Rheumatology Congress: part 1

Virtual. 23 - 26 September 2020

Published: 28 October 2020

O001

Clinical features and outcomes in sting-associated vasculopathy with onset in infancy (SAVI)

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Pediatric Rheumatology 2020, **18(Suppl 2):**O001

Introduction: STING-Associated Vasculopathy with Onset in Infancy (SAVI) is a rare autoinflammatory interferonopathy caused by gain-of-function mutations in *STING1*, characterized by peripheral vasculopathy and interstitial lung disease
Objectives: Describe the clinical and immunological manifestations of SAVI
Methods: Clinical information on 30 patients with SAVI, based on NIH evaluation (n=15) or on records and samples provided by collaborators (n=15), were retrospectively reviewed. All patients were enrolled in an IRB-approved natural history protocol. The IFN score was calculated as previously described [1]. Features of lung inflammation and damage on Computed Tomography (CT) were scored by a single radiologist (LF)
Results: 11/30 (37%) patients were female. SAVI was sporadic in 77% and familial in 23%. It was due to heterozygous mutations in 80%; only one mutation, p.R281W, present in 6 patients from 4 families, needs homozygosity to be disease-causing. The p.N154S and p.V155M mutations were most common (27% each). Disease symptoms presented in the first year of life (78%), with rash (14/27), respiratory symptoms (11/27) and fever (10/27). Median age at last evaluation was 12.6 years (range 0.4-54), 4 patients had no peripheral vasculopathy and 4 had no lung involvement. Compared to the other genotypes, the p.V155M mutation was more commonly associated with severe lung involvement (100% vs 47.6%, *p=0.01*). Table 1 lists clinical and laboratory features in SAVI. Patients failed a mean of 2.2 DMARDs or biologic, 73% received steroids; 7 patients died at a mean age of 7 years, mostly due to respiratory failure. 23 patients were treated with a JAK-inhibitor (baricitinib n=14, tofacitinib n=6, ruxolitinib n=6), for a median of 1.6 years (range 0.1-5.7). Skin ulcers improved in 9/9 patients, but recurred. Over an average of 2.6 years (range 1.1-3.9), chest CT inflammatory features improved in 6/7, with stable/improved damage in 6/7.
Conclusion: SAVI is a severe early-onset interferonopathy, that is sporadic in 77%. SAVI can present with isolated pulmonary involvement and should be suspected in patients with interstitial lung disease even in the absence of vasculopathy. The p.V155M mutation is associated with severe lung disease. Rarely, the IFN score can be negative in whole blood and positive in PBMCs. Treatment with JAK inhibitors halted progression of lung damage over an average of 2.3 years, but only partially controlled peripheral vasculopathy and did not normalize IFN score
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Funding for this study was provided by the Division of Intramural Research, NIAID, NIH

Reference

1. Kim et al. J Interferon Cytokine Res 2018;38:171–85

Disclosure of Interest

None declared

Table 1 (abstract O001). See text for description

Clinical features	n (%)	Laboratory features	n (%)	Outcomes and complications	n (%)
Rash/chilblains	26/29 (89.7%)	Elevated inflammatory markers	22/26 (84.6%)	Death	7/30 (23.3%)
Lung disease	26/30 (86.7%)	Anemia	21/27 (78%)	Lung fibrosis	12/16 (75%)
Failure to thrive/ Growth failure	22/28 (78.6%)	Thrombocytosis	15/21 (74%)	Respiratory insufficiency	11/28 (39.3%)
Fever	19/25 (76%)	Lymphopenia	12/22 (55%)	Pulmonary hypertension	4/26 (15.4%)
Clubbing	11/20 (55%)	Elevated IgG	17/24 (70.8%)	Nasal septum perforation	7/27 (25.9%)
Arthralgia/ arthritis	10/27 (37%)	Elevated IgA	16/24 (67%)	Amputations	6/30 (20%)
Myositis	5/27 (18.5%)	Autoantibodies	25/27 (92.6%)	Pathologic fractures	4/16 (25%)
Basal ganglia calcifications	2/12 (16.7%)	Elevated IFN Score	17/17 (100%)*	Short stature	15/24 (62.5%)

* In 4 patients IFN score was positive only in PBMCs

O002

Comparison of clinical and imaging features between chronic nonbacterial osteomyelitis and its mimickers: a multi-national 450 case-control study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O002

Introduction: Chronic nonbacterial osteomyelitis (CNO)/chronic recurrent multifocal osteomyelitis (CRMO) predominantly affects children and young adults. Classification criteria are not available and diagnostic criteria that were suggested have not been validated. We previously identified candidate items for the development of classification criteria.
Objectives: To refine candidate items for pediatric classification criteria for CNO by comparing clinical, laboratory and imaging features of CNO against mimicking conditions.
Methods: International multicentre collection of clinical and investigational features of cases with CNO or mimicker diseases with at least 12 months follow-up was conducted through a REDCap online database. Prevalence ratios of each collected item between CNO and mimickers were calculated. A p value of <.05 was considered significant.
Results: 450 cases were collected from 20 centers in 7 countries and 4 continents. Cases were filtered based on indicated confidence levels of diagnosis for CNO or mimickers using a cut-off of +/- 2 (moderately confident). 264 (59%) CNO cases and 145 (32%) mimicker controls were used for analysis. 41 (9%) cases were excluded. When compared to mimicker diagnoses, CNO patients were predominantly female, more frequently exhibited intermittent versus continued pain (especially of neck, back and upper torso), but less commonly had fever. Clavicular swelling was more common in CNO, while active arthritis was less common as compared to controls. CNO patients more frequently had whole body imaging (usually whole-body MRI). Symmetric patterns of bone lesions were more common in CNO. CNO frequently involved the thoracic spine, clavicle, sternum/manubrium, pelvic bones, bilateral femur, bilateral tibia, unilateral fibula, and foot bones. Imaging features concerning for infection or malignancy were less common in CNO. Lastly, complete and sustained response to antibiotic treatment is less frequent in CNO patients.
Conclusion: Using a case-based approach, key features of CNO were identified to support the development of classification criteria. Next steps will include expert panel discussions and a 1000Minds exercise.

Disclosure of Interest

Y. Zhao Consultant for: Novartis, R. Naden Consultant for: ACR/EULAR, M. Oliver: None declared, Z. Wang: None declared, E. Wu: None declared, C. Aguiar: None declared, J. Akikusa: None declared, O. Basaran: None declared, K. Cain: None declared, M. Capponi: None declared, N. Donaldson: None declared, E. Fox: None declared, A. Insalaco: None declared, A. Jansson: None declared, U. K. Akca: None declared, T. Lee: None declared, E. Marrani: None declared, K. Mahmood: None declared, E. Murray: None declared, F. Nuruzzaman: None declared, K. Onel: None declared, M. Pardeo: None declared, L. Potts: None declared, N. Rogers: None declared, A. Schnabel: None declared, G. Simonini Speaker Bureau of: Abbvie/Novartis, J. Soep: None declared, S. Stern: None declared, A. Theos: None declared, Y. Zhang: None declared, P. Ferguson Consultant for: Novartis, C. Hedrich Consultant for: Novartis, F. Dedeoglu Consultant for: Novartis, H. Girschick Consultant for: Novartis, R. Laxer Consultant for: Eli Lily Canada/Novartis/Sanofi, S. Ozen Consultant for: Novartis/SOBI

O003

Demographic features in a cohort of 101 childhood onset FMF patients with renal amyloidosis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O003

Introduction: AA Amyloidosis is the most severe complication of Familial Mediterranean Fever (FMF). Untreated amyloidosis is always progressive and typically leading to organ failure and death. Recently the rate of AA amyloidosis was reported as 8.6% in patients with a large cohort of FMF from Turkey.
Objectives: The primary aim of this study was to describe demographic, clinical, laboratory and genetic features of the patients with AA amyloidosis in a large number of childhood onset FMF patients.
Methods: In this case cohort study, patients were recruited from the nephrology and rheumatology outpatient clinics at GSM between September 2003 and February 2020. Patients who had AA amyloidosis were followed by a comprehensive patient-based registry. FMF-related AA amyloidosis was diagnosed with the positive staining pattern with Congo red dye.
Results: There were 195 patients diagnosed as amyloidosis in our registry. In total, 101 (65 males, 64.4%) of 195 patients with FMF related AA amyloidosis were diagnosed as FMF before 18-year-old.
Median age of FMF diagnosis was 13.0 (5.0-17.0) years, median age for diagnosis of amyloidosis was 21.0 (13.0-31.0) years and median age of the patients were 35.0 (20.0-49.0) years. Median (95% CI) elapse time between amyloidosis and diagnosis of FMF was 10.0 (9.3-10.6) years. Median follow up duration for our patients was 92.0 (65.0-101.0) months. Family history of FMF and amyloidosis were positive in 45 patients (44.6%) and 34 patients (33.7%), respectively.
The most common symptoms associated with the FMF episodes were fever (n=87, 86.1%), abdominal pain (n=72, 71.3%), arthritis (n=70, 69.3%), chest pain (n=65, 64.4%), vomiting (n=30, 29.7%), and mood disorder (n=26, 25.7%). Median serum hs-CRP level was 18 (9-95) mg/L (normal range <5mg/L) and median urine protein excretion was 5140 (3090-17000) mg/24 hours at the time of diagnosis for AA amyloidosis. A kidney biopsy was performed in all patients. Genetic screening showed that M694V (n=118, 61.4%) was the most common allele and M694V/M694V (n=48, 50%) was the most common mutation in our cohort. Eleven patients (10.9%) were died during the follow up due to myocardial infarction (n=9) and arrythmia (n=2). Five

patients (5%) had kidney transplantation and two patients (2%) were on dialysis. All patients had used colchicine but only 72 patients (71.3%) are on colchicine treatment currently. Twenty-eight patients were treated with biologic DMARDs (Anakinra in 12 patients (11.9%), Canakinumab in 16 patients (15.8%).
Conclusion: To the best of our knowledge, our cohort is the largest number of childhood onset FMF patients who developed AA amyloidosis. The positive family history of FMF and amyloidosis, presence of arthritis, high M694V allele frequency and elevated hs-CRP level are the most prominent findings in our cohort. FMF related AA amyloidosis is still major problem especially in the countries where the disease has high prevalence such as Turkey, Israel.

Disclosure of Interest
None declared

O004

Evaluation of the new classification criteria for PFAPA syndrome

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Introduction: Periodic Fever, Aphthous stomatitis, Pharyngitis and Cervical Adenitis (PFAPA) syndrome is characterized by regularly recurrent fever flares of early onset, accompanied by pharyngitis, cervical lymphadenopathy and oral aphthous ulcers. The diagnosis was based on the modified Marshall's criteria proposed in 1999. PFAPA is not a well-defined disease and shows a clinical overlap with inherited periodic fevers (IPF), such as Familial Mediterranean Fever (FMF), Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) and Mevalonate kinase deficiency (MVK) and Cryopyrine associated periodic syndrome (CAPS), for which a causative gene is well established. Recently new classification criteria for PFAPA and IPF have been developed during a consensus conference in Genoa in March 2017.
Objectives: To evaluate the performance of the new clinical criteria for PFAPA, FMF, MDK, TRAPS and CAPS on our cohort of patients with recurrent fever.
Methods: In the first part, we selected all patients with PFAPA, FMF, MDK, TRAPS, CAPS and UPF from 5 participating centers, and applied the new classification criteria for PFAPA. In the second part, we applied the five new sets of clinical criteria on a population of PFAPA and UPF patients from 2 centers. In the last part, we considered the 121 patients from our Swiss consultation and evaluated the clinical outcome.
Results: In the first part, we included 417 patients (187 PFAPA, 63 UPF, 12 MKD, 114 FMF, 29 TRAPS, 12 CAPS): 42% of them met 7 out of the 8 criteria to be classified as PFAPA. Based on these results, we calculated for the new PFAPA criteria a sensitivity of 80.2% and a specificity of 89.1%, and a good positive predictive value (85.7%). In the second part, we evaluated the overlap between PFAPA and the monogenic AID. We applied the five sets of criteria to 288 patients, classified by the clinician as PFAPA (n= 195) and UPF (n=93).

PFAPA (N=195)	41% PFAPA only	36% PFAP A+ MKD	10% MKD only	5% No criteria	3% FMF only	2% FMF+ MKD	1% PFAP A+ FMF	1% PFAPA+ MKD+FMF	1% PFAPA+ MKD+CAPS
UPF (N=93)	7% PFAPA only	14% PFAP A+ MKD	24% MKD only	27% No criteria	13% FMF only	3% FMF+ MKD	1% PFAP A+ FMF	3% PFAPA+ MKD+FMF	3% TRAPS only

In the third part, we evaluated the outcome in 121 patients followed in Lausanne for PFAPA (n=85) or UPF (n=36). In the PFAPA group, 88.1% had a remission of flares, 7.1% were stable and 4.8% had a flare increase. In the UPF group, 85.2% had a remission of flares, 7.4% were stable and 7.4% had a flare increase. Among all the different groups defined by the classification criteria there were no significant difference of the evolution.
Conclusion: The new criteria for PFAPA syndrome showed, when applied to a cohort of real-life patients, good sensitivity and specificity, and a good predictive value. However, when applying the 5 sets of clinical criteria to PFAPA and UPF patients, we found a large diagnostic overlap mainly between PFAPA and MKD. In the second part, we prove that when applied to patients of our cohort, the new clinical criteria were unable to distinguish PFAPA from MKD in about a third of our cohort. Clinical progression in patients with recurrent non-monogenic fever is generally favorable and is not different between the clusters.

Disclosure of Interest
None declared

O005

Gut microbiota profiling of children affected by chronic nonbacterial osteomyelitis (CNO): a potential role in the pathogenesis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O005

Introduction: Chronic non-bacterial osteomyelitis (CNO) is classified among autoinflammatory bone disorders but the exact etiology and pathogenesis are currently under investigation. The interplay between genetics, immunological and enviromental factors has been recognized as a possible causative factor so far. Emerging studies are suggesting that an altered ecology and function of microbiota (known as dysbiosis) can contribute to the occurrence or progression of a range of inflammatory diseases, affecting the balance between pro and anti-inflammatory immune responses. In a mouse model of CNO (cmo) dietary manipulation was accompanied with significant alterations of gut microbiome and significantly decreased of pro-IL-1β expression by distant neutrophils, thus resulting in protection from bone inflammation (gut-microbiota axis inflammasome).
Objectives: To assess the composition of gut microbiota in a cohort of CNO patients compared to healthy controls in order to assess its potential contribution to the pathogenesis of the disease.
Methods: In an observational cohort study, fecal samples were collected during follow up from 15 CNO patients (9 males) with a median age of 14.1 years (IQR 11.7-17.3). Four of them presented active disease at time of microbiota analysis. Microbiome maps were compared to samples from geographically- and age-matched healthy children. Gut microbiota ecology was determined by 16S ribosomal RNA-based metagenomics. Data were analyzed for their α- and β-diversity and differences in bacterial distribution were investigated by Mann Whitney and LEfSe assays.
Results: Microbiota richness, in terms of rare operational taxonomic units (OTUs), measured by the Shannon index, showed increased richness compared to healthy controls. In particular, ecological analysis revealed the presence of two distinct subjects' clusters, represented by CNO patients and healthy controls. The CNO group was characterized by a decrease of Verrucomicrobia and an increase of Actinobacteria. Especially, *Bacteroides*, *Odoribacter* and *Flavobacterium* were identified as potential microbial biomarkers for CNOs. Remarkably, the presence of *Prevotella* was only associated to the CTRL group.
Conclusion: This is the first study regarding the microbiome in CNO patients and our findings show evidence for clear dysbiosis and a

distinct beta-diversity profile in the CNO patients. The dysbiosis could actually lead to a pro-inflammatory status through the selection of specific bacterial strains associated with gut inflammation and immune response activation. These findings highlight the possibility of studying bacterial biomarkers associated with this disorder and might led to novel potential therapeutic strategies.

Disclosure of Interest
None declared

O006

Characterisation of a group of patients with PSTPIP1-associated inflammatory syndrome

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Introduction: PSTPIP1-associated inflammatory syndrome (PAID) results from mutations in the *PSTPIP1* gene and is characterized by a range of clinical phenotypes and variable expressivity. Most mutations of *PSTPIP1* lead to pyogenic phenotype. Yet, mutation c.748G>A(p.E250K) often leads to hematological symptoms associated with a variable degree of autoinflammation. Complex pathogenesis of PAID and its diverse clinical features lead to diagnostic and therapeutic challenges.
Objectives: To analyze clinical features, laboratory data and response to therapy of a group of patients with c.748G>A(p.E250K) *PSTPIP1* mutation.
Methods: We characterize 9 patients (4 females, 5 males, median age 14 years (range 3–42 years) from 6 unrelated families with the c.748G>A(p.E250K) *PSTPIP1* heterozygous mutation identified via customized panel next generation sequencing (NGS) and confirmed by Sanger sequencing.
Results: Median age at disease onset was 1 years (range birth–10 years). Most patients had various manifestations characteristic of autoinflammatory syndrome: 7/9 patients had recurrent fever; 6/9 – osteoarticular symptoms (arthralgia, arthritis, osteomyelitis, synovitis), 7/9 – dermatological symptoms (abscesses, acne, gangrenous pyoderma, vasculitis), 7/9 - lymphoproliferation, 2/9 - hepatomegaly and 4/9 - gastrointestinal symptoms. All patients had increased laboratory inflammatory markers. Yet, most patients also had a variety of hematologic abnormalities: anemia was present in 2/9 patients, neutropenia – in 1/9, pancytopenia – in 4/9, anemia and neutropenia – in 2/9, myelodysplastic syndrome - 1/9, hemophagocytic lymphohistiocytosis – in 1/9.
Tumor necrosis factor-α (TNF) inhibitor therapy was successful in 1/7 cases, had partial effect in 5/7 cases and no effect – in 1/7 cases. In responders TNF inhibitors alleviated the inflammatory symptoms but not hematologic features (Table 1).
IL-1 inhibitors, steroids, JAK inhibitors were not effective in any of the patients treated. Combination of an IL-6 inhibitor and JAK inhibitor had partial effect in two patients.
Hematopoietic stem cell transplantation (HSCT) was performed in 3 patients. Two patients are now 2 and 2,5 years post-HSCT, with mostly donor chimerism and complete absence of the disease symptoms, one patient had early graft rejection, and is 42 days after second HSCT, with full donor chimerism and alleviation of the disease symptoms.
Conclusion: Patients with p.E250K *PSTPIP1* mutation have frequent hematological manifestation different from the rest of the PAID patients and represent a therapeutic challenge. HSCT might be a viable treatment option.

Disclosure of Interest
None declared

O007

Baseline characteristics of an international longitudinal cohort of 1012 FMF patients from the Eurofever registry

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Pediatric Rheumatology 2020, **18(Suppl 2):**O007

Table 1 (abstract O006). Treatment of patients with PSTPIP1-associated inflammatory syndrome

Therapy	Patient (n)	Response		
		Full	Partial	No effect
Steroids	4	0	0	4
Anti-TNFα (adalimumab, infliximab)	6	1	4	1
Anti-TNFα (infliximab)+ Steroids	1	0	1	0
Anti-IL1 (anakinra)	1	0	0	1
Anti-IL6 (tocilizumab)	3	0	0	3
IVIG	4	0	2	2
Methotrexat	2	0	1	1
Sirolimus	3	0	2	1

Introduction: A new classification of pathogenicity of genetic variants associated to hereditary recurrent fevers[1] is available. The new Eurofever/PRINTO classification criteria (EPCC)[2] combine clinical manifestations with genotype.
Objectives: To describe the baseline characteristics of a longitudinal international cohort of familial Mediterranean fever (FMF) patients (pts) enrolled in the Eurofever registry and to evaluate the impact of EPCC criteria and new classification criteria for the pathogenicity of MEFV variants
Methods: We reviewed baseline demographic, genetic and clinical data of FMF pts included in the Eurofever registry. EPCC criteria were applied to the population. All MEFV variants were classified according to ref. 1.
Results: Since November 2009, 1175 FMF pts from 119 centers were enrolled in the registry. Clinical information was available for 1012 pts (532 males/480 females, 827 children/185 adults). For 125 pts clinical and genetic data mandatory for the application of EPCC were missing. Among the 887 remaining pts 623 (70.2%) satisfied EPCC (EPPC+), while 264 (29.8%) did not (EPPC-). Most of the EPCC- pts (172, 65.1%) displayed negative or non-informative genetics (monoallelic or biallelic benign variants, monoallelic VOUS). Eighty-nine (33.7%) and 3 (1.1%) pts with monoallelic and biallelic pathogenic variants respectively lacked FMF-associated clinical manifestations for EPCC
The differences in clinical manifestations between the EPCC+ and EPCC- pts are shown in Table 1. In EPPC+ group, the frequency of South-east Mediterranean ethnicity was higher.
At baseline 68.5% pts were treated with colchicine (438 EPCC+, 212 EPCC-). NSAIDs and steroids on demand were used in 30.8% and 16.9% in EPCC- and in 21.1% and 8.3% in EPPC+ pts respectively. Anti-IL1 treatment was used in 41 (4.1%) pts , without significative differences between the two groups.
Conclusion: The combination of EPCC and the new pathogenic variant classification criteria captured the majority of FMF pts in the Eurofever cohort in a homogeneous group. The longitudinal evaluation of EPCC+ and EPCC- pts will provide clues on the overall long-term outcome with particular interest for the efficacy, safety and tolerability of different treatments.

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2 Gattorno M, et al. Classification criteria for recurrent fevers Ann Rheum Dis 2019;78:1025–1032. doi:10.1136/annrheumdis-2019-215048

Aknowlegments
This research was financially supported by Novartis AG.

Disclosure of Interest
M. Bustaffa: None declared, I. Koné-Paut: None declared, S. Ozen: None declared, G. Amaryan: None declared, E. Papadopoulou-Alataki: None declared, R. Gallizzi: None declared, M. Carrabba: None declared, Y. Butbul Aviel: None declared, L. Cantarini: None declared, M. Alessio: None declared, J. Anton Consultant for: Novartis, Sobi, Speaker Bureau of: Novartis, Sobi, L. Obici: None declared, F. Gok: None declared, E. Batu: None declared, E. Moreno: None declared, P. Brogan: None declared, M. Trachana: None declared, G. Simonini Speaker Bureau of: Abbvie, Novartis, D. Rigante: None declared, M. Gattorno Consultant for: Novartis, Sobi, Speaker Bureau of: Novartis, Sobi, L. Rossi-Semerano : None declared

Table 1 (abstract O007). Clinical features

	Whole FMF population (887 pts)	EPCC+ (623)	EPCC- (264)	p
High risk ethnicity (South-East Mediterranean)	360	297 (47.7%)	63 (23.9%)	< 0.0001
Duration of episodes, median (25^{th} – 75^{th} p)	3 (2-3)	3 (2-3)	4 (2-4)	< 0.0001
Abdominal pain	845 (83,4%)	589 (94,5%)	166 (62,9%)	< 0.0001
Chest pain	373 (36,9%)	308 (49,8%)	39 (14,8%)	< 0.0001
Arthritis	246 (24,3%)	186 (29,9%)	38 (14,4%)	< 0.0001
Arthro-myalgia	527 (52,1%)	355 (45,1%)	355 (56,9%)	NS
Erysipela-like rash	85 (8,4%)%	72 (11,7%)	5 (1,9%)	< 0.0001
Amyloidosis	6 (0,7%)	3 (0,05%)	3 (1,1%)	NS

O008

The level of interferon alpha protein in distinct interferonopathies provides clues to the observed differential tissue involvement

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Pediatric Rheumatology 2020, **18(Suppl 2):**O008

Introduction: Whilst, by definition, up-regulation of type I interferon (IFN) signalling is common to the type I interferonopathies (T1Is), disease expression varies across this set of diseases, the basis of which remains unclear.
Objectives: To compare the levels of IFN-alpha in the cerebrospinal fluid (CSF) and serum in distinct IFN-related diseases.
Methods: We collected CSF and serum from patients with the known T1Is Aicardi-Goutières syndrome (AGS) and STING-associated vasculopathy with onset in infancy (SAVI), from individuals with presumed monogenic T1Is (pT1I), from cases of childhood-onset neuropsychiatric systemic lupus erythematosus (nSLE), and from children with non-IFN related auto-inflammation (AI) and non-inflammatory hydrocephalus (as controls). We measured IFN-alpha protein using digital-ELISA.
Results: Eighty-four and 60 measurements were recorded respectively in CSF and serum of 42 patients and 6 controls. In an intergroup comparison of the CSF data (taking one sample per analysed individual), the median level of CSF IFN-alpha was elevated in AGS, SAVI, pT1I and nSLE compared to AI and controls, with levels highest in AGS compared to all other groups. In AGS, CSF IFN-alpha concentrations were higher than in paired serum samples. In contrast, serum IFN was consistently higher compared to CSF levels in SAVI, pT1I and nSLE.
Conclusion: Whilst IFN-alpha is present in the CSF and serum of all IFN-related diseases studied here, the primary sites of IFN production in AGS and SAVI are, respectively, the CNS and the periphery. These data likely reflect tissue specificity in the expression, or biological redundancy, of the mutated gene, and/or in the generation of the endogenous self-nucleic acid ligands presumed to trigger the observed IFN response.
We thank ImmunoQure AG for sharing antibodies.

Disclosure of Interest
L. Lodi: None declared, I. Melki: None declared, V. Bondet: None declared, L. Seabra: None declared, G. I. Rice: None declared, E. Carter: None declared, A. Lepelley: None declared, M. J. Martin-Niclós: None declared, B. Al-Adba: None declared, B. Bader-Meunier: None declared, M. Barth: None declared, T. Blauwblomme: None declared, C. Bodemer: None declared, O. Boespflug-Tanguy: None declared, R. Dale: None declared, I. Desguerre: None declared, C. Ducrocq: None declared, F. Dulieu: None declared, C. Dumaine: None declared, P. Ellul: None declared, A. Hadchouel: None declared, V. Hentgen: None declared, M. Hié: None declared, M. Hully: None declared, E. Jeziorski: None declared, R. Lévy: None declared, F. Mochel: None declared, B. Neven: None declared, S. Orcesi: None declared, S. Passemard: None declared, M. Pouletty: None declared, P. Quartier: None declared, F. Renaldo: None declared, R. Seidl: None declared, S. Blanche: None declared, D. Duffy: None declared, Y. J. Crow Consultant for: Y.J.C discloses consultancy work with Biogen on behalf of the University of Edinburgh, M.-L. Frémond: None declared

O009

Standardizing care and fostering systemic autoinflammatory disease (SAID) research through the carra autoinflammatory disease network

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Pediatric Rheumatology 2020, **18(Suppl 2):**O009

Introduction: International registries have significantly enhanced the understanding of the genetics, phenotype, prognosis, and treatment of Systemic Autoinflammatory Diseases (SAIDs) but largely lack a genetically heterogeneous Northern American cohort.
Objectives: To explore developing a Childhood Arthritis and Rheumatology Research Alliance (CARRA) Autoinflammatory Disease Network.
Methods: A team within CARRA of rheumatologists, ID physicians, immunologists, otolaryngologists, geneticists, parents/patients, and members of the Autoinflammatory Alliance met in person and via teleconferences to discuss the benefits of SAIDs networks. A literature search using keywords such as "EuroFever", "pharmacosurveillance", and "autoinflammatory registry" was reviewed to identify stakeholders and methods for establishing clinics. Physicians who were involved in establishing SAIDs programs shared their experiences. To explore the feasibility of and need for this network, 17 physicians from different sites approximated total patient numbers seen in their programs, as determined by ICD-10 codes when available.
Results: The workgroup participants agreed by consensus that a CARRA Autoinflammatory Disease Network would be instrumental to improve clinical care, enhance research, facilitate international collaboration, and improve patient and family involvement in research planning. The literature search highlighted the benefits of this approach in rare diseases in preventing diagnostic delay, understanding the epigenetics of SAIDs, and providing an opportunity for pharmacosurveillance in a cohort of patients exposed to biologics in a real world setting. Data was collected from 17 sites in the US, Canada, Israel, and Ukraine, to assess the number of potential patients this network could reach. Collectively these sites (~10% of CARRA sites) care for 2493 SAID patients, including 1029 coded with periodic fever syndromes, 81 with CAPS, 786 with other defined SAIDs (including PFAPA), 160 with undefined SAIDs, and 437 with CNO/CRMO. We found significant variability in how ICD-10 codes were utilized among this small survey of US centers. ICD-10 codes were not necessarily in concordance with the physicians' diagnosis.
Conclusion: CARRA physicians manage thousands of patients in North America with SAIDs, which emphasizes the need for a CARRA Autoinflammatory Disease Network to facilitate earlier diagnoses, education, and access to expert and multidisciplinary quality care. This network will also create an infrastructure for clinical and translational research. Future work will focus on characterizing the patients seen across CARRA Registry sites. Given the genetically diverse populations in North America, an autoinflammatory network built around the CARRA Registry would facilitate collaborations with international colleagues to benefit patients worldwide.

Disclosure of Interest

G. Schulert Consultant for: Novartis and SOBI, J. Cherion: None declared, T. Wampler Muskardin Consultant for: Novartis and Regeneron, M. Twilt: None declared, S. Akoghlanian: None declared, G. Amarilyo: None declared, D. Dissanayake: None declared, K. Durrant: None declared, P. Ferguson Consultant for: Novartis, M. Gutierrez: None declared, L. Harel: None declared, J. Hausmann: None declared, M. Heshin-Bekenstein: None declared, R. Laxer: None declared, A. Lenert: None declared, S. Li: None declared, G. Licameli: None declared, G. Lionetti: None declared, I. Michelow: None declared, L. Moorthy: None declared, E. Propst: None declared, V. Saper: None declared, H. Srinivasalu: None declared, A. Thatayatikom: None declared, L. Tucker: None declared, P. Wright: None declared, C. Yildirim-Toruner: None declared, F. Dedeoglu Consultant for: Novartis, S. Lapidus: None declared

O010

Evaluation of the thyroid disorders in children with familial mediterranean fever

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Pediatric Rheumatology 2020, **18(Suppl 2):**O010

Introduction: Autoimmune thyroid diseases is the most frequent organ-specific autoimmune disease. Although it is well-known that autoimmune thyroid diseases are more common in most of the autoimmune connective tissue diseases, the relationship between autoinflammatory diseases like familial Mediterranean fever (FMF) and autoimmune thyroid diseases has not well-evaluated yet and still remains unclear.
Objectives: The objective of this study was to evaluate the frequency of autoimmune diseases of the thyroid gland in children with FMF.
Methods: A total of 133 children aged <18 years with FMF and 70 healthy controls were included in the study. Thyroxine (fT4), thyroid stimulating hormone (TSH), thyroid peroxidase (TPO) and thyroglobulin (TG) antibodies, and thyroid ultrasound findings of all participant were evaluated.
Results: One hundred thirty-three patients with FMF [72 female and 61 male] and 70 healthy controls (n=40 female/30 male) were enrolled in the study. The mean free T4 levels of the patients and control groups were 1.25 ± 0.13 ng /ml and 1.35 ± 0.27 ng / mL, respectively (p=0.20). The mean TSH levels were 2.86 ± 1.72 mcU / mL in patients group and 3.1 ± 1.55 mcU / mL in control group. There was no statistical difference in TSH values between two groups (p=0.76) (**table1**)
There were five patients with increased levels of antibodies (2 of them positive for anti TPO and 3 of them positive for both of the antibodies) in patients with FMF and all of them were euthyroid. Four of these patients with high autoantibodies were pubertal and 1 of them were prepubertal. Two cases of control group had positive thyroid antibodies and they were euthyroid, too. Heterogeneity in thyroid parenchyma was observed in 1 of 5 patients with high autoantibodies in patients with FMF and 1 of 2 patients with high autoantibodies of the control. Thus, the frequency of Hashimoto's thyroiditis was 0.7 % in the cases with FMF and 1,2 % in control group.
In the FMF group, one patient had overt hypothyroidism and 5 patients had subclinical hypothyroidism. In the control group, subclinical hypothyroidism was detected in 3 patients and overt hypothyroidism was detected in 2 patients. The antibodies of the patients with overt and subclinical hypothyroidism in both groups were negative and the ultrasound findings were normal.
Conclusion: Although the relationship between thyroid abnormalities and FMF has been reported before, we did not find a deterioration in thyroid functions in children with FMF. Our results suggest that there is no need for routine screening of serum thyroid function tests and thyroid antibody levels in patients with FMF in the absence of clinical symptoms or family history.

Disclosure of Interest

None declared

Table 1 (abstract O010). The comparison of the thyroid function tests and the ultrasound findings of the patient group and the healthy controls

	Patient group (n=133) (mean ± SD) / n (%)	Control group (n=70) (mean ± SD) / n (%)	p value
Mean age (years)	11.09 ± 4.19	10.4 ± 4.4	0,776
Thyroid stimulating hormone (mcU / mL)	2.86 ± 1.72	3.1 ± 1.55	0,76
Free thyroxine (ng /ml)	1.25 ± 0.13	1.35 ± 0.27	0,20
Anti-TPO† or/and Anti-Tg‡ positivity	5 (3.7)	2 (2.8)	0,718
Mean volume of right lobe	3,39±0,92	2,84±1,1	0,125
Mean volume of left lobe	2,8±1,2	2,6±0,78	0,431
Subclinical hypothyroid	5 (3,7%)	1 (1,25%)	0,340
Overt hypothyroid	3 (2,25%)	2 (2,5%)	0,916

O011

Galectin-3: a new biomarker for differentiating PFAPA (periodic fever, adenitis, pharyngitis, aphthous stomatitis) syndrome from familial mediterranean fever

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Pediatric Rheumatology 2020, **18(Suppl 2):**O011

Introduction: Periodic fever, aphthosis, pharyngitis, and adenitis (PFAPA) syndrome is an autoinflammatory recurrent fever syndrome of early childhood. In regions endemic for familial Mediterranean fever (FMF), differentiating PFAPA syndrome from FMF could be challenging in some cases. Galectin-3 is a lectin with regulatory functions in apoptosis and inflammation.
Objectives: We aimed to test whether galectin-3 could be a biomarker for differentiating PFAPA syndrome from FMF.
Methods: Patients with PFAPA syndrome, FMF, cyropyrin-associated periodic syndrome (CAPS), and streptococcal pharyngitis were included in this cross-sectional study along with healthy controls. Serum galectin-3 levels were measured using enzyme-linked immunosorbent assay.
Results: Ninety-three patients (42 patients with PFAPA, 39 with FMF, 8 with CAPS, and 4 with streptococcal pharyngitis) and 17 healthy controls were included. Blood samples were drawn during attacks from 23 PFAPA and 7 FMF patients, and during attack-free periods from 24 PFAPA, 35 FMF, and 8 CAPS patients. The median serum galectin-3 level in the PFAPA attack group (1.117 ng/ml) was significantly lower than the levels in healthy control (2.367 ng/ml), streptococcal pharyngitis (3.021 ng/ml), FMF attack (2.402 ng/ml), and FMF-attack-free groups (2.797 ng/ml) (p=0.005, 0.04, 0.01, and <0.001, respectively). PFAPA attack-free group also had lower galectin-3 levels compared to FMF attack-free group (1.571 vs. 2.797 ng/ml, respectively; p=0.008). Serum galectin-3 levels did not differ significantly between CAPS patients and attack-free PFAPA patients (1.439 ng/ml vs. 1.571 ng/ml, respectively; p=0.78).
Conclusion: Galectin-3 may serve as a biomarker to differentiate PFAPA syndrome from FMF. Further studies with larger number of patients could validate its role as a biomarker.

Disclosure of Interest
None declared

O012

Long-term effectiveness of canakinumab in aid – interim analysis of the CAPS subgroup from the reliance registry

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Pediatric Rheumatology 2020, **18(Suppl 2):**O012

Introduction: In the treatment of monogenic autoinflammatory diseases (AID), a heterogeneous group of diseases with excessive interleukin (IL)-1ß release and severe systemic and organ inflammation, the anti-IL-1 inhibitor canakinumab (CAN) has been associated with rapid remission of symptoms in clinical trials as well as in real-life[1,2].
[1]Lachmann et al. N Engl J Med. 2009;360(23):2416-25
[2]Kuemmerle-Deschner et al. Rheumatology (Oxford). 2016;55(4):689-96
[1]Lachmann et al. N Engl J Med. 2009;360(23):2416-25
[2]Kuemmerle-Deschner et al. Rheumatology (Oxford). 2016;55(4):689-96
[3]De Benedetti et al. N Engl. J Med. 2018;378(20):1908-1919
Objectives: The aim of the Reliance registry is to explore long-term effectiveness and safety of CAN under routine clinical practise conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndromes, including Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal onset multisystem inflammatory disease (NOMID)/chronic infantile neurological cutaneous and articular syndrome (CINCA), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).
Methods: This prospective, non-interventional, observational study is based in Germany with a 3-year follow-up and enrolls pediatric (from 2 years) and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD routinely receiving CAN. In 6-monthly visits, clinical data and patient-reported outcomes are assessed. Study endpoints are long-term effectiveness and safety of CAN. Here, the CAPS cohort was analyzed.
Results: This 18-month interim-analysis includes 78 CAPS patients (49% females) enrolled by September 2019. Mean age at baseline was 25 years and mean duration of prior CAN treatment was 5.7 years. 64 patients (82%) had MWS, 2 FCAS, 7 NOMID/CINCA, 3 atypical CAPS and 2 lacked subtype diagnosis. Disease activity, fatigue and social impairment by patients' assessment, days absent from school/work, inflammatory markers, and remission by physician assessment were evaluated at 6-monthly intervals starting at baseline with last update at 18 months of follow-up (table 1). The results demonstrate sustained remission and disease control as evaluated parameters remained stable over time. Serious adverse events were reported for 10 patients including papillitis, pyrexia, chest pain, tonsillitis, appendicitis, circulatory collapse, skin disorders, TIA, and preterm delivery.
Conclusion: The 18-month interim analysis of the RELIANCE study, the longest running real-life CAN registry, demonstrates that long-term CAN treatment is safe and effective in CAPS patients.

Disclosure of Interest
J. Kuemmerle-Deschner Consultant for: Novartis, AbbVie, SOBI, Speaker Bureau of: Novartis, AbbVie, Sobi, B. Kortus-Götze Speaker Bureau of: Novartis, M. Borte: None declared, I. Foeldvari Consultant for: Novartis, G. Horneff Speaker Bureau of: Abbvie, Chugai, Roche, Novartis, Pfizer, MSD, Bayer, A. Janda: None declared, T. Kallinich Speaker Bureau of: SOBI, Roche, CSL, Novartis, P. Oommen: None declared, C. Schuetz: None declared, F. Weller-Heinemann Speaker Bureau of: Novartis, J. Weber-Arden Employee of: Novartis, N. Blank Speaker Bureau of: SOBI, Novartis

Table 1 (abstract O012). See text for description

	Baseline	6 months	12 months	18 months
Number of patients, N	78	51	42	29
Mean age, years (SD)	25 (4; 79)	22 (4; 79)	20 (4; 58)	22 (4; 54)
Patient's assessment of disease activity 0-10, mean (min; max)	2.2 (0; 7)	1.8 (0; 7)	2.4 (0; 7)	2.8 (0; 8)
Patient's assessment of fatigue 0-10	2.9 (0; 9)	2.4 (0; 8)	2.8 (0; 8)	1.7 (0; 7)
Number (%) of patients without impairment of social life by disease	16 (49)	29 (76)	20 (61)	14 (67)
Number (%) of patients with days absent from school/work	25 (32.5)	11 (22)	14 (34)	15 (52)
Inflammatory markers, CRP/SAA, mean (mg/dL)	0.4 3.2	0.4 2.1	0.3 0.8	0.2 0.5
Number (%) of patients in disease remission (physician assessment)	55 (72)	38 (76)	29 (71)	22 (76)

O013

Clinical, diagnostic and therapeutic features of children with chronic non-bacterial osteomyelitis (CNO) – an analysis of the German National Pediatric Rheumatologic Database 2009-2018

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Pediatric Rheumatology 2020, **18(Suppl 2):**O013

Introduction: An analysis of data was performed, investigating clinical, diagnostic and therapeutic features of juvenile patients with CNO.
Objectives: The objective of this investigation was to collect data of clinical and diagnostic features of patients with CNO during the first year of disease course.
Methods: Patients with diagnosis of CNO, disease duration < 13 months and a first registration into the National Pediatric Rheumatologic Database (NPRD) between 2009 and 2018 were included in this cross-sectional analysis. The data analyzed, included age, gender and routine laboratory parameters. Skin involvement as well as clinical and radiological data was documented in addition to therapeutics applied. Well-being and pain were assessed via numerical rating scales (NRS) and the functional ability by the C-HAQ.
Results: Of 774 documented patients, 62.8 % are female with a median age of 11 years. Symptoms at first visit included fever (>38°C) in 77/593 patients (13.0 %) and CRP > 1 mg/dl in 107/593 patients (18.0 %). HLA-B27 was positive in 48 patients (7.4 %), while the mean ESR was 12 mm/h. 14.8 % of the patients showed skin involvement, most of them psoriasiform. In 406 cases, X-ray was performed at the first visit, showing osteosclerosis/ -lysis in 34 % and hyperostosis in 14.5 % of the cases. In 177/406 patients, no changes were detected in conventional X-rays. MRI scan was performed in 648 cases, and 81.5 % showed a positive T2 signal. In 589 patients, clinical active lesions were documented, most frequently affected sites were tibia (29,7 %), pelvis (28,0 %) and femur (27,8 %). The spine was affected in 96 individuals (16.3 %). 48.2 % showed monofocal lesions, 6.5 % presented with 6 or more. In most patients, radiologically active lesions corresponded to the clinical sites. Main locations were tibia, pelvis and femur in 36,5 %, 32,5 %, and 31,2 %, respectively. Therapeutically, 78.2 % of the patients received nonsteroidal anti-inflammatory drugs (NSAIDs), 6.2 % glucocorticoid treatment, 10.8 % of the patients (71/657) obtained disease modifying anti-rheumatic drugs (DMARDs) (methotrexate 4.4 %, sulfasalazine 3.7 %, etanercept 1.4 %) and 5.2 % bisphosphonates at the time of documentation. The evaluation of the patient`s questionnaire showed pain VAS (0-10) of 2.0, C-HAQ (range 0-3) of 0.13 and overall well-being (NRS 0-10) of 2.0. Diagnostic criteria for enthesitis-related arthritis are fulfilled in 16/672 patients (2.4 %).
Conclusion: To our knowledge, the NPRD cohort presents the largest cohort of children suffering from CNO. Clinical and diagnostic parameters of these patients at disease-onset and in the first year of disease course were analyzed. At initial presentation one third of the patients presented with clinical symptoms (fever, local redness and/or elevated inflammatory markers (CRP, ESR)). Conventional X-ray scans did not show any changes in almost 50 %, but more than 80% showed positive T2-signaling in the MRI. Most patients were treated with NSAIDs, only a small group received additional therapies like conventional or biological DMARDs, steroids or bisphosphonates.
In contrast to adult SAPHO patients during the first year of treatment, pediatric patients did not present with diagnostic criteria consistent with enthesitis-related arthritis (ERA). Evaluating the patients' questionnaires concerning QoL, no strong impairment due to CNO could be shown.

Disclosure of Interest
None declared

O014

Paediatric sarcoidosis: phenotype of a retrospective cohort of biopsy-proven patients

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Pediatric Rheumatology 2020, **18(Suppl 2):**O014

Introduction: Paediatric sarcoidosis is a multisystemic inflammatory condition characterised by the formation of non-caseating granulomata that may lead to end-organ damage. Diagnosis is challenging as a compatible clinical-radiographic presentation with histopathologic confirmation is needed. Caution must be exercised to exclude granulomata of infectious aetiology as well as those seen in immunodeficiencies associated with immune dysregulation. Little is known about this rare disease's presentation and outcome in children. We report a retrospective cohort of children with biopsy-confirmed sarcoidosis.
Objectives: To describe the phenotype of children with biopsy-proven sarcoidosis, their treatment and the course of the disease on various treatments.
Methods: Patients' notes were reviewed retrospectively, and multisystem involvement identified. We included patients with biopsies consistent with sarcoidosis or granulomatous inflammation which were performed or reviewed at our centre between 2010 and 2020. Excluded were gut biopsies, samples suggestive of an infectious diagnosis and immunodeficiencies with immune dysregulation.
Results: We identified 42 children with biopsy-proven sarcoidosis. Mean age at diagnosis was 9.4 years; male to female ratio 0.68. Twenty-seven patients were of Afro-Caribbean descent, 7 Asian, 5 Caucasian and 1 of mixed race. Tissues biopsied included lymph node, skin, kidney, liver, lung, submandibular, lacrimal and salivary gland, eye, spleen, bone, brain and synovium.
28 patients had lymphadenopathy, 16 glandular involvement (13 parotid, 16 other glands including submandibular, lacrimal, thyroid), 17 liver, 17 pancreas, 13 renal (including 3 with nephrocalcinosis), 11 spleen, 27 skin, 14 lung involvement, 11 arthritis, 4 tenosynovitis, 3 hearing loss, 2 bone, 1 cerebral, and 25 eye involvement (including 19 with uveitis).
Remarkable laboratory findings were as follows: 9 patients had hypercalcaemia, 16 raised amylase, 4 raised lipase and 30 raised ACE levels; 12 patients had abnormal renal function, 13 abnormal liver function. 13 patients were tested for NOD2 mutations, which were present in 5.
38 patients received treatment for sarcoidosis. Of those, 37 received steroids, 16 intravenous followed by oral steroids, 18 oral steroids only and 18 received steroid eye drops; 36 patients received disease-modifying antirheumatic drugs (DMARDS) including 26 methotrexate, 11 mycophenolate mofetil and 10 azathioprine; 4 patients received hydroxychloroquine, 5 cyclophosphamide; 10 received biologic therapy including 9 anti-TNF, 2 interleukin-1 blockade, one JAK inhibitor, one IL-6 blocker and 1 rituximab.
All patients had a good response to steroids, and most responded to methotrexate. The treatment of a subset of patients was escalated to include anti-TNF treatment, owing to grumbling disease activity. Although most of the patients were able to wean off regular steroids, the majority remained on long-term DMARDS to maintain disease control.
Conclusion: Our study suggests that non-necrotizing granulomatous inflammation on biopsy, multiorgan involvement, response to steroids and chronic course appear to be the hallmarks of paediatric

sarcoidosis. DMARDs, in particular methotrexate, were used with efficacy. When response was partial, addition of an anti-TNF was efficacious at controlling the disease, particularly in ocular sarcoidosis. Additional organ involvement occurs over time when the disease is not fully controlled. However, no biomarkers are available to assess disease activity apart from ACE, which does not appear sensitive enough. Prospective cohort studies are needed to define this rare paediatric disease.

Disclosure of Interest
None declared

O015

Transition readiness assessment from pediatric to adult services in rheumatic diseases

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Pediatric Rheumatology 2020, **18(Suppl 2):**O015

Introduction: Pediatric rheumatic diseases are chronic illness, which requires special and continuity of health care throughout adulthood. The transition of care should be developed and adjusted according to the readiness of each child, so the individualized readiness assessment should be performed before transferring patients to adult care. Transition Readiness Assessment Questionnaire (TRAQ) is one of the validity and reliability tools, which is used for the assessment of transition-related skills in patients with chronic illness. Although TRAQ had been used in previous studies in European countries, there is limited data in pediatric rheumatic diseases especially in Asian countries, where cultural differences. Therefore, the development of a validated and reliable tool in the Thai language is needed.
Objectives: To cross-culturally adapt and validate Thai version of TRAQ and assess transition readiness in pediatric rheumatic diseases in Thailand.
Methods: This is a cross-sectional study design. TRAQ was translated into the Thai language and adapted to Thai culture and lifestyle. Forward translation and backward translation were performed by three different translators. After completing the translation process, the TRAQ was validated for the final version. Then the TRAQ Thai version was completed by participants aged 15 – 24-year-old, who was diagnosed with rheumatic diseases. The demographic data, including age, sex, socioeconomic status, diagnosis, duration of disease, medication, and disease activity were reviewed from medical records. Descriptive analysis and logistic regression analysis were used in this study.
Results: A total of 123 participants were included in this study. The mean age was 17.81 ± 2.19 years. The mean TRAQ score was 3.90 ± 0.68. There were significantly higher TRAQ scores in participants, who involved these parameters; 1) aged more than 18 years, 2) education in a Bachelor's degree program, 3) a transition clinic attendance, 4) a transition discussion with the doctor, and 5) an independent clinic visit (table 1). In multivariate analysis, a higher education level and an independent clinic visit were predictors for a higher TRAQ score with OR 4.64, 95%CI (1.68 – 12.80) and 4.07, 95%CI (1.35 – 12.22), respectively. The appointment keeping and tracking health issues were two domains in the questionnaire that had a lower score than others. Inactive disease status and dependent visit were factors that associated with participants, who had lower scores in these 2 domains, with OR 5.60, 95%CI (1.20 – 26.14) and 4.13, 95%CI (1.60 – 10.67), respectively.
Conclusion: The Thai version of TRAQ was validated in rheumatic disease populations with good performance. Patients, who had a higher education level and visited the clinic on their own, had a higher chance of successful transit to adult care.

Disclosure of Interest
None declared

Table 1 (abstract O015). Comparison of TRAQ score in different parameters

Parameters	TRAQ score (mean ± SD)		*P* value
	Yes	No	
Age ≥ 18 years	4.26 ± 0.42	3.70 ± 0.71	< 0.01
Education in a Bachelor's degree program	4.30 ± 0.35	3.76 ± 0.71	< 0.01
Transition clinic attendance	4.30 ± 0.50	3.85 ± 0.69	0.03
Receiving transition discussion	4.15 ± 0.56	3.80 ± 0.69	0.04
Independent clinic visit	4.32 ± 0.53	3.78 ± 0.67	< 0.01

O016

Early implementation of treatment with etanercept increases the likelihood to achieve remission

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Pediatric Rheumatology 2020, **18(Suppl 2):**O016

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease in children and adolescents. A consistent therapy is required to avoid consequential damage and permanent loss of function. Biologic disease modifying anti-rheumatic drugs (bDMARDs) provide a well-accepted option for treatment of patients with a severe course of JIA. Etanercept (ETA) is still the most commonly prescribed bDMARD for JIA in Germany.
Objectives: To analyze adherence to treatment with ETA with special attention on discontinuation after achieving an inactive disease and recurrence of active disease after ETA withdrawal.
Methods: Data from two ongoing prospective, multicenter, non-interventional registries BiKeR and JuMBO were used for the analysis. JuMBO is the follow-up study to BiKeR and follows patients who have reached the age of 18. Both registers provide treatment data, individual trajectories of clinical data and outcomes from childhood into adulthood in JIA patients treated with bDMARDs and csDMARDs. Clinical disease characteristics, such as disease activity, were reported by the rheumatologists in addition to patient-reported outcomes at each six-months follow-up. Start and end dates for DMARDs as well as reasons for discontinuation were reported by the rheumatologists. Remission was defined as inactive disease defined by the Wallace Criteria.
Results: Data from 2,500 patients who were included in BiKeR and had an age ≥18 at the time of analysis were considered. A subset of 1,535 were enrolled in JuMBO. The mean follow-up was 8.6 (SD 4.2) years for the JuMBO patients. The majority of them had polyarthritis (35%), followed by enthesitis-related arthritis (20%). A total of 1,779 (68.8% of 2,584) patients were ever treated with ETA, providing 2,178 ETA treatment courses. There were 1,724 (67%) patients with first, 338 patients with a second and 54 with a third course of ETA treatment course. 710 (41.2%) discontinued ETA by ineffectiveness in the first course with similar rates of discontinuation due to ineffectiveness in the first and second course. A total of 332 (+/-MTX, 19.3%) discontinued ETA after achieving remission in the first ETA course. Among those, 129 (38.9%) patients did not require treatment with any other bDMARD subsequently until last follow-up (3.9 years, SD 3.5), while 169 (50.9%) re-started treatment with ETA, 14 (4.2%) with adalimumab and 4 with other bDMARDs. The likelihood of discontinuing ETA due to an inactive disease was positively associated with a younger age (hazard ratio (HR) 1.08, p<0.001), persistent oligoarthritis (HR 1.89, p=0.004), a shorter duration between JIA onset and ETA start (HR 1.10, p<0.001) as well as a good response to therapy within the first six months of treatment (HR 1.11, p<0.001). 209 (of

332) had ETA monotherapy at withdrawal. Of those, 77% (n=161) experienced recurrence of disease with a mean time to flare of 12.1 (SD 13.7) months. 129 patients restarted bDMARD therapy (n=117 ETA). We could not identify any correlates for the risk of flare. 70% re-achieved remission and 20% again discontinued therapy thereafter.
Conclusion: The study confirms the good effectiveness of ETA, even in the re-treatment of patients with JIA. Our data highlight the association of an early bDMARD treatment with a higher likelihood to achieve an inactive disease indicating a window of opportunity.

Disclosure of Interest
None declared

O017

Safety of biologicals in juvenile idiopathic arthritis: a risk analysis from the biker register

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Pediatric Rheumatology 2020, **18(Suppl 2):**O017

Introduction: The pharmacotherapy with biologicals is characterized by a high efficiency with comparatively good safety.
Objectives: Using large patient numbers from the BIKER register even rare risks can be detected as well as influencing factors .
Methods: The BIKER database was used to identify adverse events of special interest (AESI). A cohort of biologic-naïve JIA patients treated with methotrexate (MTX) was used as control. The influence of biographical factors, comorbidities, pre- and concomitant therapy and disease activity was analysed univariate and multivariate.
Results: 2856 non-systemic polyarticular JIA patients with a total of 2808 treatment courses with biologics (Etanercept n=1816, Adalimumab n=633, Tocilizumab n=178, Abatacept n=74, Golimumab n=60, Infliximab n=47) and 970 control patients were included. NSAIDs were used in 2930 (78%) treatment courses, systemic steroids in 1241 (33%), MTX in 2815 (65%), other DMARDs in 349 (9%). Pre-existing comorbidities were more frequent in the biologics cohort (1007 (36%) vs. 203 (20%); p<0.001). There were 2265 adverse events (AE) with biologics (81% of courses) compared to 832 in the control cohort (86%; p< 0.001). Of these, 232 AE were classified as serious (SAE) in the biologics (8.3%) compared to 34 (3.5%) in the control cohort (p<0.001).
AESI with biologics were medically important infection n=106, opportunistic infection n=28, uveitis n=100, cytopenia n=31, hepatic event n=26, inflammatory bowel disease n=18, anaphylaxis n=14, depressive disorder n=14, evolving psoriasis n=12, other autoimmunopathy n=11, bleeding event n=5 and pregnancy n=5. Univariate analysis revealed a number of factors significantly associated with the occurrence of AESI: Anaphylaxis n=14, cytopenia n=10, hepatic event n=14, serious infection n=28, opportunistic infection n=13, Uveitis n=24, Psoriasis, n=15, IBD n= 15,Depression, n=7. Results of multivariate analysis: association with serious infections are outlined in table 1.
Conclusion: Various AESIs were associated with several patient characteristics, comorbidities, pretreatment and the kind of biologic used. Interestingly, protective factors also were defined such as older age and ANA positivity for serious infections and higher active joint count and higher age for uveitis. The knowledge of these influencing factors enables an individual risk assessment and can significantly influence the choice of the biological agent.

Disclosure of Interest
None declared

Table 1 (abstract O017). Significant factors in multivariate analysis for 8 Adverse Events of Special Interest. Odd's ratio (95% CI) is given

Anaphylaxis	Cytopenia	Hepatic event	Serious infection	Uveitis	Psoriasis	IBD	Depression
Infliximab 57.8 (15.1-222)	Endocrine comorbidity 4.7 (1.6-13.9)	Tocilizumab 4,1 (1.5-11.1	Golimumab 4.7 (1.5-14.8)	Previous uveitis 4.8(3.2-7.3)	Premedication Abatacept 7.4 (1.5-51)	Infliximab 20.7 (1.8-241)	Vascular events 18.5 (2.1-161)
Respiratory comorbidity 7.2 (1.4-38)	Tocilizumab 3.7 (1.6-6.7)	Systemic steroids 3.7 (1.6-8.7)	Gastrointest. comorbidity 3.7 (1.2-11.4)	ESR 1.2 (1.1-1.3)#	Premedication Adalimumab 7.4 (1.4-40)	Hepatic comorbidity 15.9 (1.6-156)	Pretreatment MTX 1.4 (1.1-1.8)
Premedication i.a. steroids 7.1 (2.3-22.3)	Pretreatment with Steroids 3.2 (1.3-7.6)	BMI 1.5 (1.1-2.2)*	Adalimumab 2.7 (1.4-5.3)	Active joint count 0.8 (0.6-0.9)*	Adalimumab 7.1 (2.0-26)	Gastrointest. comorbidity 8.8 (1.6-48)	
Tocilizumab 5.9 (1.2-29.5)		Age 0.4 (0.3-0.3/*	Etanercept 2.22 (1.3-3.8)	BMI 0.7 (0.5-0.9)*	Psoriatic arthritis 5.9 (1.7-20)	Etanercept 7.4 (1.7-32.3)	
Age 0.5 (0.3-0.9)*			JADAS 10 1.2 (1.2-1.4)*	Age 0.6 (0.4-0.8)*	Premedication i.a. steroids 4.3 (1.4-13.5)	Cardial comorbidity 6.4 (1.1-36.9)	Physician global VAS 0.8 (0.6-1.0)
			Age 0.6 (0.5-0.8)*			Premedication I.a. steroids 2.6 (1.0-6.8)	
			ANA positive 0.6 (0.4-0.9)				

increment for each 10 mm (ESR); *increment for each 5 years (age), each 5kg/m2, each 5 joints or 5 points (JADAS)

O018

Vaccination working party of pres- past, present and future

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Pediatric Rheumatology 2020, **18(Suppl 2):**O018

Introduction: Vaccination WP has its first meeting at PRES congress in Athens 2017. Officially it was established in 2018 PRES congress in Lisbon, Portugal. One of the main reasons for establishing this WP was low level of evidence on which recommendation for vaccination in children with rheumatic diseases (RD) was based and it was concluded that in following years we need more solid evidence to answer numerous remaining questions. The first task was to create the platform for future multicentre studies. We gathered data from 25 countries about the variability of vaccination practices across the globe and presented it as the first Vaccination WP poster. There were considerable qualitative and quantitative differences amongst countries in their vaccination programmes, coverage and in parent obligation to vaccinate the child.
Objectives: The group identified many problems in this field including vaccine coverage in children with RD, the attitude of physicians towards vaccinations, the hesitancy of parents to vaccinate their children and among other the main issue was safety and immunogenicity of live attenuated vaccines, in particular MMR and varicella vaccine in children treated with different

immunosuppressive and anti-inflammatory drugs including the 'biologics'. Another unanswered question was also long term immunogenicity of vaccines in children with RD.
Methods: We created on line data collection on vaccine coverage, on attitude of physicians towards vaccinations in children with RD and on safety of booster MMR/V vaccine in children with RD on immunosuppressive therapy.
Results: In the 2019 PRES congress the group presented 2 abstracts: Live attenuated vaccines in pediatric rheumatic diseases are safe: Multicenter, retrospective data collection that was presented in YIM and in the congress plenary session as oral presentation by Veronica Moshe and An international survey on approaches towards immunization in children with rheumatic diseases: a report of the PRES Vaccinations Working Group in YIM and congress as poster presenation by Elena Moraitis. Recently, the article »Live attenuated MMR/V booster vaccines in children with rheumatic diseases on immunosuppressive therapy are safe: Multicenter, retrospective data collection" was published in Vaccine.
In 2020 we collected the data on Influenza vaccine uptake which was low in majority of participating countries.
Conclusion: The main task for the future is prospective study on MMR/V safety and immunogenicity in children with RD on immunosuppressive therapy.
In conclusion we believe that there are many tasks in front of us. Infections remain the main adverse event of immunosuppressive drugs that we use with great success for treatment of children with RD. And even more so in this terrible time of corona epidemics when we realised again how endanger can we be because of infection and that vaccine can be the only solution to the problem in such times.

Disclosure of Interest
None declared

O019

Attainment of inactive disease following discontinuation of adalimumab monotherapy in patients with era

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Pediatric Rheumatology 2020, **18(Suppl 2):**O019

Introduction: Enthesitis Related Arhtritis (ERA) is one of the most challenging JIA subtypes in terms of drug management and duration of treatment.
Objectives: We present the results of a retrospective study regarding clinical remission sustainment and potential relapse-associated factors in children with ERA treated with TNF-inhibitor (adalimumab -ADA).
Methods: This was a retrospective case study including patients with ERA (based on ILAR criteria) who received ADA from January 2012 to December 2017. All subjects had clinically inactive disease (clinical remission on medication (CRM) and Juvenile Spondylarthritis Disease Activity (JSpADA) remission criteria) for at least 2 years on treatment. Demographics, clinical, laboratory parameters as well data on medication exposure and clinical outcome were documented. Data were analyzed using STATA 15.
Results: In a total of 35(17 girls) patients with inactive ERA(median age 12.5 years), ADA treatment was discontinued. Median treatment duration was 2.8 years. Median time to achieve clinically inactive disease was 5.2 months (range 3.8-7.8). Discontinuation was gradual; in 40% of patients we performed gradual dose reduction while dose spacing was performed in 60% of patients. In 29 patients ADA treatment was successfully ceased. Out of these 29 patients, 3 (10%) developed a single episode of peripheral mono-arthritis managed by intra-articular joint injection while 3 (10%) had a flare of anterior uveitis managed with topical steroids; the rest remained in flare-free clinical remission (>2 years). 6(19%) patients considerably flared during the follow-up period and were restarted on ADA. Median duration of remission following ADA withdrawal was 5 months (range 3.6-11.6). Subgroup analysis showed that patients with unilateral (92%) vs bilateral (74%) sacroiliitis (p=0.06) and patients with shorter disease duration (0.5 vs 1.1 years, p=0.03) had a higher chance of successful withdrawal. In addition, patients with accompanying uveitis were more prone to require drug re-initiation(p=0.04). Time to achieve clinically inactive disease, rise of inflammatory markers at initiation of ADA, presence of enthesitis, peripheral arthritis as well as the tender joint count at diagnosis did not affect the primary outcome. Relapse rate decreased proportionally to time [66.5% relapse(< 6m) vs 33.5%(>6m), p=0.07]. The relapse percentages were identical in the dose-reduction versus gradual spacing mode of discontinuation groups. Age, gender, range of inflammatory markers at diagnosis did not affect clinical outcome.
Conclusion: This was a retrospective study regarding discontinuation of ADA used as monotherapy in patients with ERA (and associated sacroiliitis), following attainment of clinical disease remission, showing optimistic results. TNFi are generally effective in inducing and maintaining remission in ERA and ankylosing spondylitis(AS) patients and therefore long-term therapy is recommended. Overall, biologic-naïve patients demonstrate a swift and sustained response to TNFi; however majority of studies also ensue a synthetic DMARD. Our study demonstrated that ADA withdrawal is feasible in a significant proportion of ERA patients, provided anti-TNFi is initiated promptly. Patients with shorter disease duration and unilateral sacroiliitis showed a higher chance of attaining long-term remission. Prolonging the duration of treatment in clinical remission before discontinuation may show favorable results in contrast to other studies endeavoring earlier discontinuation.

Disclosure of Interest
None declared

O020

Canakinumab, on a reduced dose or a prolonged dose interval without concmitant corticosteroids and methotrexate, maintains clinical remission in systemic juvenile idiopathic arthritis patients

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Pediatric Rheumatology 2020, **18(Suppl 2):**O020

Introduction: Treatment with canakinumab (CAN), a selective, human anti-IL-1β monoclonal antibody, has shown sustained therapeutic effect along with corticosteroid dose reduction/discontinuation in patients with systemic juvenile idiopathic arthritis (sJIA), in a long-term extension study (NCT00891046).
Objectives: To evaluate the efficacy and safety of 2 different canakinumab tapering regimens in sJIA patients who were in clinical remission (NCT02296424).
Methods: This Phase 3b/4 study had two parts. In Part I 182 patients, n=84 with inactive disease from the extension study1 (cohort 1) and n=96 CAN-naïve patients (cohort 2) with active disease were administered subcutaneous CAN 4 mg/kg q4w. Per protocol titration off corticosteroids and/or methotrexate was attempted during Part I. Eligible patients (inactive disease for 24 consecutive weeks and being corticosteroid- and methotrexate-free for at least 4 weeks) advanced to Part II. Patients were randomised to either a 3-step CAN dose reduction regimen (2mg/kg/q4w, followed by tapering to 1 mg/kg/q4w and then discontinuation) or dose interval prolongation regimen (4mg/kg q8w, followed by tapering to 4 mg/kg/q12w and then

discontinuation); patients advanced to the next tapering step if inactive disease was maintained for 24 weeks. The primary objective was to evaluate if at least 40% of patients were able to maintain inactive disease status for at least 24 consecutive weeks on either 2mg/kg q4w or 4mg/kg q8w.
Results: In Part II, a total of 75 patients were randomised to a dose reduction (n=38) or dose interval prolongation (n=37) CAN tapering regimen. The proportion of patients who maintained inactive disease for 24 consecutive weeks significantly exceeded the predefined threshold of 40% of Step 1 in both treatment arms: CAN reduced dose (71%; 2 mg/kg q4w) and in prolonged dose interval (84%; 4 mg/kg q8w). A total of 68% (26/38) and 79% (30/37) of the dose reduction and interval prolongation arms, respectively were successful in Step 2, while only 33% (25/75) of patients successfully discontinued CAN and maintained inactive disease for 24 consecutive weeks. Adverse events (AEs) and serious AEs observed within the 2 treatment cohorts and across Parts I and II were similar without any specific pattern or relationship to patients' disease status at baseline or treatment regimen. The most frequent AEs were common infections such as nasopharyngitis, upper respiratory tract infection, and pharyngitis followed by sJIA-related events such as rash, pyrexia and arthralgia. Clinical laboratory abnormalities were consistent with expected findings in patients with active sJIA and the known safety profile of CAN.
Conclusion: sJIA patients who are able to maintain inactive disease status on CAN monotherapy can successfully taper CAN by either reducing the dose or prolonging the dosing interval. However, only a minority of patients successfully discontinued CAN treatment for 24 weeks. The safety profile for both CAN titration regimens was similar and consistent with other CAN sJIA studies. No new safety signals were identified.

Disclosure of Interest
P. Quartier Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi,SOBI, Speaker Bureau of: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, SOBI, E. Alexeeva: None declared, C. Wouters Consultant for: GSK, Roche, Pfizer, I. Calvo: None declared, T. Kallinich Speaker Bureau of: Sobi, Roche, Novartis, CLB, B. Magnusson: None declared, N. Wulffraat Consultant for: Novartis, X. Wei Employee of: Novartis, A. Martini: None declared

O021
Long-term safety profile of anakinra in patients with systemic juvenile idiopathic arthritis
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Pediatric Rheumatology 2020, **18(Suppl 2):**O021

Introduction: Systemic juvenile idiopathic arthritis (sJIA) is characterized by extra-articular manifestations, as fever and rash, and rarely associated by a potentially lethal complication as macrophage activation syndrome (MAS). Anakinra is a recombinant human interleukin (IL)-1 receptor antagonist whose efficacy and safety profile has been studied for patients with sJIA.
Objectives: To evaluate the long-term safety profile of anakinra in patients with sJIA in current clinical practice.
Methods: Data from patients with sJIA treated with anakinra and enrolled in Pharmachild registry before 30 September 2018 was retrospectively analyzed (EUPAS28378). The study endpoints were the occurrence of non-serious adverse events (AEs) of at least moderate severity and serious AEs (SAEs), including MAS; the duration of anakinra treatment and reasons for discontinuation. All endpoints were analyzed overall and stratified by 6 months time windows.
Results: 306 patients were enrolled with both genders equally represented. Anakinra was administered at the median age of 8.0 years and after a median of 0.6 years from the disease onset. Almost half of the patients (n=146; 46%) were continuously treated with anakinra for at least 12 months, 34.0% for at least 18 months and 28.1% for at least 24 months. A total of 201 AEs was reported during a total of 509.3 patient years (py) of treatment with an overall incidence rate (IR) of 39.5 (95% CI 30.8-50.6) per 100 py, mostly represented by infections (52 events, 25.9%; IR 10.2/100 py). 56 SAEs were reported (IR 11.0/100 py; 95% CI 7.9-15.2), whereof 13 infections (23.2%; IR 2.6/100 py), and 11 MAS episodes (19.6%; IR 2.2/100 py). The IR/100 py of AEs was higher during the first 6 months of treatment and gradually decreased over time. Ten patients (3.3%) had a history of MAS before anakinra start, 9 of these patients did not experience any new MAS episode after anakinra start. 8 patients developed MAS several months after anakinra discontinuation. Discontinuation of treatment occurred at least once in 233 patients (76%) more often during the first 6 months and decreased over time and reasons were overall secondary to inefficacy (43%), remission (31%) or AEs and intolerance (15.0%). No deaths occurred during anakinra treatment while 3 deaths occurred after anakinra discontinuation (5 months, 3 years, and 5 years after discontinuation, respectively). No malignancies were reported neither during treatment with anakinra nor after discontinuation.
Conclusion: The results of the present study confirm the long-term safety profile of anakinra in sJIA patients without any new safety findings. Long-term treatment with anakinra in sJIA patients was well tolerated, with a decreasing overall incidence rate of AEs.

Disclosure of Interest
G. Giancane: None declared, R. Papa: None declared, S. Vastert Consultant for: SOBI and Novarts + unrestricted research grant from SOBI in collaboration with a public private funding opportunity of the Dutch National Science Organisation, F. Bagnasco: None declared, J. Swart: None declared, E. Alexeeva Speaker Bureau of: Novartis and has received research grants from Roche, Pfizer, Centocor, Novartis, P. Quartier Consultant for: AbbVie, Bristol-Myers Squibb, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi and Swedish Orphan Biovitrum, I. Kone-Paut Consultant for: AbbVie, Pfizer, Roche, CHUGAI, Novartis, Sobi, Novimmune, J. Anton Consultant for: Sobi, Novartis, Roche, Speaker Bureau of: Sobi, Novartis, Roche, S. Sawhney: None declared, F. Sztajnbok: None declared, S. Kamphuis: None declared, T. Herlin: None declared, V. Panaviene: None declared, R. Cuttica Consultant for: Bristol Myers Squibb, Centocor, Glaxo Smith Kline, Janssen, Lilly, Novartis, Pfizer, Roche, Sanofi Aventis., W. M. Saad Suwairi: None declared, H. Sanner: None declared, C. Pallotti: None declared, K. Franck-Larsson Employee of: Sobi, H. Malmström Employee of: Sobi, S. Cederholm Employee of: Sobi, N. Wulffraat: None declared, N. Ruperto Consultant for: NR has received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi.

O022
Early treatment and IL1RN SNPS affect response to anakinra in systemic juvenile idiopathic arthritis
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Pediatric Rheumatology 2020, **18(Suppl 2):**O022

Introduction: Systemic juvenile idiopathic arthritis (sJIA) represents 10-20% of all chronic arthritis during childhood. The interleukin 1 (IL-1) plays a pivotal role in the pathogenesis of the disease. Indeed, several studies confirmed the therapeutic efficacy of anakinra (recombinant IL-1 receptor antagonist) in a significant portion of patients with sJIA, especially in the first phase of disease. The use of anakinra as first-line therapy can benefit from the so-called "window of

opportunity", for which the evolution of the disease can be modified preventing the onset of chronic arthritis. Despite a good response to anakinra in a high percentage of patients, there is a subset of non-responders. The early identification of non-responder patients is of primary importance to avoid the progression towards chronic arthritis. Some single nucleotide polymorphisms (SNPs) in *IL1RN* gene have been found associated with sJIA, and recently, a cluster of SNPs in the *IL1RN* non-translated region has been suggested as a possible predictor of non-response to anakinra.
Objectives: The aim of this study was to evaluate the impact of early treatment and genetic variants in *IL1RN* gene on the response to anakinra in sJIA.
Methods: Response to anakinra was considered as clinically inactive disease (CID) at 6 months, without glucocorticoids treatment. Demographic, clinical and laboratory characteristics of 56 patients were analyzed in univariate and multivariate analysis as predictors of response to treatment. Six SNPs in *IL1RN* gene were genotyped by qPCR or Sanger sequencing. Haplotype mapping was performed with Haploview software and *IL1RN* mRNA expression in whole blood from patients before anakinra initiation was assessed by qPCR.
Results: After 6 months of treatment, 73.2% of patients met the criteria for CID off glucocorticoids. In univariate analysis the variable strongly related with the response was disease duration from onset to anakinra initiation, with an optimal cut-off at 3 months. Patients who started anakinra after 3 months from disease onset had an 8-fold higher risk of non-response at 6 months. We confirmed that the 6 *IL1RN* SNPs were inherited as a common haplotype in our cohort of patients. We found that homozygosity for at least one high expression SNP correlates with higher *IL1RN* mRNA levels and was associated with a 6 fold higher risk of non-response, independently of disease duration.
Conclusion: Our results confirm the important role of early IL-1 inhibition and suggest that genetic *IL1RN* variants predict non-response to therapy with IL-1 blockade in patients with sJIA.

Disclosure of Interest
None declared

O023

Pharmacokinetics-pharmacodynamics of hydroxychloroquine in childhood-onset systemic lupus erythematosus

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Pediatric Rheumatology 2020, **18(Suppl 2):**O023

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a chronic, autoimmune multisystem inflammatory disease that is associated with sizable morbidity and mortality. Hydroxychloroquine (HCQ) is an antimalarial agent given to patients with systemic lupus erythematosus (SLE) as first-line therapy with accumulating evidence on its role in reducing mortality and morbidity. HCQ is known to alleviate cSLE skin and musculoskeletal disease, along with decreasing disease activity and flare. Despite longstanding use of HCQ in children patients, the effect of HCQ in pediatric population and the potential need for dose adjustments remains unknown.
Objectives: To study the pharmacokinetics/ pharmacodynamics relationships of HCQ in cSLE
Methods: We performed a population-pharmacokinetic analysis using samples from patients' medical records in Necker- Enfants-malades Hospital and Robert-Debré hospital from 2016 to 2018. cSLE flares were defined using the SLE Disease Activity Index (SLEDAI); flare was denoted by a SLEDAI score of > 6. Hydroxychloroquine blood concentration was measured using high-performance liquid chromatography with fluorometric detection. Population pharmacokinetic/pharmacodynamic parameters were estimated using the nonlinear mixed-effects modelling software Monolix (version 2019R2).
Results: 144 results of blood samples were obtained from 48 child patients (45 girls). The mean age was 15.2 ±2.3 years; the median body weight was 56.1 ± 18.2 kg. Most subjects took HCQ as 400 mg per day (300 ± 113 mg/d). We found large interindividual variations in blood HCQ concentrations; the mean HCQ blood concentration was 685 ng/mL, range [100-2509]. HCQ apparent blood clearance CL/F was dependent on patients body weight (positive effect according to the allometric rule) and platelet count (negative effect). The mean SLEDAI score war 4.2 [0 -19]. Patients with active cSLE had a lower mean blood HCQ concentration than patients with inactive cSLE (536 ± 294 vs 758 ± 490 ng/mL, $p < 0.05$). When considering blood HCQ concentration ≥ 1000 ng/mL, 42/48 of patients had inactive cSLE. The joint model for HCQ concentration and probability of active disease status confirmed that HCQ concentration and treatment duration were significant predictors of disease status
Conclusion: We developed the first population-pharmacokinetic/ pharmacodynamic model for hydroxychloroquine in childhood-onset systemic lupus erythematosus. Whole blood HCQ concentrations are associated with cSLE disease activity. To confirm these results, a prospective pharmacokinetic / pharmacodynamic analysis is necessary

Disclosure of Interest
None declared

O024

'It gives the treatment structure': patient and parental perspectives on treating to target in juvenile-onset systemic lupus erythematosus treat

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Pediatric Rheumatology 2020, **18(Suppl 2):**O024

Introduction: 'Treat to target' (T2T), in which treatment is adjusted or escalated until a specific target is achieved, is now part of routine clinical care in many areas of medicine. It has been proposed as a strategy to improve management of juvenile-onset systemic lupus erythematosus (JSLE), using existing treatments in a more structured way. The TARGET LUPUS research programme; 'Targeting disease, Agreeing Recommendations and reducing Glucocorticoids through Effective Treatment, in LUPUS' has been established in order to develop a JSLE T2T study. There is currently little guidance on JSLE patient/parental views on the concept of T2T.
Objectives: To explore, in-depth, the views of JSLE patients and parents on the treatment targets, outcome measures and study designs for T2T being considered by TARGET LUPUS, in light of their previous treatment and care.
Methods: Topic guided semi-structured interviews explored what it means to JSLE patients to be 'well', and their views on potential T2T study targets e.g. Lupus Low Disease Activity State (LLDAS). As part of the interviews, patients and parents completed health-related quality of life (HRQOL) and fatigue tools and were then asked about their views of the tools and how well these captured their experiences. The concept of T2T was also explored, and patient and parental views on the proposed study and potential study designs were sought. Analysis of audio recorded interviews was informed by thematic approaches.
Results: 24 semi-structured interviews were conducted with 12 JSLE patients (aged 9-18 years) and 12 parents from six UK hospitals. Most patients reported feeling very well at the time of the interview, with several commenting that they felt completely back to normal. Most parents also classed their children as feeling well. However, several parents rated their child's wellbeing as worse than their child had themselves. Both patients and parents tended to class joint pain, muscle aches/weakness and rash as

consistent with low disease activity. When asked about symptoms/signs that had not previously experienced during their disease course patients and parents often regarded as these signifying high disease activity. Of the three HRQOL questionnaires assessed, both patients and parents favoured the Peds QL Rheumatology Module, as they felt it provided the clearest picture of both wellbeing and functioning. Almost all patients and parents thought it was important to have a specific questionnaire focusing on fatigue. Most families felt that reducing corticosteroids would be a good treatment target. Almost all families liked the idea of a T2T approach to treatment, commenting that it would structure their treatment and enable more frequent clinic visits where needed. However, some were concerned about the impact of increased visits on schooling and parental work and suggested holding monthly visits until medication is stable, and then visits could become less frequent.

Conclusion: This study has provided insights on patient and parental perspectives on treatment targets, outcomes measures and indicated that the concept of T2T is acceptable to families in principle. These findings will be shared with JSLE experts, including patients and families during future international consensus meetings on further defining a treatment target and treatment strategy which is acceptable to both patients, families and clinical teams.

Disclosure of Interest
None declared

O025

A national multicentre study on severe paediatric recurrent idiopathic pericarditis treated with IL-1 blockers: appropriateness of the standard of care and pros and cons of anti-IL-1 treatments

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Pediatric Rheumatology 2020, **18(Suppl 2):**O025

Introduction: Recurrent pericarditis (RP) is a rare cause of morbidity in children. Non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids and colchicine are the standard of care in adults. Recently, anakinra has been proven to be effective in patients with steroid-dependence and colchicine resistance.

Objectives: To analyse, in a cohort of paediatric patients with RP undergoing to anti-IL-1 treatment for resistance to standard treatments, the appropriateness of the first line treatments, the long-term efficacy of different IL1-blockers and the percentage of patients achieving a drug-free remission.

Methods: Paediatric patients with RP pericarditis followed by Italian centers of paediatric rheumatology or cardiology and treated with IL1 inhibitors were included in the study. The efficacy of treatment with IL1-blockers was evaluated trough an annualized relapse. A bivariate logistic regression analysis wad used to identify variables associated to an increased probability to withdraw the biological treatment without relapses.

Results: 58 patients were enrolled in the study. Overall, NSAIDS, colchicine and steroids were used in 56, 49 and 48 patients, respectively. 8/18 and 6/38 patients without a complete response to treatment with NSAIDs and colchicine, respectively, were not receiving an adequate dosage according to ESC guidelines. 4/48 patients treated with glucocorticoids were receiving the proper dosage of < 0,5 mg/kg/day of prednisone or equivalent. Steroidal-dependence was observed in 45 patients.

Anakinra and canakinumab were used in 57 and 6 patients respectively. In 57 patients treated with anakinra the annualized relapse rate (ARR) before treatment was of 3.05 and 0.28 ($p < 0.0001$) during daily treatment; however, an increase in the number of relapses was then observed after the reduction or discontinuation of treatment (ARR=0.83, $p<.0001$). In the 6 patients treated with canakinumab he ARR was 2.3 and 1.46, before and during treatment, respectively.

At last follow-up, only 9 patients had withdrawn all treatment. None of the variables analysed were associated with a statistically significance between the group of these patients and those 49 in which the withdrawal was not possible, due to recurrence of the disease.

Conclusion: This study confirm the effectiveness of IL-1 blockade in paediatric patients with recurrent pericarditis; however, most of the patients require prolonged treatment to maintain relapse-free remission. In our cohort of patients the rate of response was higher for anakinra then for canakinumab.

Disclosure of Interest
R. Caorsi Consultant for: Sobi, Novartis, A. Insalaco: None declared, F. Bovis: None declared, G. Martini: None declared, M. Cattalini: None declared, M. Chinali: None declared, A. Rimini: None declared, C. Longo: None declared, S. Federici: None declared, C. Celani: None declared, G. Filocamo: None declared, R. Consolini: None declared, C. Maggio: None declared, G. Fadanelli: None declared, F. Licciardi: None declared, M. Romano: None declared, B. Teruzzi: None declared, A. Taddio: None declared, A. Miniaci: None declared, F. La Torre: None declared, A. De Fanti: None declared, G. Cavalli: None declared, B. Bigucci: None declared, R. Gallizzi: None declared, M. Chinello: None declared, A. Brucato: None declared, M. Imazio: None declared, R. Cimaz: None declared, F. De Benedetti: None declared, M. Gattorno Consultant for: Sobi, Novartis

O026

Evaluation of flare rate and tapering strategies in juvenile idiopathic arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O026

Introduction: Biological treatment (BT) has changed the perspectives of Juvenile Idiopathic Arthritis (JIA) patients, but it remains unclear the time point when and how to taper or to withdraw treatment, neither the effect of treatment withdrawal after remission is achieved.

Objectives: To assess the course of the disease after tapering or stopping BT in a cohort of JIA patients. Tapering strategies and median time to flare were analyzed.
Methods: A retrospective, descriptive study was conducted in a cohort of JIA patients followed up in a Pediatric and Transition Unit of a referral hospital and who had received BT between 2000 and 2019. All JIA patients with at least one attempt of tapering were included. Remission was defined according to Wallace criteria for remission.
Results: 131 JIA patients and 219 BT were reviewed. 198 de-escalations in 108 (49,3%) BT in 95 (72,5%) JIA patients were identified and included. 67,7% of the patients were female. The median age at JIA diagnosis was 5 years [IQR (2-12)] and the median age at the beginning of tapering was 17 years [IQR (11,8-26)]. Patients were in remission a median of 9 months [IQR (6-17)]. Main BT tapered were: TNF inhibitors (76,3%), IL6 inhibitors (15,2%) and IL1 inhibitors (6,5%). Conventional DMARDs (cDMARDs) were administrated in combination with BT in 40,4% of the deescalations. Regarding JIA categories: 44 (22,2%) were Oligoarticular Persistent, 36 (18,2%) were Oligoarticular Extended, 32 (16,2%) were Systemic JIA, 31 (15,7%) were Enthesitis related Arthritis, 19 (16,2%) were Psoriatic Arthritis, 16 (8,1%) were Polyarticular Rheumatoid Factor positive, 16 (8,1%) were Polyarticular Rheumatoid Factor negative and 5 (2,5%) were Undifferentiated. 8 (6,3%) patients were lost in follow-up.
The 171/198 (86,3%) cases started a de-escalation. The most frequent tapering strategy was prolonged interval between applications (90,6%), combined strategy (5,8%) and lower dosage (3,5%). The median remaining dose administrated was 50% [IQR (50, 75)].
Twenty-seven (13,6%) cases withdrawn BT abruptly. The main causes of abrupt BT withdrawal were: remission (33,3%), pregnancy (29,6%), active infection (14,8%) and vaccination (14,8%).
Forty-five (26,3%) cases stopped BT after tapering. Median time to withdrawal was 11 months [IQR (6-22)]. The main causes of withdrawal after tapering were remission (66,7%), pregnancy (11,1%), infections (6,7%) and vaccination (4,4%).
There was no difference in remission rates after withdrawal among cases with previous tapering or abrupt discontinuation [Median time of remission on withdrawal after tapering 5 +-(1,1), median time of remission among abrupt withdrawal 7 +-(2,6), Log rank=0,946]. After 6 months of withdrawal 48,1% of cases that stopped abruptly and 56,1% of cases that stopped after tapering had presented a flare. 10/72 (13,8%) cases are currently on remission without BT during follow-up, 9,7% without any treatment and 4,1% with cDMARDs.
BT was tapered without withdrawal in 126 (63,6%) cases. Remission rates during tapering are specified in table 1. 40 (20%) cases continue tapered without a flare after a median of 77 months [IQR (36,3-111,3)] of follow-up.
Conclusion: - There was no difference in remission rates among patients that discontinuated BT after tapering or after abrupt discontinuation. After 6 months of withdrawal 48,1% of cases that stopped abruptly and 56,1% of cases that stopped after tapering had presented a flare.
- Tapering without withdrawal is safe: 79,8% of cases at 6 months and 47,4% of cases at 24 months that tapered without withdrawal remained on sustained remission.

Disclosure of Interest
None declared

Table 1 (abstract O026). Remission rates among cases tapered without withdrawal during follow-up.. n=126

Time, months	Cases on remission, n %
6	101 (79,8)
12	86 (68,1)
24	60 (47,4)
Currently on remission	40 (31,8)

O027

Should etanercept be avoided in certain patients with juvenile idiopathic arthritis due to risk of developing inflammatory bowel disease?

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Pediatric Rheumatology 2020, **18(Suppl 2):**O027

Introduction: Inflammatory bowel disease is a relatively rare comorbidity in patients with juvenile idiopathic arthritis but is known to have an important negative impact on quality of life. It is suggested that IBD development is associated with use of etanercept but due to its low incidence, thus far this has not been proven.
Objectives: The aim of this study was to determine risk factors for developing IBD in JIA patients and evaluate the possible relationship between medication and IBD development.
Methods: In this study, Pharmachild, the largest international JIA registry was used. Enrollment of patients was facilitated by members of the Paediatric Rheumatology INternational Trials Organisation (PRINTO). Risk factors for IBD where identified both before and after adjustment for confounders. A prediction model was developed using multivariable logistic regression analysis in a backward procedure based on likelihood ratio tests. To identify associations between drugs of interest and IBD development, patients who developed IBD were matched to similar controls based on the variables in the prediction model. Odds ratios were calculated using conditional logistic regression analysis.
Results: 8,942 patients were included in this study of which 48 (0.5%) developed IBD. Age at JIA onset was significantly higher in patients with IBD (8.94 years vs 5.33 years p=0.000) and there was a lower female predominance in the IBD group (52.1% vs 68.0% p=0.029). Family history was significantly more positive for autoimmune disease in IBD patients (43.8% vs 29.0% p=0.037) and enthesitis-related arthritis (ERA) was more frequently observed (39.6% vs 10.8% p=0.000). The model with the best discriminative performance included the variables age, gender, ERA and the total number of first and second degree relatives with a history of autoimmune disease and had an AUC of 0.721 (95% CI 0.646-0.796). Analyses on IBD patients with available onset date (n =27) matched to non-IBD controls (n = 129) showed that patients treated with ETN had a 6.88 and 7.45 times higher odds for developing IBD within 3 and 6 months respectively, compared to control patients that did not receive ETN at similar disease duration (Table 1). In addition, both patients using ETN and MTX dual therapy and patients using ETN without MTX had higher odds for developing IBD. Use of other biologicals and MTX without ETN were not significantly associated with IBD.
Conclusion: In this study, ERA patients were at an increased risk of developing IBD. The most important risk factors for developing IBD were age, gender, ERA subtype and family history of autoimmune disease. In addition, patients using ETN had higher odds of developing IBD while we did not find a protective role of MTX for the development of IBD. Therefore, we recommend to prescribe other biologicals than ETN to JIA patients with a higher risk of developing IBD.

Disclosure of Interest
None declared

Table 1 (abstract O027). Odds ratios for the development of IBD

	3 months before IBD OR (95% CI)	6 months before IBD OR (95% CI)	>6 months before IBD OR (95% CI)
Drug therapy			
Methotrexate	**2.87 (1.16 – 7.07)**	**3.15 (1.24 – 8.03)**	2.93 (0.66 – 13.05)
MTX without ETN	1.11 (0.40 – 3.10)	1.02 (0.37 – 2.83)	0.57 (0.21 – 1.56)
Etanercept	**6.88 (2.51 – 18.81)**	**7.45 (2.75 – 20.16)**	2.38 (0.92 – 6.12)
ETN without MTX	**3.13 (1.08 – 9.03)**	**3.6 (1.12 – 11.08)**	-
ETN + MTX	**7.12 (2.03 – 25.01)**	**6.46 (2.06 – 20.27)**	**2.73 (1.07 – 6.99)**
Infliximab	9.21 (0.83 – 102.62)	9.21 (0.83 – 102.62)	2.27 (0.49 – 10.48)
Adalimumab	2.24 (0.14 – 35.9)	1.49 (0.13 – 17.34)	0.8 (0.18 – 3.46)

O028

Early start of biological treatment in juvenile idiopathic arthritis: does a therapeutic window exist in real life?

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Pediatric Rheumatology 2020, **18(Suppl 2):**O028

Introduction: Biological therapy (BT) has changed the treatment and perspectives of JIA patients but little is known about when is the best moment to start BT and the impact of this prompt initiation.
Objectives: To analyse the response to BT of Juvenile Idiopathic Arthritis (JIA) patients according to the time when the BT was started
Methods: A retrospective, descriptive study was conducted on JIA patients followed up in a referal hospital that started BT up to 24 months after diagnosis from 2000 to 2018. Disease activity was measured, at 2 years after diagnosis, according to Wallace criteria for remission (absence of: active arthirits, active uveitis, fever, rash or any other manifestation attributable to JIA, normal CRP and ESR, PGA indicating no active disease) for at least 6 months.
Results: 55 JIA patients that started BT up to 24 months from diagnosis were analyzed. 69,1% were girls with a median age at diagnosis of 8 years old [IQR(3-13)], median age at the start of BT of 9 years old [IQR(3-13)]. Regarding JIA categories: 25,5% were Oligoarticular Persistent (OligP), 18,2% Systemic JIA (sJIA), 16,4% Entesitis related Arthritis (ERA), 12,7% Psoriatic Arthritis (APso) and Polyarticular RF- (PolyRF-), 5,5% Oligoarticular Extended (OligE) and Polyarticular RF+ (PolyRF+), 3,6% Undifferentiated (Und). 20% of patients had uveitis during followup. Conventional DMARD (cDMARD) was indicated in 83,6% of patients (95,7% Methotrexate) at diagnosis [median 0 months IQR(0-2,3)]. At the end of followup (2 years) only 30,9% of patients continued with cDMARDs. The main causes of discontinuation were: adverse events (46,7%), remission (36,7%). TNF inhibitors were precribed in 81,8% of patients and 18,2% of patients recieved two BT during the first 2 years from diagnosis. 54,5% of BT were indicated during the first 6 months from diagnosis, 27,3% from 7 to 12 months, 12,7% from 13 to 18 months, 5,5% from 19 to 24 months.
After 2 years from diagnosis, 78,2% of patients were on remission and 21,8% active. Among patients with active disease: 75% had arthritis, 16,7% had uveitis and 8,3% had both. There were no differences regarding disease activity among patients with uveitis and neither taking cDMARDs. Regarding JIA categories: 66,7% of OligE, 57,1% of PolyRF- and 57,1% of APso patients were active at 2 years from diagnosis when compared to the other categories (p= 0.004).
Patients on remission at 24 months from diagnosis started sooner the BT than active patients [CI 95% (0,46-8,29) p=0,029]. The time when the BT was started was correlated to the activity at 2 years (K= 0,294 p=0,029). When the BT was prescribed after 7,5months from diagnosis it was correlated, in a COR curve, with a higher probability of active disease at 2 years(S= 0,67 E= 0,63). There was a correlation, among patients on remission at 2 years, between prompt start of BT and less time to reach remission (K= -0,345 p=0,024). Patients with active disease at 2 years, regardless of moment of BT iniciation, required more BT during follow-up (p=0,002).
Conclusion: Prompt iniciation of BT was correlated with a better outcome. JIA patients that started BT early after diagnosis had a higher probability of remission after 2 years. Starting BT after 7,5 months was correlated with a higher probability of active disease at 2 years. Active disease at 24 months was correlated with presistent active disease during follow-up.

Disclosure of Interest
None declared

O029

Autologous hematopoietic stem cell transplantation in rheumatologic diseases: the experience of a third-level hospital in Mexico

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Pediatric Rheumatology 2020, **18(Suppl 2):**O029

Introduction: Autologous hematopoietic stem cell transplantation (AHSCT) is an alternative treatment for patients with refractory rheumatologic disease (RD). AHSCT can re-establish immunological tolerance and induce complete remission of the disease.
Objectives: To report our experience of AHSCT in patients with refractory RD [diffuse cutaneous systemic sclerosis (dcSSc) and systemic juvenile idiopathic arthritis (sJIA)] at the Hospital Infantil de México Federico Gómez.
Methods: We included pediatric patients from 0 to 16 years with refractory dcSSc and sJIA, whom underwent AHSCT. We carried out a retrospective analysis of these cases.
Results: The present study was carried out from January 2018 to December 2019. We report 6 patients. 33% of patients with dcSSc and 67% sJIA. 83% were female. The mean age at the time of diagnosis was 12.8. The median time interval from diagnosis to AHSC T was 52 months. Regarding the dcSSc patients, received an average of 4 nonbiologic disease-modifying antirheumatic drugs (DMARDs) and 1 biologic agent prior to AHSCT. The sJIA patients received an average of 1.5 nonbiologic DMARDs and 2 biologic agents prior to AHSCT. The peripheral stem cells were mobilized with cyclophosphamide (CYC) and granulocyte colony-stimulating factor and harvested by leukapheresis and subsequently selected for CD34+ cells, on day 0 were infused, after compliance with the conditioning adjustment (CYC was given on days -8, -7 and -6 and antithymocyte globulin on days -5, -4, -3, -2 y -1). All patients received acyclovir, cefepime and fluconazole for infection prophylaxis. We follow-up the patients a median of 28.5 weeks. Patients with dcSSc experienced resolution of dyspnea, digital ulcers, decrease 33% the mRss and the number of Raynaud's phenomenon events. There were no significant changes in lung function tests, HRCT of the lungs and EGDS in dcSSc. All patients with JIAs had 0 joints with active arthritis, we documented a decrease of CRP 95% and VSG 64% after AHSCT. The cHAQ score improved 98% and the DAS 28 score 61%. The total of patients with dcSSc are in complete remission. Of the patients with AIJs, 66% have complete remission and 33% partial remission. No mortality has been reported.
Conclusion: To our best knowledge, this is the first study in Mexico that describes the use of AHSCT in patients with refractory dcSSc and sJIA. AHSCT is a viable, effective and safe procedure in dcSSc and sJIA. AHSCT can slow the progression of rheumatologic disease, however, it does not reverse established damage. We must investigate poor prognosis factors that allow us to recognize patients with a high probability of rapid disease progression in order to select them for the AHSCT in a timely manner.

Disclosure of Interest
None declared

Table 1 (abstract O029). Baseline characteristics of the patients with refractory rheumatologic disease

Gender	Age (years)	Diagnosis	Time (month)	Damaged organ	Pre-transplant treatment	Post-transplant treatment	Complications	Status
F	11	dcSSc	26	Skin + Lung + Digestive	HCQ + MTX + MMF + CYC	HCQ	Catheter-related sepsis	Complete remission
F	17	dcSSc	31	Skin + Lung + Digestive	HCQ + MTX + MMF + CYC + RTX	HCQ	Malabsorption Syndrome	Complete remission
F	16	sJIA	73	MAS	MTX + LFN + TOCI + IVIG + HLH-2004	HCQ	Catheter-related sepsis + CMV infection	Complete remission
F	8	sJIA	65	———	MTX + LFN + TOCI + ABA + ETA	LFN	———	Partial remission
M	14	sJIA	33	MAS	MTX + TOCI + ETA + IVIG + HLH-2004	MTX + TOCI	Catheter-related sepsis + Septic shock + Anaphylaxis + Adenovirus-induced hemorrhagic cystitis	Partial remission
F	11	sJIA	84	———	MTX + TOCI + ETA	HCQ	———	Complete remission

O030

Examining health outcomes in juvenile idiopathic arthritis- a genetic epidemiology study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O030

Introduction: Juvenile idiopathic arthritis (JIA) is the most common paediatric rheumatic disease, however there is limited data on other health-related outcomes in JIA patients.
Objectives: The aims of this study were to use publicly available genome-wide association study (GWAS) datasets to interrogate the genetic correlation between JIA and a broad range of health-related traits. We then sought to examine whether JIA was causally associated with any correlated traits.
Methods: We used publicly available JIA GWAS data (sample size 15872) and the LDHub platform to implement linkage disequilibrium score regression (LDSC) to explore genetic correlation (r_g) between JIA and 832 other health traits across the life course. Results were adjusted for multiple testing based on the false discovery rate (FDR). For non-autoimmune traits correlated with JIA (FDR-adjusted p value, P_{adj}, <0.05), we then conducted two sample Mendelian randomisation (2SMR) to examine evidence of causality. We employed multiple sensitivity analyses to ensure the evidence was robust. MR estimates for continuous outcomes are reported as beta coefficients and for binary outcomes are transformed onto the odds ratio scale.
Results: We found robust evidence of positive genetic correlation between JIA and seven human traits: "rheumatoid arthritis" (r_g 0.63, P_{adj} 0.029), "coeliac disease" (r_g g 0.58, P_{adj} 0.032), "systemic lupus erythematosus" (r_g 0.40, P_{adj} 0.032), "coronary artery disease" (CAD, r_g 0.42,P 6.0x10^{-3}), "hypothyroidism/myxoedema" (r_g 0.61, P_{adj} 4.1x10^{-5}), "number of non-cancer illnesses" (r_g 0.42, P_{adj} 0.016) and "paternal health" (r_g 0.57, P_{adj} 0.032). There was robust evidence of negative correlation with "strenuous sports" (r_g -0.52, P_{adj} 0.032). In addition, we found some evidence for genetic correlation between JIA and a number of unfavourable cardiometabolic traits. Using 2SMR we identified robust evidence for a causal relationship between genetically predicted JIA and "number of non-cancer illnesses"(2SMR causal estimate beta 0.021, 0.008-0.034). The 2SMR estimate for genetically predicted JIA and CAD (OR 1.05, 95% CI 0.98-1.12), "paternal health" (OR 1.05, 95% CI 0.98-1.13) and "strenuous sports" (OR 0.98, 95% CI 0.96-1.00) provides very little evidence of a causal relationship between these traits and JIA despite their high genetic correlation.
Conclusion: We show evidence of genetic correlation between JIA and a several novel and important long-term health outcomes, particularly coronary artery disease and other systemic and organ-specific autoimmune disorders. Although 2SMR analysis suggests the association between JIA and CAD is one of correlation rather than causation, our findings support the observational literature regarding the need for cardiovascular risk assessment and management of JIA patients, and the consideration of routine thyroid function monitoring and coeliac screening.

Disclosure of Interest
None declared

O031

Patients with periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome have differential methylation in intron regions of PIK3AP1 and SPON2 genes

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Pediatric Rheumatology 2020, **18(Suppl 2):**O031

Introduction: Periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome is the most common periodic fever syndrome in children, often grouped together with hereditary periodic fever syndromes, although its cause and hereditary nature remain unexplained. Genes known to be involved in inflammation seem to contribute to a predisposition to PFAPA syndrome, suggesting complex genetic inheritance.
Objectives: We investigated whether a differential DNA methylation was present in DNA from peripheral blood mononuclear cells in patients with PFAPA versus a group of healthy young individuals.
Methods: A whole epigenome analysis (Methylated DNA Immunoprecipitation (MeDIP) and Methyl-CpG-binding domain (MBD)) was performed using pooled DNA libraries enriched for methylated genomic regions. Of identified candidate genes, two most significantly different regions were further evaluated with methylation specific restriction enzymes coupled with qPCR (MSRE-qPCR).
Results: MSRE-qPCR proved to be a quick and reliable method to confirm results from MeDIP and MBD. Differential methylation was observed in patients with PFAPA. The analysis showed that the first intron region of *PIK3AP1* (BCAP) is hypermethylated (P< 0.0001) and that the fifth intron region of the *SPON2* (spondin-2) is differentially methylated (hypomethylated (P=0.001) and hypermethylated (P=0.0191)) in patients with PFAPA compared to healthy individuals. Both B cell adapter protein (BCAP) as PI3K binding inhibitor of inflammation and spondin-2 as a pattern recognition molecule and integrin ligand could play a role in etiology of PFAPA.
Conclusion: Our findings indicate that BCAP and spondin-2 could be involved in the pathogenesis of PFAPA, their role and the effect of changed DNA methylation in PFAPA etiology and autoinflammation need further investigation.

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Disclosure of Interest
None declared

O032

Cell damage and pathogen-associated TLR4 ligands fundamentally differ in their ability to induce type I interferon expression

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Introduction: Damage and pathogen-associated molecular patterns (DAMPs, PAMPs) can strongly activate innate immune cells via sensors such as toll-like receptors (TLRs). DAMPs are particularly important players in sterile inflammation. In diseases such as systemic juvenile idiopathic arthritis (systemic JIA) and disease-complicating macrophage activation syndrome (MAS) the TLR4-signaling DAMPs S100A8/A9 and A12 are highly overexpressed and are thought to trigger and perpetuate inflammation. However, TLR4-signaling is not exclusively pro-inflammatory. Upon receptor internalization, an alternative pathway is initiated, which induces prominent type I interferon (T1-IFN) expression.
Objectives: We recently reported on a critical role of IFNa/b in regulating IL-18 expression in hyperinflammation and MAS, which results in its sensitivity to JAK/STAT-inhibition in both murine models as well as patients (Verweyen *et al.*, Am J Respir Crit Care Med, 2020). While this study was largely built on PAMP (LPS) stimulations, we next wondered whether a purely sterile inflammatory environment as in systemic JIA can be sufficient to already induce T1-IFN expression and may thus operate as driver of the high IL-18 levels observed in disease.
Methods: In human PBMCs we investigated pro-inflammatory as well as IFN-related gene expression resulting from LPS, S100A8/A9, S100A12, serum amyloid A (SAA), Apolipoprotein A1 (ApoA1), HMGB1 and type I or type II interferon-stimulations. Different concentrations and stimulation times as well as inhibitors for LPS-signaling and LPS-binding protein (LBP) were tested. Stimulation-induced TLR4-internalization was analyzed by flow cytometry.
Results: In contrast to previous results obtained from experiments built on LPS-stimulations (Verweyen *et al.*, Am J Respir Crit Care Med, 2020), we initially observed, that S100A12-treatment of primary human monocytes did not result in comparable *IL18* expression. Broadened analyses of pro-inflammatory and IFN-related gene expression in LPS, S100A12, IFNa or IFNg-treated human PBMCs revealed, that in contrast to LPS, S100A12 - even when far beyond physiological levels - failed in inducing *IFI27*, *IFI44L*, *IFIT1*, *ISG15* and *RSAD2* expression. *IL1A*, *IL1B*, *IL1RN* and *IL6* expression was induced at levels comparable to LPS. When investigating stimulated cells by flow cytometry, we observed no TLR4-internalization by S100A12-treated human monocytes. *Vice versa*, inhibition of LBP, which has been assigned a fundamental role in TLR4-internalization, impaired LPS-induced receptor endocytosis, which resulted in abrogation of T1-IFN-related gene expression as observed with S100A12 treatment. When testing stimulations with other TLR4-dependent DAMPs (S100A8/A9, SAA, ApoA1, HMGB1) alongside with S100A12 we universally observed pro-inflammatory but no *IFIT1*, *ISG15* and *RSAD2* expression compared to LPS.
Conclusion: In contrast to LPS, TLR4-dependent DAMPs fail to enable LBP-driven receptor internalization. In consequence, this restricts DAMP-signaling to the MyD88-dependent pro-inflammatory pathway and excludes TRIF-dependent T1-IFN expression. As T1-IFN acts as natural negative regulator of IL-1, while it is strictly required for *IL18* expression, this has fundamental consequences on how TLR4-dependent DAMPs shape a sterile inflammatory environment in diseases such as systemic JIA.

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Disclosure of Interest
None declared

O033

Sex differences in juvenile-onset SLE susceptibility and cardiovascular risk could be associated with altered Treg phenotype and lipoprotein metabolism

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Introduction: Males and females have altered immune responses resulting in variation in autoimmune and cardiovascular risk (CVR). Recently, these differences have played a role in the inflammatory response to COVID-19 infection. Sex differences exist in the frequency and activity of immune-cell subsets but mechanisms underlying sexual dimorphism remain unknown. Our previous work identified a link between immune cell function and lipid metabolism. We hypothesised that sex hormones could influence immune cell differentiation via changes in lipid metabolism and this could be altered in autoimmune diseases such as juvenile-onset systemic lupus erythematosus (JSLE), a disease that emerges during puberty, results in an increased CVR and has a strong female prevalence.
Objectives: We investigated sex differences in T-cell subset frequency and function during adolescence in healthy donors and JSLE patients, including the relationship with lipid metabolism and CVR.
Methods: Flow cytometry and qPCR were used to measure metabolic marker expression on 44 immune cell subsets from 39 teenage healthy controls (HCs, 17 male, 22 female, mean age 19), 35 age matched JSLE patients (12 male, 23 female, mean age 19), pre puberty HCs (10 males and 10 females, mean age 8) and individuals with gender dysphoria undergoing cross-sex hormone therapy (10 biologic males and 10 biologic females). Analysis of metabolic biomarkers, including lipoprotein composition, was performed on matching serum using nuclear magnetic resonance.
Results: HC responder (Tresp) and regulatory (Treg) T-cell subsets displayed the strongest immune profile differences by sex with significantly increased Tregs (p= 0.036) and reduced Tresp (p= 0.001) frequencies in males compared to females. HC Male Tregs had an increased suppressive capacity, IL-4 production (p= 0.019) (supported by increased GATA-3 expression) and plasma membrane glycosphingolipid (GSL) expression (p= 0.038) compared to Tregs from HC females. GSL changes were mirrored by increased expression of GSL synthesis enzyme UGCG (p= 0.042) in male Tregs, suggesting a sex-specific alteration in lipid metabolism related to Treg function.
Metabolomic lipoprotein analysis of matching serum revealed that teenage HC males had significantly reduced atheroprotective high density lipoprotein subsets and increased atherogenic very low density lipoprotein (VLDL) subsets compared to HC females. These differences were not observed pre-puberty but were induced

appropriately by sex hormone treatment in gender dysphoria individuals; suggesting that sex hormones regulate lipid metabolism in vivo. VLDL subsets from HC males were preferentially enriched with triglycerides and correlated positively with activated Treg subsets compared to VLDL from HC females where no such relationship was seen. Furthermore, Tregs cultured with VLDL isolated from either HC males or females recapitulated the male and female Treg phenotype respectively. Strikingly, sex differences in Treg frequency, phenotype, lipid metabolism and serum lipoproteins were lost in patients with JSLE. This loss of sexual dimorphism in JSLE patients involved the development of a more atherogenic metabolomic profile and pro-inflammatory T-cell phenotype in females.
Conclusion: Potential defects in sex hormone signalling in patients with JSLE may lead to a loss of differential male/female lipid taxonomy. Defective lipoprotein metabolism in JSLE could alter immune cell plasma membrane lipids and immune cell function and contribute to increased CVR in female JSLE patients.

Disclosure of Interest
None declared

O034

Examining the role of IFN-I and Langerhans cell ADAM17 in lupus photosensitivity

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Introduction: Photosensitivity resulting in inflammatory skin lesions is a hallmark of cutaneous lupus. Lesions can be disfiguring and have a negative impact on quality of life. Understanding photosensitivity is critical to developing better treatment. Our lab showed ADAM17, a metalloprotease found on Langerhans cells (LCs), is activated by UVR and is critical for limiting UVR-induced keratinocyte apoptosis and skin inflammation through cleavage and activation of epidermal growth factor receptor (EGFR) ligands. Two photosensitive SLE models showed reduced LC ADAM17 expression with evidence for dysfunction in human SLE, suggesting that photosensitivity is at least in part due to dysfunctional LCs. A prominent IFN signature has been documented in the blood and skin of SLE patients and could be an upstream mediator of ADAM17. We thus hypothesized that Type I IFN downregulates LC ADAM 17 activity resulting in photosensitive rash in SLE.
Objectives: Our primary objective was to examine gene expression patterns in non-lesional skin of human and murine lupus skin. We seek to develop an LC ADAM17- deficient gene expression signature and hypothesize the presence of a prominent IFN signature further demonstrating a potential link between interferon and ADAM17 downregulation.
Methods: Transcriptomics of non-lesional skin from discoid lupus (DLE) and healthy controls and of MRL and MRL/lpr mice were compared. Human data was gathered from unpublished data from Krueger et al (2014) using microarray in DLE lesions compared to psoriasis and healthy skin. We performed RNA seq on non-lesional skin of MRL and MRL/lpr mice. Data were analyzed in R using edgeR. Gene set analyses were performed with QuSAGE and plots were generated using a custom Shiny platform developed by the HSS Genomics Center. To examine whether LCs show an IFN-I regulated gene signature, we are currently sorting LCs from both UVR-exposed and non-exposed WT and Adam 17 fl/fl Langerin Cre mice for RNA seq. Using the IRB approved method of suction blistering to sample immune cells in the skin, our plan is to gather LCs from the skin of SLE patients to determine LC ADAM17 activity and whether this correlates with interferon signature via RNA seq.
Results: IFN-I regulated genes were among the most differentially regulated genes in non-lesional skin in both human and the MRL/lpr lupus mouse model. Many interferon regulated genes were found to be highly expressed in both (Fig 1A, D). Pathway analysis further showed that IFN-I-regulated genes were among the most differentially regulated pathways in disease vs control skin for both humans and mice (Fig 1B, E). Preliminary results from the analysis of ADAM17fl/fl Langerin Cre mice are expected in the next several months.
Conclusion: Microarray results suggest an elevated IFN signature in non-lesional skin of DLE patients with a similar IFN signature found in MRL/lpr mice via RNA sequencing. We anticipate that we will detect a reduction in ADAM17 activity in non-lesional skin of human SLE patients and find a correlation with IFN signature, supporting a potential role for IFN-I in dysregulating ADAM17 in lupus photosensitivity. These findings could help to understand why type I IFN targeted therapies are having success in SLE skin disease and may lead to targeting of ADAM17 for lupus. In the future, we hope to determine whether the gene signature associated with ADAM17 deficiency can be seen in other inflammatory skin conditions, such as dermatomyositis.

Disclosure of Interest
None declared

O035

Synovial tissue resident memory T cells mediate arthritis flares

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Introduction: Resident memory T cells (T_{RM}) are site-specific memory T cells that take up long-term residence in peripheral tissues and aid in local immune defense. T_{RM} have also been implicated in autoimmune diseases by driving localized recurrent inflammation.
Objectives: As chronic arthritis is characterized by recurrent site-specific joint inflammation, we sought to investigate the role of T_{RM} in joint-specific memory.
Methods: We performed 10x genomics droplet-based single cell RNA sequencing and immune repertoire profiling on memory T cells disaggregated from human rheumatoid arthritis synovium to evaluate transcriptomic signature. We also used Mantra multispectral immunofluorescence microscopy to evaluate T cells expressing common T_{RM} protein markers in human arthritic synovial tissue sections. To assess the functional contribution of T_{RM} cells in arthritis in vivo, we generated a novel murine model of joint-specific recurrent synovitis. We utilized adoptive transfer, in vitro metabolic and migration assays, in vivo cell labeling, and localized depletion strategies to characterize T_{RM} cells in the synovium and their functional role in arthritis flare.
Results: We identified cells with the phenotypic and transcriptomic signature of T_{RM} within human arthritic synovium. These cells were primarily CD8+ and exhibited restricted T cell receptor clonotypes as well as a pro-inflammatory gene expression profile. Adoptive transfer studies in our animal model of joint-specific recurrent inflammation confirmed that arthritis flares were mediated by antigen-specific CD8+ T cells that remained within previously inflamed joints during remission. These cells were bone fide T_{RM}, as confirmed through surface signature, failure to migrate in vivo or in vitro, preferential uptake of free fatty acids, and long-term residency. Site-specific depletion of synovial T cells during remission markedly ameliorated disease recurrence, confirming a role of synovial T_{RM} in arthritis flares.

Conclusion: Here, we demonstrate that synovial T_{RM} present in human inflamed synovium are a targetable mediator of joint-specific memory in arthritis.

Disclosure of Interest
None declared

O036

An active proNGF/p75NTR axis in arthritis patients influences cytokine production in synovial fibroblasts

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Introduction: Inflammation has been associated with a marked increase in the basal levels of NGF in tissues, but how NGF and its immature form proNGF, regulate cell functions and mediator release during inflammatory responses is still largely unknown. In this study, we investigated the effects of proNGF, the biological active NGF precursor, on inflammatory cytokine production in synovial fibroblasts to clarify whether changes in proNGF concentration or in the expression of its specific receptor p75NTR are involved in joint inflammation.
Objectives: To investigate whether proNGF and its specific receptor p75NTR modulate distinct pro-inflammatory pathways in synovial fibroblasts of chronic arthritis patients and whether p75NTR/proNGF axis inhibition dampens inflammatory cytokine production.
Methods: NGF expressions, TrkA, p75NTR expression and signaling in synovial fibroblasts from arthritis patients were evaluated by quantitative PCR (qPCR) and Western Blot Analysis. Specific ELISA were used to analyze NGF, proNGF and cytokine production. *In vitro* inhibition of p75NTR was performed using a synthetic inhibitors (LM11A-31) that blocks the binding site of proNGF.
Results: High amounts of proNGF were detected in the synovial fluid of chronic arthritis patients. *In vitro* stimulation of patient synoviocytes with recombinant cytokines strongly enhanced the release of proNGF in conditioned media as well as the expression of p75NTR. Inhibition of p75NTR significantly decreased the release of inflammatory mediators as IL-6, IL-1β, IL-8, MCP1. To recreate *ex vivo* the condition of an inflamed synovia, synovial fibroblasts were cultured in media enriched with 30% synovial fluid (SF) obtained from active Juvenile Idiopathic Arthritis (JIA) patients and that contained high concentration of inflammatory mediators and high proNGF amounts. As expected, synoviocytes cultured in 30% SF significantly enhanced the release of IL-6 and other inflammatory cytokines in the conditioned media. The inhibition of proNGF binding to p75NTR using LM11A-31, strongly decreased inflammatory cytokines release. This reduction was even more substantial of the one obtained using monoclonal antibodies against IL-6 R (tocilizumab), IL-1β (canakinumab) and TNFα (infliximab) commonly used for arthritis treatment. The analysis of the intracellular pathways in LM11A-31 treated synoviocytes showed a decreased phosphorylation of MAPK downstream molecules like p38 and JNK, indicating that inhibition of proNGF binding to p75NTR results in a decreased activity of the pro-inflammatory cascade response.
Conclusion: Inflammatory stimuli induce both p75NTR expression and the release of proNGF in synoviocytes. Blocking the binding of proNGF to its receptor p75NTR, using LM11A-31 inhibitor, strongly reduces in synoviocytes the release of inflammatory mediators, suggesting that enhanced p75NTR expression levels might have a crucial role in the chronicity of the inflammatory response and prospect the use of p75NTR inhibitors as a new therapeutic approach to chronic arthritis.

Disclosure of Interest
None declared

O037

Coexistence of synovial T lymphocytes driving and regulating chronic inflammation in juvenile idiopathic arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O037

Introduction: T lymphocytes accumulate in inflamed tissues of patients with juvenile idiopathic arthritis (JIA) and they can express pro-inflammatory cytokines upon re-stimulation in vitro. This and a significant genetic linkage of JIA to MHC genes suggest that T lymphocytes play an important role in the pathogenesis of this disease. But their role in established disease is less clear.
Objectives: We aimed to define the transcriptional and clonal identity of autoreactive memory T cells in patients with JIA.
Methods: We isolated paired samples of antigen-experienced conventional CD4+CD45RO+CD25lo T helper memory cells (T_{cons}), regulatory CD4+CD45RO+CD127loCD25hi T memory cells (T_{regs}) and cytotoxic CD8+CD45RO+ T memory cells (CTLs) by flow cytometry from the synovial fluid (SF) and the blood of seven patients with JIA. Subsequently, we performed single-cell sequencing combined with T cell receptor (TCR) sequencing on 74.891 cells to dissect their cell heterogeneity due to their transcriptional profiles and clonal repertoire. We then performed shared nearest neighbor-clustering using dimensional reduction analysis by t-distributed stochastic neighbor embedding (t-SNE).
Results: Our data reveal transcriptional heterogeneity among the different subsets of T memory cells both in peripheral blood as well as in cells derived from inflammatory tissues. TCR sequencing and gene expression of TCR signaling-induced genes enabled us to distinguish autoreactive from bystander memory T cells. Gene expression profiles of expanded recently activated clonotypes showed elevated expression of *PDCD1* (encoding for PD-1) compared to non-enriched bystander T helper memory cells from the inflamed tissue. A PD-1^{+}*TOX*$^{+}$*EOMES*$^{+}$ population of $CD4^{+}$ T lymphocytes expressed immune regulatory genes and genes attracting myeloid cells. A PD-1^{+}*TOX*$^{+}$*BHLHE40*$^{+}$ population of $CD4^{+}$, and a mirror population of $CD8^{+}$ T lymphocytes

expressed genes driving inflammation as well as genes supporting B lymphocyte activation. This dichotomy among *PDCD1*-expressing cells represents a general, lineage-transcending signature of memory T lymphocytes in chronic inflammation, since both $CD4^+$ and $CD8^+$ T memory cells possess analogous populations. Finally, we identified autoreactive T lymphocyte clones and transcriptional signatures of recirculating SF-derived cells in the blood of JIA patients.
Conclusion: Taken together, these results might offer a basis for developing diagnostic and therapeutic strategies for patients with JIA i), by developing biomarkers on the basis of recirculating autoreactive memory T cells and ii), by treating patients with agents to selectively deplete memory T cells driving pathology in chronic inflammation.

Disclosure of Interest
None declared

O038

Identification of a regulatory pathway governing expression of TRAF1 via a JIA-associated non-coding variant

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Pediatric Rheumatology 2020, **18(Suppl 2):**O038

Introduction: Over the past decade, genome-wide association studies (GWAS) have identified TRAF1/C5 locus as a risk locus for rheumatoid diseases including RA and JIA(1, 2), and TRAF1 negatively regulates Toll-like receptor signaling(3). However, the exact risk variant within that locus and its underlying mechanism regulating TRAF1 expression is still not known.
Objectives: We aim to identify non-coding variant in TRAF1/C5 locus governing the expression of TRAF1 gene and its regulatory pathway.
Methods: Single-nucleotide polymorphisms (SNPs) in linkage disequilibrium (LD) with the most disease associated SNP in TRAF1/C5 locus from immunochip data (5 thousands JIA patients and 14 thousands health controls) were high-throughput screened by SNP-seq(4). Top candidates' regulatory function were further validated by Electrophoretic mobility shift assay (EMSA) and luciferase reporter assay. Then the transcriptional factor that might binds to the functional variant after validation was tested by CHIP-qPCR, oligo pulldown assay as well as supershift assay. Finally, the association between this transcriptional factor and TRAF1 gene expression were analyzed by RNAi knockdown experiment.
Results: After screening by SNP-seq, EMSA and luciferase reporter assay, rs7034653 was found to be the best functional non-coding variant in TRAF1/C5 locus that is associated with JIA. EMSA shows that protein from monocyte nuclear extract has a preferential binding to protective allele A than the risk allele G of rs7034653, and that binding preference likely regulates higher gene expression as shown by luciferase reporter assay, which is consistent of existing eQTL data that shows higher expression of TRAF1 in protective allele than risk allele in human monocytes. Furthermore, this variant is found to be able to bind to AP1 transcriptional factor FRA2. Suppressed expression of FRA2 by RNAi leads to lower expression of TRAF1 after LPS stimulation in THP-1 monocytic cell line.
Conclusion: Non-coding variant rs7034653 in TRAF1/C5 locus likely regulates TRAF1 gene expression in monocytes through binding to transcriptional factor FRA2.

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Disclosure of Interest
None declared

O039

A novel loss-of-function mutation in LACC1 underlies hereditary juvenile arthritis with extended intra-familial phenotypic heterogeneity

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Introduction: Recent clinical reports link early-onset hereditary JIA with likely-pathogenic homozygous variants in the *Laccase (multicopper oxidoreductase) domain-containing 1* gene - *LACC1* (*C13orf31*, *FAMIN*, MIM 613409). Interestingly, a shared *LACC1* likely-pathogenic variant was independently reported in association with either monogenic JIA or severe pediatric Crohn's disease..
Several associations studied have linked *LACC1* risk variants with increased susceptibility to leprosy and to various autoimmune disorders, including ulcerative colitis, psoriasis, Behcet and ankylosing spondylitis.
Objectives: To reports the intra-familial phenotypic heterogeneity associated with early onset Juvenile Idiopathic Arthritis (JIA) secondary to *LACC1* disruption, and to describe its effect on infalmatory pathways.
Methods: Whole exome sequencing (WES) in a consanguineous Israeli-Muslim family with autosomal recessive polyarticular JIA and extra-articular involvement including renal amyloidosis and Crohn's disease. Expression studies of an identified homozygous truncating variant variant in *LACC1* in patient-derived macrophages (Mϕ) and Cytokine profile analysis in WT and LACC1-disrupted Mϕ.
Results: Whole exome sequencing (WES) in a consanguineous Israeli-Muslim family with autosomal recessive polyarticular JIA and extra-articular involvement including renal amyloidosis and Crohn's disease, identified a novel homozygous truncating variant (p.Glu348Ter) in *LACC1* as underlying the disease. The p.Glu348Ter variant is predicted to cause premature stop of the LACC1 protein sequences, is absent from ethnically-matched control samples and from public variation databases, and is predicted harmful by prediction software. Expression studies of p.Glu348Ter-LACC1 in patient-derived macrophages (Mϕ) indicate lack of endogenous RNA transcription and protein expression, most probably secondary to nonsense-mediated mRNA decay. Cytokine profile analysis in WT and LACC1-disrupted Mϕ indicate increased levels of pro-inflammatory chemokines and cytokines in affected as compared to WT cells, thereby implicating a role for *LACC1* disruption in pro-inflammatory molecular pathways.
All the described family members with JIA showed remarkable response to Tocilizumab therapy, causing sustained improvement of their arthritis, and resolution of amyloidosis in the affected family member.
Conclusion: Taken together, our findings reinforce the role of LACC1 disruption in autosomal recessive JIA, extend the clinical spectrum and the intra-familial heterogeneity of the disease-associated

phenotype, and suggest an inhibitory role for wild-type *LACC1* on pro-inflammatory pathways.

Disclosure of Interest
None declared

O040

Roles of intestinal barrier and microbe-associated molecular patterns in the pathogenesis of inflammatory arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O040

Introduction: Juvenile idiopathic arthritis (JIA) is the most common childhood-onset chronic rheumatic disease. The cause of JIA remains unknown. A growing body of evidence suggest that intestinal microbiota and intestinal barrier dysfunction may play a pivotal role in the pathophysiology of JIA. Furthermore, some publications suggest a putative role of Microbe-Associated Molecular Patterns (MAMPs) for the development of murine models of arthritis. In order to develop new treatment approaches for inflammatory arthritis it is necessary to better understand the putative link between intestinal barrier dysfunction and development of inflammatory arthritis.
Objectives: To study the link between changes in the intestinal permeability, systemic translocation of microbial components and development of arthritis in mice.
Methods: We used the collagen induced arthritis (CIA)model and IL1Ra KO mice that is a spontaneous model of arthritis. Severity was assessed by a clinical score. Intestinal permeability was studied *ex vivo* using translocation of labelled marker in Ussing chambers.
Results: Oral treatment with carrageenan (CGN) increased intestinal permeability (mean 859 vs 313pmol/cm^2/h, p<0.01) and was associated with a more severe arthritis (mean 3.6 vs 1.3, p<0.01). In accordance with previous publications on intestinal-conditional HNF4aKO mice, we observed increased intestinal permeability (794 vs 379 pmol/cm^2/h, p<0.05). Furthermore, they exhibited a higher score of collagen-induced arthritis (1.7 vs 0.77, p<0.05). The worsening effect of CGN on arthritis was also confirmed in IL1RaKO mice (mean 2.7 vs 0.5, p<0.05). Treatment with CGN and deleting intestinal HNF4a were associated to an increased *ex vivo* translocation of muramyldipeptide (MDP) (respectively p=0.001 and p=0.03) and lipopolysaccharide (LPS)(p=0.04 and p=0.04). Oral treatment with probiotic Vsl3 reduced intestinal permeability (mean 277 vs 667 pmol/cm^2/h, p<0.05) and decreased *ex vivo* translocation of muramyldipeptide (MDP) (p=0.01) and lipopolysaccharide (LPS)(p=0.01). Furthermore, VSL3 tended to decrease the severity of arthritis in the CIA (mean 3.7 vs 11.3,p=0.07) and in the IL1RaKO (mean 2.2 vs 0.4, p<0.05) mouse models. While oral treatment with MDP and LPS did not affect the intestinal permeability, it exacerbated collagen induced arthritis (mean 3.2 vs CTRL mean 0, p<0.01). The worsening effect of treatment with MDP and LPS was also confirmed in the IL1RaKO arthritis model (mean 2.9 vs 0.5, p<0.01).
Conclusion: Changing the intestinal permeability impacted on the severity of arthritis. Bioavailable MDP and LPS contribute to the development of arthritis. Further experiments are necessary to understand how exactly systemic MAMPs leads to worsening of arthritis.

Disclosure of Interest
None declared

O041

Application of systems biology-based in silico tools to optimize treatment strategy in Still's disease

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Pediatric Rheumatology 2020, **18(Suppl 2):**O041

Introduction: Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult Onset Still's Disease (AOSD) are manifestations of an autoinflammatory disorder with complex pathophysiology and significant morbidity, together also termed Still's disease.
Objectives: To investigate the optimal treat-to-target strategy for Still's disease by in silico models based on systems biology.
Methods: Molecular characteristics of Still's disease and data on biological inhibitors of interleukin (IL)-1 (anakinra, canakinumab), IL-6 (tocilizumab, sarilumab), glucocorticoids as well as conventional disease-modifying anti-rheumatic drugs (DMARDs, methotrexate) were used to construct in silico mechanisms of action (MoA) models by means of Therapeutic Performance Mapping System technology (TPMS). TPMS combines artificial neuronal networks (ANN), sampling-based methods and artificial intelligence. The models were validated with publicly available expression data from sJIA patients.
Results: Biologicals demonstrated more pathophysiology-directed efficiency than non-biological drugs. IL-1 blockade mainly acts on the innate immune system, while IL-6 signaling blockade has a weaker activity on the innate immunity and rather affects the adaptive immunity (Table 1). The MoA models showed that the IL-1β inhibitor canakinumab is more efficient than the IL-6 receptor inhibiting antibody tocilizumab in the autoinflammatory/systemic phases of Still's disease. MoA models reproduced 67% of the information obtained from expression data.
Conclusion: Systems biology-based modelling supported the preferred use of biologics as immunomodulatory treatment strategy for Still's disease. This further encourages early IL-1β blockade in initial autoinflammatory/systemic phases of Still's disease to prevent the development of disease or drug-related complications. Further studies are needed to determine the optimal timeframe of the window of opportunity for canakinumab treatment.

Disclosure of Interest
M. Coma Employee of: Anaxomics Biotech, C. Segú-Vergés Employee of: Anaxomics Biotech, C. Kessel: None declared, S. Smeets Employee of: Novartis, D. Foell Consultant for: Novartis, Chugai-Roche, Paid Instructor for: Novartis, Pfizer and SOBI, A. Aldea Employee of: Novartis

Table 1 (abstract O041). Summary of ANN scores. A) Global Still's disease evaluation. B) Immune system component. ANN scores mean the probability of the resulted relationship is true positive: +++ correspond to values >78% (p-value<0.05); ++ correspond to values > 59% (p-values <0.15) and; + correspond to values > 38% (p-value<0.25)

A) Still's disease molecular definition		Biologics				Non-biologics	
		Anakinra	Canakinumab	Sarilumab	Tocilizumab	Methotrexate	Prednisone
Still's disease		+++ (81%)	+++ (86%)	+++ (85%)	+++ (85%)	- (5%)	++ (70%)
	Systemic profile	+++ (80%)	+++ (88%)	+++ (85%)	+++ (85%)	- (4%)	++ (70%)
	Rheumatic profile	+++ (87%)	+++ (92%)	+++ (81%)	+++ (81%)	- (9%)	++ (64%)
B) Immune system components		**Biologics**				**Non-biologics**	
		Anakinra	**Canakinumab**	**Sarilumab**	**Tocilizumab**	**Methotrexate**	**Prednisone**
Innate immune system deregulation		++ (71%)	++ (71%)	+ (55%)	+ (55%)	- (10%)	++ (65%)
Adaptive immune system	T-cell response activation	+ (45%)	- (37%)	++ (71%)	++ (71%)	- (25%)	+ (47%)
	Defective immune regulation	- (19%)	- (37%)	+ (47%)	+ (47%)	- (15%)	+ (50%)

O042

Interferon-γ drives the expression of T-bet in naïve B cells of patients with paediatric systemic lupus erythematosus

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Introduction: Paediatric systemic lupus erythematosus (pSLE) is an autoimmune disorder of childhood characterized by the production of autoantibodies against nuclear antigens. In the last decade, several studies showed an up-regulation of genes induced by type I interferons (IFNα) in peripheral blood and tissues of pSLE patients[2]. It has been reported that the expression of this group of genes, known as the type I IFN signature, correlates with disease activity[2]. More recently, also the type II interferon (IFNγ) has been implicated in pSLE; however, its precise role has not been clarified yet[3].
Objectives: To investigate the role of IFNγ in the pathogenesis of pSLE evaluating: 1) the expression levels of IFNγ-related genes in the peripheral blood of pSLE patients; 2) the expression of T-bet in B cells of pSLE patients; the induction of T-bet in B cells by IFNγ.
Methods: Expression levels of IFNα-induced genes (IFI27, IFI44L, IFIT1, RSAD2, ISG15, SIGLEC1), IFNγ and IFNγ-induced genes (CXCL9, CXCL10, IDO1) were analysed by quantitative PCR (qPCR) in whole blood of pSLE patients and healthy donors (HDs). We developed a type II IFN score similarly to the type I IFN score described by Crow[4]. Expression of T-bet in B cells was evaluated by flow cytometry. Peripheral blood mononuclear cells (PBMCs) from 5 HDs were stimulated *in vitro* with recombinant human IFNγ and IFNα2b; expression of T-bet was evaluated by flow cytometry. Serum levels of CXCL9 were evaluated by ELISA. For each patient, SLEDAI was calculated.
Results: Expression levels of both IFNα and IFNγ-induced genes were upregulated in patients with pSLE (n=39). The type II IFN score significantly correlated with the SLEDAI (r = 0.33, P = 0.03). As previously reported, also the type I IFN score significantly correlated with SLEDAI (r = 0.50, P < 0.01). We also found increased serum levels of CXCL9 in pSLE patients compared to HDs (mean±SD HD 333±117pg/mL, SLE 2125±4885pg/mL, P=0.0003). Thus, patients with pSLE have increased activity of IFNγ .
B cells play a crucial role in the pathogenesis of SLE. In murine models of SLE, IFNγ was shown to activate B cells to make autoantibodies[4]. We evaluated the expression of T-bet (a transcription factor that is thought to be induced specifically IFNγ) in B cells: we observed a population of B cells expressing T-bet in the naïve compartment in patients with pSLE. The frequency of T-bet+ naïve B cells correlated with SLEDAI. To confirm the induction of T-bet in B cells by IFNγ, we stimulated PBMCs of HD with either IFNγ or IFNα: both chemokines induced the expression of T-bet in naïve B cells. Since it is known that IFNα can induce the expression of IFNγ, we stimulated cells with IFNα and an antibody blocking IFNγ: in this setting IFNα did not upregulate the expression of T-bet in B cells.
Conclusion: Our data suggest a potential role of IFNγ in the pathogenesis of pSLE. IFNγ-induced genes in whole blood and CXCL9 in serum were increased in pSLE patients. IFNγ specifically induced the expression of T-bet in naïve B cells. We observed an expansion of T-bet+ naïve B cells in patients with pSLE. Thus, IFNγ is hyperactiaved in SLE, inducing the aberrant expression of T-bet in naïve B cells. Further research is needed to dissect the role of IFNγ-activated B cells in pSLE.

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Disclosure of Interest

None declared

O043

In vitro analysis of standard of care drugs on the IFN type I signature; aspirin and hydroxychloroquine the old kids on the block

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Pediatric Rheumatology 2020, **18(Suppl 2):**O043

Introduction: Childhood-onset Systemic Lupus Erythematosus (cSLE) is prototypic Interferon (IFN) driven autoimmune disease characterized by an increased expression of type-I IFN stimulated genes, known as the IFN signature. The inhibitory effects of various drugs like Hydroxychloroquine and more recently Aspirin on IFN inductions routes led to the idea that some standard of care drugs might be the cause of a low IFN score observed in a subgroup of treated patients. For this, testing these, but also other standard of care immunosuppressive agents in an *in vitro* model for their effect on IFN activation would lead to new knowledge and a broader view of the mechanisms that lead to a patient having an increased expression of the IFN signature or not.
Objectives: To study the effect of immunosuppressive medication on the type-I IFN signature in an *in vitro* model
Methods: Freshly isolated human PBMCs were stimulated with or without CpG-A or Imiquimod (IQ) or transfected with the cGAS agonist G3-YSD to induce IFN upregulation through the TLR7/9- and DNA Sensing Receptor-pathway respectively. To assess the direct role of the drugs on the downstream pathway of the IFNAR PBMCs were stimulated with IFN-a2b. Aspirin, diclofenac, HCQ, Mycophenolate Mofetil (MMF) and prednisone were added separately to these cultures followed by analysis of MxA by qPCR. Cell viability in all culture conditions was above 85%.
Results: The IFN signature induced by CpG-A, IQ, G3-YSD and IFN-a2b was significantly reduced after addition of Aspirin in three separate experiments. Addition of diclofenac showed a trend towards reduced levels in all conditions. HCQ was able to significantly reduced the CpG-A and IQ induced IFN activation while MMF and prednisone did not show an effect in any of the culture conditions.
Conclusion: The IFN signature induced through various routes was significantly reduced by Aspirin and HCQ in an in vitro model. Combining both clinical and *in vitro* data from our longitudinal cohort will elucidate the effect of different immunosuppressive drugs on the type-I IFN signature in cSLE.

Disclosure of Interest

None declared

O044

Subchondral high T2 signal in pediatric sacroiliac joint MRI: a normal finding that can mimic sacroiliitis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O044

Introduction: Understanding of the normal magnetic resonance imaging (MRI) appearance of the developing sacroiliac joint (SIJ) is important for distinguishing normal developmental variations from disease. Subchondral signal changes in SIJ in children can give rise to diagnostic challenges and false positive diagnoses of sacroiliitis, as they can mimic bone marrow edema (BME).
Objectives: To determine how subchondral signal intensity on T2-weighted images in SI-joints in children varies with age, sex and closure of segmental apophyses of the sacrum.

Methods: MRI of 502 SIJ in 251 children (132 girls), mean age 12.4 years (range 6.1-18.0), were obtained. Ethics committee approval was obtained, informed consent was signed by all children and parents. 127/251 had asymptomatic joints and were imaged for non-rheumatologic reasons in whom we added semi-coronal T1 and STIR of the SI joints, and 124 had low back pain but no sign of sacroiliitis on initial clinical MRI review. Before the main reading exercise, images of 10 participants (20 SIJ) who had been excluded from the study were used for multi-step calibration exercises. Three calibration rounds were conducted over 8 months. Subchondral high signal ('flaring') was defined as increased signal in subarticular bone on STIR images compared to normal bone marrow in the centre of S1 and S2 vertebral bodies. After calibration, three subspecialist radiologists independently scored subchondral signal changes from 0-3 in 4 locations: vertical sacral (along the lateral apophyses of the sacrum), horizontal sacral (along the intersegmental apophyses), iliac (vertically along iliac side of SIJ), and iliac crest (horizontally along iliac wing upper margin), separately for left and right sides. The degree of closure of sacral segmental apophyses was graded as well. Readers were blinded to demographic, clinical and other imaging findings. Associations between patient age, sex, signal changes and apophyseal closure were analysed.
Results: Rimlike subchondral increased T2 signal or 'flaring' was commonly seen in children at the margins of the SI joints, and is far more common on the sacral side (72% vs 16%, p<.001). It was symmetrical in >90% of children. Iliac flaring scores were always lower than sacral, except for 1 child. Signal changes decreased as sacral apophyses closed, and were seen in <20% of subjects with fully closed apophyses. Signal changes were more frequent in boys, and peaked in intensity later than for girls (ages 8-12 vs. 7-10). Subchondral signal in iliac crests was high throughout childhood and did not correlate with other locations. We found no significant difference between left/right side, boys/girls nor between both groups.
Conclusion: Rimlike subchondral high T2 signal 'flaring' is commonly observed at MRI of sacroiliac joints in children, and should not be confused with pathology. It is generally sacral-predominant, symmetrical, and seen in less than 1/5 of children after segmental apophyses are closed. Flaring that is asymmetrical, greater in ilium than sacrum, or intense in a teenager with closed apophyses, is unusual for normal children and raises concern for pathologic bone marrow edema. Subchondral signal in iliac crests is high throughout childhood and cannot be used for reference in diagnostic criteria. Accurately distinguishing between normal and pathologic pediatric subchondral sacroiliac joint signal changes requires understanding the patterns of normal variation, to avoid misdiagnosis of sacroiliitis.

Disclosure of Interest
None declared

O045

Foot and ankle MRI in JIA: development and preliminary validation of a paediatric-targeted MRI scoring system for the assessment of disease activity and damage

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Pediatric Rheumatology 2020, **18(Suppl 2):**O045

Introduction: Arthritis of the ankle occurs commonly in all subtypes of JIA and might cause considerable functional impairment. Clinical assessment of this region is often challenging due to the multiplicity of joint recesses and surrounding tendons.
Objectives: (1) to explore the value of MRI in the assessment of the ankle/foot; (2) to set-up a MRI scoring system to assess disease activity and damage in this region, and provide preliminary evidence of its validity in JIA patients.
Methods: 101 patients with JIA and clinical ankle/foot involvement were recruited from the Paediatric Rheumatology of Gaslini Institute and Ospedale Pediatrico Bambino Gesù between 2015 and 2018The clinically more affected ankle/foot was investigated with MRI and radiography (CR). One-year MRIs follow-up were available in 53 patients. Images were scored according to a MRI semi-quantitative score developed for the purpose, which included grading of synovitis, bone marrow oedema (BMO), bone erosions and cartilage lesions. Validation procedures included analysis of reliability, construct validity and responsiveness to change. Foot and ankle MRIs, obtained from 39 age-matched healthy controls, were included to evaluate the discriminant ability.
Results: Concordance between MRI and clinical evaluation in the assessment of disease activity was poor at the subtalar (70% of patients showed synovits on MRI whereas this joint was clinically involved in 39% of them) and talonavicular joints (54.4% of patients had synovitis on MRI versus 11% of patients with clinical active disease). MRI visualized tenosinovitis in 68.3% of patients, while clinical examination revealed tendons involvement in 19.8% of them. BMO was visualised in 49/101 (48.5%) patients. Bone erosions and cartilage damage were detected by MRI in 56/101 (56%) and 37/101 patients (36.6%), respectively. The MRI score showed an excellent inter-reader agreement for synovitis, tenosynovitis, BMO, bone erosions and cartilage damage scores (inter-class-correlation coefficient>0.9 for each items). The MRI synovitis and tenosynovitis scores were moderately correlated with clinical variables reflecting disease activity, such as the total count of swollen joints (r 0.44 and r 0.54) and the JADAS-71 (r 0.46 and r 0.47). The median values of MRI bone erosion and cartilage scores were significantly higher in patients with radiographic damage compared to patients without structural damage on CR ($p<0.05$). The responsiveness to change was satisfactory for the MRI synovitis (standardized response mean (SRM) 1.09) and tenosynovitis (SRM 0.85) scores, moderate for the MRI bone erosion score (SRM 0.41) and poor for the BMO score (SRM 0.27). MRI revealed synovitis in 6/39 (15%) healthy children; one healthy child showed bone profile changes resembling bone erosion. BMO was detected in 20/40 (50%) healthy children.
Conclusion: Foot and ankle MRI is more sensitive than clinical evaluation to identify the single anatomic components that are affected by the disease, with relevant implications for therapeutic intervention. The proposed paediatric MRI score appears to be a reliable and valid tool for assessing disease activity and damage in JIA patients with foot and ankle involvement. BMO is present in a relevant percentage of healthy children, thus significantly limiting its prognostic value.

Disclosure of Interest
None declared

O046

Early achievement of jadas acceptable disease activity is strongly predictive of one-year remission in etanercept-treated polyarticular JIA patients: results from a biker cohort

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Pediatric Rheumatology 2020, **18(Suppl 2):**O046

Introduction: Although an early onset of clinical improvement is thought to be a key factor in determining treatment success in juvenile idiopathic arthritis (JIA), the minimal early treatment response required to achieve remission remains undefined.
Objectives: We assessed Juvenile Arthritis Disease Activity Score (JADAS) and American College of Rheumatology (ACR) criteria for response to treatment at 3 months as a predictor of treatment success at one year in polyarticular JIA (pJIA) using a well-defined cohort of pJIA patients newly starting etanercept.
Methods: Patients from the German Biologics registry for Pediatric Rheumatology (BiKeR) with a diagnosis of pJIA initiating etanercept treatment were identified. Response to treatment at 3 months was determined according to JADAS improvement of disease activity[1], JADAS acceptable (ADA, JADAS≤5.4) and minimal disease activity (MDA, JADAS≤3.8), as well as to ACR improvement criteria. Primary outcome measures at one year were JADAS remission (JADAS≤1) and ACR defined inactive disease. Data were analysed using intention-to-treat.
Results: Altogether, 968 patients (758 females, 78.3%) with pJIA (491/132 RF negative/positive polyarthritis, 293 extended oligoarthritis, 52 PsA) were included. Mean age and disease duration at baseline were respectively 11.2±4.2 and 4.1±3.5 years. Achievement of JADAS improvement, ADA or MDA at 3 months correlated to 2.2 (1.5-3.3), 5.0 (3.5-7.2) and 5.4 (3.9-7.5) times higher odds to achieve JADAS remission, and to 2.6 (1.8-3.9), 3.7 (2.7-5.3) and 4.7 (3.4-6.5) times higher odds to achieve ACR inactive disease at one year compared to failure to meet these criteria, respectively. Achievement of ACR30/50/70 response at 3 months was associated to 2.3 (1.5-3.5), 2.2 (1.5-3.1) and 3.2 (2.3-4.3) times higher likelihood to achieve JADAS remission, and to 2.3 (1.6-3.5), 2.5 (1.7-3.5) and 3.1 (2.3-4.3) times higher likelihood to achieve ACR inactive disease at one year compared to failure to meet these responses, respectively. Failure to achieve a response to treatment, JADAS or ACR-defined, at 3 months showed a high negative predictive value (NPV) for attainment of JADAS remission or ACR inactive disease at one year (s. table).
Conclusion: Achievement of JADAS ADA / MDA at 3 months was significantly associated with better remission outcome at one year in etanercept-treated pJIA. Conversely, ACR30/50/70 and JADAS improvement did not strongly predict treatment success at one year. Our data suggest that, in a treat-to-target concept, attainment of at least JADAS ADA at 3 months may be meaningful.

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Disclosure of Interest
G. Armaroli: None declared, A. Klein: None declared, K. Minden: None declared, I. Foeldvari Consultant for: Chugai, Novartis, A. Hospach Speaker Bureau of: Chugai, Roche, Novartis, F. Weller-Heinemann: None declared, R. Trauzeddel: None declared, J. Kuemmerle-Deschner Consultant for: Novartis, Sobi, G. Horneff Speaker Bureau of: Pfizer, Abbvie, Chugai, Novartis

Table 1 (abstract O046). See text for description

	Response at 1 year							
	JADAS remission				ACR inactive disease			
Response at 3 months	Rate (%)	OR (95%CI)	P value	NPV (%)	Rate (%)	OR (95%CI)	P value	NPV (%)
JADAS impr	42	2.2 (1.5-3.3)	<0.0001	76	41	2.6 (1.8-3.9)	<0.0001	79
JADAS ADA	50	5.0 (3.5-7.2)	<0.0001	83	47	3.7 (2.7-5.3)	<0.0001	81
JADAS MDA	56	5.4 (3.9-7.5)	<0.0001	81	54	4.7 (3.4-6.5)	<0.0001	80
ACR30	42	2.3 (1.5-3.5)	<0.0001	76	41	2.3 (1.6-3.5)	<0.0001	77
ACR50	43	2.2 (1.5-3.1)	<0.0001	74	43	2.5 (1.7-3.5)	<0.0001	77
ACR70	51	3.2 (2.3-4.3)	<0.0001	75	50	3.1 (2.3-4.3)	<0.0001	76

O047
Patient-reported adverse events and treatment adherence in JIA: analysis of two large international cohorts
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Pediatric Rheumatology 2020, **18(Suppl 2):**O047

Introduction: Juvenile idiopathic arthritis (JIA) patients may experience significant adverse effects (AEs) from medications. AEs may negatively affect patients' well-being and reduce treatment compliance, ultimately compromising patient outcomes.
Objectives: 1) To assess the frequency of patient-reported adverse events (AEs) and their effects on well-being, health-related quality of life (HRQoL) and school activity.
2) To investigate treatment non-adherence and its determinants, focusing on the possible impact of AEs.
Methods: Data on 13704 visits of 8402 patients were obtained from two large multi-center international studies, the pharmacovigilance registry Pharmachild and The EPidemiology, treatment and Outcome of Childhood Arthritis (EPOCA) cohort. Subjects who were on medications at the time of visit were included. AEs, currently prescribed medications, root of administration, disease-related school problems, self-reported treatment adherence (as a dichotomic variable), reasons for non-compliance, patient overall well-being (PGA), physician global assessment (MD-global) and VAS-rated pain intensity were collected through the Juvenile Arthritis Multidimensional Assessment Report (JAMAR). HRQoL was assessed through a ten items Likert-type HRQoL scale encompassing a physical health (PhH) and psychosocial health (PsH) subscale, with higher scores indicating worse outcomes. The effects of AEs on PGA, PsH scale, school problems, and the determinants of therapy non-compliance were analyzed using General Linear and Generalized Mixed Effects Models with random intercepts per individual.
Results: AEs were reported by 29,49% of patients. Experiencing one or more AEs was associated to worse PGA (β 0.377, η^2 0.011, $p < 0.001$) and PsH score (β 0.618, η^2 0.024, $p < 0.001$) and school problems (OR 1.82, 95%CI 1.64-2.01, $p < .001$) after adjustment for MD-global, PhH and pain levels. Mood swings, sleep problems and weight gain showed the highest impact on PsH; frequency of the main AEs and regression estimates for outcomes are depicted in the table. Treatment non-adherence was reported by 9,27% of subjects. The most frequently cited reasons for non-adherence were drug refusal by the child (n=200) and fear of adverse events (n=142). Self-reported medication adherence was negatively associated to combination treatment with conventional and biologic DMARDs (OR 0.40, 95%CI 0.26-0.62, $p < .001$) and subcutaneous administration (OR 0.13, 95%CI 0.09-0.20, $p < .001$). Nausea predicted non-compliance due to fear of AEs (OR 13.93, 95%CI 5.02-38.65, $p < .001$).
Conclusion: AEs have a substantial impact on patients' quality of life, functioning and therapy adherence in JIA. Understanding treatment-related burden is vital to achieve good therapeutic compliance and improve outcomes in JIA.

Disclosure of Interest
None declared

Table 1 (abstract O047). See text for description

AEs	Frequency (%)	PGA		PsH Scale	
		β	p	β	p
Nausea	11.4	0.061	0.221	0.065	0.279
Headache	6.5	0.155	0.010	0.385	< .001
Gastric pain	6.1	0.182	0.003	0.293	< .001
Mood swings	5.4	0.548	< .001	153.654	< .001
Vomit	4.8	0.058	0.406	0.065	0.432
Sleep problems	3.5	0.253	0.002	0.659	< .001
Injection site reaction	3.3	0.164	0.034	0.097	0.287
Weight gain	3.2	0.113	0.157	0.499	< .001

O048

Tofacitinib for the treatment of polyarticular course juvenile idiopathic arthritis: patient-reported outcomes in a phase 3, randomised, double-blind, placebo-controlled withdrawal study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O048

Introduction: Tofacitinib is an oral Janus kinase inhibitor that is being investigated for juvenile idiopathic arthritis (JIA).

Objectives: To evaluate the impact of tofacitinib on parent/patient-reported outcomes (PROs) in patients (pts) with polyarticular course JIA (pcJIA: extended oligoarthritis, systemic JIA without systemic features, rheumatoid factor-positive polyarthritis or rheumatoid factor-negative polyarthritis).

Methods: This was a Phase 3, randomised, double-blind (DB), placebo (PBO)-controlled withdrawal study in pts aged 2–<18 years with pcJIA, psoriatic arthritis or enthesitis-related arthritis. In the 18-week open-label (OL) phase (Part 1), pts received tofacitinib (5 mg twice daily or weight-based equivalent dose in pts <40 kg). Pts with ≥JIA ACR30 response at Week (W)18 were blindly randomised 1:1 to continue receiving tofacitinib or switch to PBO in the DB phase (Part 2; W18–44). This post hoc analysis assessed PROs in pts with pcJIA in Parts 1 and 2 including: mean values for the 3 Childhood Health Assessment Questionnaire (CHAQ) domains (Disability Index, parent/pt assessment of child pain and parent/pt assessment of child overall well-being) and mean scores for the 15 Child Health Questionnaire (CHQ) health concepts, and the CHQ physical (PhS) and psychosocial (PsS) Summary Scores.

Results: In Part 1, 184 pts with pcJIA received OL tofacitinib; of these, 142 were blindly randomised in Part 2 to continue receiving tofacitinib or switch to PBO. Improvements in the 3 CHAQ domains occurred from Part 1 baseline (BL) up to W18 with tofacitinib (Table). At W44, each CHAQ domain had improved from Part 2 BL (W18) by a numerically greater extent with tofacitinib vs PBO (Table). Mean scores for the 15 CHQ health concepts, and the PhS (Table), improved from Part 1 BL to W18 with tofacitinib, with these improvements generally sustained with tofacitinib and PBO in Part 2. The CHQ PsS was within the range of a healthy normative population (ie mean 50 [standard deviation 10]) at Part 1 BL and remained as such throughout the study (Table).

Conclusion: In pts with pcJIA, tofacitinib demonstrated sustained improvements in PROs, as measured by the CHAQ and CHQ.

Acknowledgements

Study sponsored by Pfizer Inc. Medical writing support was provided by Emma Deeks, CMC Connect, and funded by Pfizer Inc.

Trial registration identifying number: ClinicalTrials.gov (NCT02592434)

Disclosure of Interest

N. Ruperto Grant / Research Support from: Bristol-Myers Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer Inc, Roche and Sobi, Consultant for: AbbVie, Ablynx, AstraZeneca-MedImmune, Bristol-Myers Squibb, Biogen, Boehringer Ingelheim, Eli Lilly, EMD Serono, GSK, Janssen, Merck, Novartis, Pfizer Inc, Roche, R-Pharm, Sanofi, Servier, Sinergie, Sobi and Takeda, Speaker Bureau of: AbbVie, Ablynx, AstraZeneca-MedImmune, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, EMD Serono, GSK, Janssen, Merck, Novartis and Roche, D. J. Lovell Grant / Research Support from: AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche and UBC, Consultant for: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GSK, Novartis, Pfizer Inc, Roche, Takeda, UBC and Wyeth; and is a DSMB chairperson for NIH and Forest Research, E. Alexeeva: None declared, J. Chaitow: None declared, P. Chiraseveenuprapund Grant / Research Support from: Pfizer Inc, Consultant for: CARRA and Novartis, M. Erguven: None declared, B. Gottlieb Grant / Research Support from: AbbVie, Janssen, Pfizer Inc and UCB, S. Knupp Oliveira: None declared, M. Klein-Gitelman Grant / Research Support from: AbbVie, Bristol-Myers Squibb, CARRA, LFA, NIH, Pfizer Inc, UCB, Consultant for: AbbVie, S. Ozen Consultant for: Novartis and Pfizer Inc, Speaker Bureau of: Sobi, C. Saad Magalhaes: None declared, D. Gruben Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Germino Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Posner Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Suehiro Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Stockert Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Martini Consultant for: Janssen, Novartis and Pfizer Inc, Speaker Bureau of: AbbVie, Eli Lilly, EMD Serono, Janssen, Novartis and Pfizer Inc, H. I. Brunner Grant / Research Support from: AstraZeneca-MedImmune, Bristol-Myers Squibb, Novartis and Pfizer Inc, Consultant for: AbbVie, AstraZeneca-MedImmune, Bayer, Biocon, Bristol-Myers Squibb, Boehringer Ingelheim, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche and R-Pharm, Speaker Bureau of: GSK, Novartis and Roche

Table 1 (abstract O048). CHAQ and CHQ in pts with pcJIA

	Part 1		Part 2			
	Tofacitinib[a]		Tofacitinib[a]		PBO	
	Part 1 BL	W18	Part 2 BL	W44	Part 2 BL	W44
CHAQ domain,[b] mean (SE)	**N=184**	**N=154**	**N=72**	**N=49**	**N=70**	**N=33**
Disability Index	1.01 (0.05)	0.51 (0.05)	0.47 (0.06)	0.29 (0.07)	0.48 (0.07)	0.33 (0.08)
Parent/pt assessment of child pain	5.20 (0.20)	2.07 (0.17)	1.86 (0.23)	1.02 (0.22)	1.95 (0.23)	1.71 (0.33)
Parent/pt assessment of child overall well-being	4.91 (0.19)	2.09 (0.16)	1.94 (0.22)	0.99 (0.17)	1.89 (0.23)	1.36 (0.29)
CHQ score,[b] mean (SE)	**N=182**	**N=150**	**N=71**	**N=49**	**N=67**	**N=31**
Physical Summary Score	30.24 (1.14)	43.73 (0.91)	45.28 (1.11)	48.68 (1.32)	43.97 (1.41)	44.53 (2.08)
Psychosocial Summary Score	47.82 (0.78)	52.41 (0.74)	52.49 (1.05)	52.23 (1.33)	52.30 (1.08)	54.13 (1.48)

[a]5 mg twice daily or weight-based equivalent dose in pts <40 kg
[b]Missing data not imputed
BL=baseline; CHAQ=Childhood Health Assessment Questionnaire; CHQ=Child Health Questionnaire; N=number of pts; pcJIA=polyarticular course juvenile idiopathic arthritis; PBO=placebo; pt=patient; SE=standard error; W=Week

O049

Predictors of clinical remission in children with extended oligoarticular arthritis, enthesitis-related arthritis, or psoriatic arthritis treated with etanercept in the clipper studies

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Pediatric Rheumatology 2020, **18(Suppl 2):**O049

Introduction: CLIPPER is an ongoing, 8-year, phase 3b, multicenter, open-label study of the safety and efficacy of etanercept in the treatment of juvenile idiopathic arthritis (JIA) categorized as extended oligoarticular arthritis (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA).
Objectives: To identify predictors of sustained 6-month clinical remission on medication using long-term data from CLIP PER.
Methods: Previously reported baseline characteristics of the 127 children enrolled in CLIPPER (60 eoJIA [2–17 years], 38 ERA [12–17 years], and 29 PsA [12–17 years])[1] were analyzed post hoc as possible predictors of the attainment of clinical remission on medication (per the JIA ACR criteria or Juvenile Arthritis Disease Activity Score 71-joint [JADAS] criteria) sustained for 6 consecutive months using univariate logistic regression models and stepwise multivariate models. Clinical response and disease activity status after 4, 8, and 12 weeks of treatment were also evaluated as predictors. Analyses were based on observed cases in CLIPPER and 6 years of follow-up in the CLIPPER2 extension.
Results: Univariate analyses showed that baseline Patient/Parent Global Assessment score, JIA ACR inactive disease (IA) at Week 12, JADAS low disease activity (LDA) at Week 12, and JADAS IA at Week 12 were associated with the attainment of 6-month remission according to both JIA ACR criteria and JADAS criteria (**Table**). Multivariate analyses showed that age at onset and JADAS LDA at Week 12 were predictors of 6-month remission according to JIA ACR criteria, whereas JADAS LDA at Week 12 was a predictor according to JADAS criteria.
Conclusion: JADAS LDA at Week 12 of etanercept treatment was a predictor of attaining sustained 6-month clinical remission on medication according to JIA ACR criteria and JADAS criteria during the CLIPPER studies. Younger age at onset was also a predictor according to JIA ACR criteria.

Table 1 (abstract O049). Predictors of sustained 6-month clinical remission on medication during the CLIPPER studies

Univariate analyses		
Patient characteristic	**Definition of remission**	
	JIA ACR (N=127)	**JADAS (N=127)**
	OR (95% CI)	**OR (95% CI)**
Age at onset (≤7.61 years vs older)	5.17 (2.31, 11.57)	1.93 (0.90, 4.14)
Patient/Parent Global Assessment score (≤2.5 vs >2.5)	2.67 (1.13, 6.28)	2.75 (1.13, 6.67)
JIA ACR IA at Week 12 (Yes vs No)	5.06 (1.51, 16.99)	4.64 (1.24, 17.38)
JADAS LDA at Week 12 (Yes vs No)	5.83 (2.60, 13.06)	7.06 (3.02, 16.51)
JADAS IA at Week 12 (Yes vs No)	7.00 (2.14, 22.89)	4.10 (1.26, 13.29)
Multivariate analyses		
Definition of remission and patient characteristic	**OR (95% CI)**	
JIA ACR		
Age at onset (≤7.61 years vs older)	7.19 (2.71, 19.09)	
JADAS LDA at Week 12 (Yes vs No)	6.29 (2.46, 16.06)	
JADAS		
JADAS LDA at Week 12 (Yes vs No)	7.68 (3.08, 19.14)	

CI: confidence interval; IA: inactive disease; LDA: low disease activity; OR: odds ratio

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Trial registration identifying number: NCT0962741, NCT01421069.

Disclosure of Interest
J. Vojinović: None declared, V. Chasnyk: None declared, J. Dehoorne: None declared, V. Panaviene: None declared, J. Akikusa: None declared, T. Avcin Consultant for: AbbVie, Alexion, Octapharma, and Takeda, Speaker Bureau of: AbbVie, Octapharma, and Takeda, J. Chaitow: None declared, B. Lauwerys: None declared, J. Antón Grant / Research Support from: AbbVie, Eli Lilly, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi, and Sobi, Consultant for: AbbVie, GSK, Novartis, and Sobi, Speaker Bureau of: Novartis and Sobi, I. Penades: None declared, B. Flato: None declared, A. Boteanu: None declared, H.-I. Huppertz: None declared, J. Jaller: None declared, D. Graham Shareholder of: Pfizer, Employee of: Pfizer, C. Borlenghi Shareholder of: Pfizer, Employee of: Pfizer, B. Vlahos Shareholder of: Pfizer, Employee of: Pfizer, C. Zang Shareholder of: Pfizer, Employee of: Pfizer, N. Ruperto Grant / Research Support from: Bristol-Myers Squibb, Eli Lilly, Novartis, Pfizer, Roche, and Sobi, Consultant for: Astrazeneca-Medimmune, Aurinia, Biogen, Bristol-Myers Squibb, Centrical Global, Domain Therapeutics, Eli Lilly, EMD Serono, GSK, Idorsia, Janssen, Novartis, Pfizer, Sinergie, and Sobi

O050
Evaluation of anti-HBS and anti-VZV antibody levels in juvenile idiopathic arthritis patients treated with classical disease modifying drugs and biologics

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Pediatric Rheumatology 2020, **18(Suppl 2):**O050

Introduction: Juvenile idiopathic arthritis(JIA) is the most common chronic arthritis in children. The effects of classical disease modifying anti-rheumatic drugs(DMARDs) and biological drugs on vaccine responses in patients are controversial.
Objectives: The aim of our study was to evaluate the childhood vaccine responses against hepatitis B and varicella zoster virus of patients with JIA using classical DMARDs and biologic drugs.
Methods: Our study included 95 JIA patients who received classical DMARDs (methotrexate,salazopyrin,leflunomide,cyclosporine, hydroxychloroquine), 95 JIA patients who received biological drugs(anti-TNF, anti-IL-6, anti-IL-1 and CTLA4-Ig) and 91 healthy controls between the ages of 2-19 years. All participants were vaccinated according to our country's routine vaccination program in infancy. The anti-HBs and anti-VZV IgG antibody levels of participants were evaluated. Also the patients receiving DMARDs and biologic treatments were assessed within each group separately.

Results: Anti-HBs and anti-VZV IgG titers were not different in patients with DMARDs, patients with biologics and healthy controls(p= 0.094), (p=0.22) . The duration of biologic treatment was longer in patients with anti-HBs negative in biologic group(p=0.023), and was found to be a risk factor for anti-HBs negativity (OR:0.978 95%CI 0.961-0.966, p=0.012) in univariate logistic regression. However, the duration of biological treatment did not affect anti-VZV positivity(p= 0,553). Significant relationship was not detected between the duration of DMARDs therapy and anti-HBs(p=0.721) and anti-VZV(p= 0.560) positivity.

Conclusion: We found that the anti-HBs and anti-VZV positivity are not different in patients with JIA from healthy controls. However, the duration of biologic therapy is a risk factor for negative anti-HBs titers.

Disclosure of Interest
None declared

Table 1 (abstract O050). Comparison of the characteristics of controls, patients with DMARDs and patients with biologics

Variable	Control (n=91)	Patients with DMARDs (n=95)	Patients with biologics (n=95)	p value
Age, year (median, range)	13,0(4-18)	12,52(2,08-18,17)	13,58(2,91-19,75)	-
Gender				-
Female(n, %)	45(49.5%)	59(62.1%)	60(63.2%)	
Male(n, %)	46(50.5%)	36(37.9%)	35(36.8%)	
JIA subtypes(n, %)				-
Oligoartikülar JIA	-	59(62,1%)	31(33.7%)	
ERA	-	18(18.95%)	24(24.2%)	
RF- polyarticular JIA	-	8(8.42%)	24(25.2%)	
RF+ polyarticular JIA	-	5(5.26%)	2(2.1%)	
Systemic JIA	-	5(5.26%)	9(9.5%)	
Psoriatic arthritis	-	-	3(3.16%)	
Undifferantiated	-	-	2(2.1%)	
DMARDs duration, months (median, range)	-	15,0(1-105)	37,05(1-140)	0,000
Biologic duration, months (median, range)	-	-	30,6(1,33-115,0)	-
Anti-HBs(n, %)				
Positive(>10 IU/L)	50(54.9%)	67(70.5%)	64(67.4%)	0,065
Negative(<10 IU/L)	41(45.1%)	28 (29.5%)	31(32.6%)	
Anti-VZV IgG(n, %)	81(89%)	77(81.1%)	81(85.3%)	0,313
Positive(>110 IU/L)	10(11%)	18(18.9%)	14(14.7%)	
Negative(<110 IU/L)				
Anti-HBs titer(IU/L)	12,95 (2-1000) (±140,53)	19,47 (2-1000) (±205,4)	26,1 (2-1000) (±180,97)	0,094
(median, range) (±SD)	916,0 (0-5000) (±1294,8)	484 (0-5000) (±1426,1)	430 (0-5000) (±1460,81)	
Anti-VZV IgG titer(IU/L)				0,223
(median, range) (±SD)				

DMARDs, disease modifying anti-rheumatic drugs; ERA, enthesitis related arthritis; JIA, juvenile idiopathic arthritis; RF, rheumatoid factor

O051

Validity and reliability of four parent/patient reported outcome measures for Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O051

Introduction: In the last years, the interest in the assessment of parent- and child-reported outcomes (PCROs) in paediatric rheumatic diseases is gaining increasing importance. These measures reflect the parent and child perception of the disease course and effectiveness of therapeutic interventions and may facilitate concordance with physician's choices, improve adherence to treatment, and participation in a shared decision -making strategy. Moreover, the availability of reliable PCROs could be crucial for remote monitoring of patients when in person clinical evaluation may be difficult or even not possible.

Objectives: Aim of this work is to provide further evidence of validity and reliability for four PCRO measures included in the OMERACT JIA core domain set: the evaluation of the child's pain and of the child's level of disease activity, the assessment of the morning stiffness (MS) duration, and an active joint count for parent/patient proxy or self-assessment.

Methods: Pain and disease activity were rated on a 21-numbered circle scale corresponding to the traditional VAS (0=no pain; 10=extreme pain). MS was measured with a 5-point Likert scale. The proxy- and self-assessment of active joints was obtained by rating the presence of pain or swelling in the following joints or joint groups: cervical spine, lumbo-sacral spine, shoulders, elbows, wrists, small hand joints, hips, knees, ankles, and small foot joints. To each joint or joint group, one point was given in case of monolateral involvement, two points in case of bilateral involvement. Patients were included in a multinational dataset of patients enrolled in the Epidemiology Treatment and Outcome of Childhood Arthritis study. Criterion validity was assessed by examining the correlation of the four tested measures with physician centered measures, ESR, and composite disease activity scores. To further assess the validity of the tools correlations of the measure with the cJADAS10 were computed after grouping patients by ILAR category, by geographic area, and by education level. Reliability was assessed in a subset of subjects with Spearman correlations and intraclass correlation coefficients (ICC), comparing two visits 7-14 days apart.

Results: A total of 8,848 parents and 6,204 patients had all the evaluations available. Correlations of tested measures were in the moderate range (0.4–0-7) with physician centered measures and in the poor range (< 0.4) with ESR. The level of correlation of the tested parent measures with the cJADAS10 remained stable after grouping patients by ILAR category. In the same analysis with patients grouped in eight geographic areas, correlation levels were similar, although, on average, they were higher in Latin America and slightly lower in North America. The levels of correlation with the cJADAS10 were similar in subjects in which the level of education of the parent filling the questionnaire was elementary or lower, high school, or degree, respectively. In 442 parents and 344 children, correlations between first and second assessment was > 0.7 for all measures; ICC

ranged between 0.79 and 0.87 for parents and 0.81 and 0.88 for children.
Conclusion: The four tested PCROs showed good criterion validity and excellent reliability. These tools can be considered for remote patient assessment, when in person evaluation might not be possible.

Disclosure of Interest
C. Trincianti: None declared, E. H. P. Van Dijkhuizen: None declared, S. Calandra: None declared, L. De Miglio: None declared, M. Mazzoni: None declared, F. Ridella: None declared, T. Herlin: None declared, M. Cattalini: None declared, H. Sanner: None declared, G. Susic: None declared, F. Sztajnbok: None declared, D. Maritsi: None declared, T. Constantin: None declared, N. Ruperto Consultant for: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi., Speaker Bureau of: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi., A. Ravelli: None declared, A. Consolaro: None declared

O052
Longitudinal effectiveness of abatacept in Juvenile Idiopathic Arthritis (JIA): results from an ongoing JIA registry
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Pediatric Rheumatology 2020, **18(Suppl 2):**O052

Introduction: Abatacept (ABA) is a selective T-cell co-stimulation modulator approved for use in JIA. Efficacy and safety of ABA in patients (pts) with JIA has been demonstrated previously in two Phase III studies.[1,2]
Objectives: Provide data from a real-world setting for longitudinal effectiveness of IV and SC ABA in pts with JIA.
Methods: By protocol, clinical sites in the Pediatric Rheumatology Collaborative Study Group and Paediatric Rheumatology International Trial Organization enrolled pts with JIA currently taking or starting IV or SC ABA. Planned duration of follow-up (FU) is 10 yrs; data were collected up to 31 Mar 2018. Effectiveness was assessed at day of entry into registry (baseline; BL), 3 and 6 mos and 1, 2, 3, 4 and 5 yrs. Safety data were collected at each visit.
Results: 438 were enrolled; 435 were included in the analysis, 346/435 (80%) were female. At BL, 17 (4%) pts were aged 2–5 yrs and median age was 13.6 yrs; JIA disease duration was 4.4 yrs; ABA treatment duration 6.5 mos, number of active joints 1 (mean 2.7). JIA categories were systemic (2%), oligo (23%), poly RF– (55%), poly RF+ (10%), psoriatic (3%), enthesitis-related (3%) and undifferentiated (4%). Total ABA exposure was 474.0 pt-yrs. At 1-yr FU, pts had low MD Global Disease Activity, low Juvenile Arthritis Multidimensional Assessment Report scores and improved joint assessments (Table 1). A higher percentage of pts achieved clinically inactive disease after 1 yr FU vs BL (32 vs 45; Table 1). This trend continued despite low numbers of pts with 4 and 5 yrs of FU. There were 5 serious infections reported (incidence rate [IR] 0.66 /100 pt-yrs of FU, 95% CI: 0.22, 1.55; IR 0.79/100 pt-yrs on treatment, 95% CI: 0.26, 1.84). There were 15 autoimmune events (9 new onset) in 14 patients (IR 1.98/100 pt-yrs of FU, 95% CI: 0.66, 4.65; IR 2.37/100 pt-yrs on treatment, 95% CI: 0.78, 5.52). No malignancies or TB reported. There was 1 death (unrelated pre-existing cardiac problems).
Conclusion: In this real-world JIA cohort, abatacept was safe and well-tolerated with no new safety risks identified. This longitudinal analysis further supports the persistent effectiveness of abatacept in pts with JIA.

References
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Trial registration identifying number: NCT01357668

Disclosure of Interest
N. Ruperto Consultant for: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Employee of: The IRCCS Istituto Giannina Gaslini (IGG), where NR works as a full-time public employee, has received contributions from Bristol-Myers Squibb Company, Eli Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties. The registry is funded by Bristol-Myers Squibb Company, Speaker Bureau of: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, D. Lovell Consultant for: consultant: AstraZeneca, Boehringer Ingelheim, F Hoffman-La Roche, GlaxoSmithKline, Novartis, UCB; principal/co-principal investigator: Bristol-Myers Squibb Company, F Hoffman-La Roche, Janssen, Pfizer, UCB; board member: Forest Research, N. Tzaribachev: None declared, E. Morgan: None declared, G. Simonini Consultant for: AbbVie, Novartis, Speaker Bureau of: AbbVie, Novartis, T. Griffin: None declared, E. Alexeeva Consultant for: grant/research support and consulting fees: AbbVie, Novartis, Pfizer, Roche, Speaker Bureau of: AbbVie, Novartis, Pfizer, Roche, J. Bohnsack: None declared, A. Zeft Shareholder of: Merck, Opko Health, Teva, G. Horneff Consultant for: AbbVie, Novartis, Pfizer, Sanofi, Speaker Bureau of: AbbVie, Novartis, Pfizer, Sanofi, R. Vehe: None declared, V. Stanevica: None declared, S. Tarvin: None declared, M. Trachana Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, Novartis Hellas, Speaker Bureau of: Novartis Hellas, F Hoffman-La Roche, Pfizer, A. Huber: None declared, I. Orban: None declared, J. Dare Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, F Hoffman-La Roche, Pfizer, UCB, Employee of: Centene Corporation, I. Foeldvari Consultant for: Amgen, Bristol-Myers Squibb Company, Eli Lilly, Novartis, Pfizer, Sanofi, P. Quartier Consultant for: consultant: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum; board member: Sanofi, Speaker Bureau of: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum, A. Dominique Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, T. D. Kou Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, R. Wong Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, A. Martini Consultant for: Aurinia, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, Janssen, Pfizer, H. Brunner Consultant for: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GlaxoSmithKline, F Hoffman-La Roche, Novartis, Pfizer, Takeda, UCB, Wyeth (funds paid to employer), Speaker Bureau of: F Hoffman-La Roche, GlaxoSmithKline, Novartis

Table 1 (abstract O052). Assessment of disease activity and impact

Endpoint	BL n= 435	3 mos n=348	6 mos n=319	1 yr n= 296	2 yrs n= 189	3 yrs n= 75	4 yrs n= 21	5 yrs n=3
MD Global Disease Activity[a]	2.0 (0.1)	1.6 (0.1)	1.6 (0.1)	1.2 (0.1)	1.1 (0.1)	1.0 (0.2)	1.0 (0.3)	1.0 (0.6)
Clinical inactive disease (Wallace criteria), %	32	31	37	45	49	47	48	33
No. joints with active arthritis	2.7 (0.3)	2.1 (0.2)	2.2 (0.2)	1.8 (0.2)	1.7 (0.3)	1.8 (0.5)	1.1 (0.4)	0.3 (0.3)
JAMAR functional scale[b]								
Child	5.4 (0.3)	4.7 (0.3)	4.3 (0.3)	4.1 (0.4)	3.6 (0.4)	3.8 (0.6)	4.5 (1.2)	0.7 (0.3)
Parent	6.1 (0.4)	5.7 (0.4)	4.5 (0.4)	3.8 (0.4)	3.2 (0.4)	3.8 (0.8)	4.3 (2.1)	1.0 (–)
JAMAR HRQoL[c]								
Child	7.2 (0.3)	6.0 (0.3)	5.7 (0.3)	5.2 (0.3)	4.5 (0.4)	6.2 (0.7)	7.0 (1.4)	1.0 (0.6)
Parent	7.2 (0.3)	6.4 (0.3)	6.1 (0.3)	5.3 (0.4)	4.4 (0.5)	4.7 (0.8)	6.4 (2.2)	1.0 (–)

Mean (SE), unless otherwise indicated
[a]Visual analogue scale 0–10; 0=inactive; [b]range 0–15, 0=no functional limitation; [c]range 0–15, 0=best possible HRQoL
HRQoL=health-related quality of life; JAMAR=Juvenile Arthritis Multidimensional Assessment Report; MD=physician

O053

Determinants of discordance between criteria for inactive disease and low disease activity in Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O053

Introduction: It is currently agreed that disease remission should be an over-riding goal in the management of juvenile idiopathic arthritis (JIA), but the existence of multiple ways in which this target can be assessed in the clinical setting makes its definition more challenging.
Objectives: To assess concordance among criteria for inactive disease (ID) and low disease activity (LDA) in JIA, and to seek for factors driving discordance.
Methods: The frequency of fulfillment of existing ID and LDA definitions was evaluated in 10186 patients extracted from three cross-sectional datasets. Patients were divided in the "functional phenotypes" of oligoarthritis and polyarthritis. Concordance between criteria was examined through Venn diagrams. The role of each individual component in explaining discordance between criteria was assessed by calculating the absolute number and percentage of instances in which the component was responsible for discrepancy between definitions.
Results: ID criteria were met by 31.2 to 41% of patients with oligoarthritis and by 26.5 to 33% of patients with polyarthritis. LDA criteria were met by 44.8 to 62.4% of patients with oligoarthritis and by 44.6 to 50.4% of patients with polyarthritis. There was a 63.2 to 67.1% overlap between ID criteria and a 67.9 to 85% overlap between LDA criteria. The parent global assessment of child's well-being and the physician global assessment of disease activity were responsible for the majority of instances of discordance among ID criteria (9.2-17.5% and 9.6-12%, respectively).
Conclusion: We found fair concordance between definitions of ID and LDA in JIA, with the main drivers of discordance being the physician and parent global assessments. This observation highlights the need for further studies aimed to compare the relationship between physician- and parent-perceived remission and remission assessed by objective measures of inflammatory activity.

Disclosure of Interest

G. Giancane: None declared, C. Campone: None declared, M. F. Gicchino: None declared, A. Alongi: None declared, C. Bava: None declared, S. Rosina: None declared, Y. Boyko: None declared, N. Martin: None declared, Y. El Miedany: None declared, M. Harjacek: None declared, S. Hashad: None declared, M. Ioseliani: None declared, R. Burgos-Vargas: None declared, R. Joos: None declared, C. Scott: None declared, M. Hofer: None declared, Z. M. Ayala: None declared, M. Ekelund: None declared, S. Al-Abrawi: None declared, M.-F. Aiche: None declared, X. Norambuena: None declared, J. A. Melo-Gomes: None declared, N. Ruperto Employee of: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties, Speaker Bureau of: Ablynx, Astrazeneca-Medimmune, Aurinia, Biogen, Boehringer, Bristol Myers and Squibb, Centrical Global, Domain Therapeutics, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Idorsia, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi, Servier, Sinergie, and Sobi, A. Consolaro: None declared, A. Ravelli Consultant for: AbbVie, BMS, Pfizer, Hoffman LaRoche, Novartis, Centocor, "Francesco Angelini" and Reckitt Benckiser

O054

Clinical outcomes of Juvenile Arthritis in adulthood: a systematic review

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Pediatric Rheumatology 2020, **18(Suppl 2):**O054

Introduction: Juvenile arthritis (JA) is the most common pediatric rheumatic disease, potentially having permanent functional impacts on patients long after initial diagnosis. There has not been a comprehensive review of these studies to collate and assess the quality of their information.
Objectives: The purpose of this systematic review is to summarize clinical outcomes in adults with JA (age >16) and assessing quality of

current literature. We aim to identify areas of knowledge and methodological deficits that should be improved in future studies.
Methods: The systematic review was conducted in MEDLINE and EMBASE (2000-2017) by an academic librarian. Inclusion criteria included prognosis studies focused on quantitative outcomes related to JA, primary data, and adult outcomes.
The quality of publications was assessed using QUality In Prognosis Studies (QUIPS) risk-of-bias tool. QUIPS is classified into six domains of bias - study population, attrition, outcome, prognostic factor, confounding factor and statistical analysis. Papers were graded by trained reviewers who assigned a risk-of-bias grading (low/ moderate/ high) to the overall domain. We identified and extracted all statistically significant study outcomes and information related to studies. Statistical modelling was extracted to help determine the significance and validity of the results.
Results: 56 of 12 243 papers were included in this study for analysis. The majority (50.8%) of studies were cross-sectional, and the most common study queries were disease (34.9%), functional status/psychosocial (22.2%), temporomandibular joint (11.1%), and uveitis (9.5%) outcomes. 13 publications (21%) were repeat publications of non-unique cohorts, with the majority of these using the same cohort from Norway.
In terms of QUIPS, study confounding (95%), participation (81%) and attrition (82.1%) domains had the largest proportion of studies with moderate to high levels of bias.
In disease outcomes, the most common reported were remission (36%), and use of DMARDs (71%). HAQ functional status was reported with a median score of 0.49, signifying mild disability. VAS pain scale had a median score of 6.51 cm. DMARDs and NSAIDs usage ever were reported with 42.8% and 63.3% respectively. Uveitis was reported in 22.9% patients.
Out of 56 papers, 35 performed statistical multivariable modelling. Within each study topic there were no multivariable models of similar outcomes to allow for identification of consistent prognostic factors.
Conclusion: Only 2 (3.1%) truly longitudinal studies focused on the adult outcomes of JA patients. We therefore do not know the disease course information of adults with JA. The evidence in the studies had a high risk of bias in confounding factors, population and attrition, thus should be interpreted with caution. One theme that is not as prevalent is the effectiveness of medication and the complications with medication over time.
Limitations in our paper include being consistent in extracting the many categories of information. There are subjective biases in rating QUIPS as well. Another drawback exists in working with already presented results in published articles, which make come with biases in the information that is presented.
The majority of the studies have high levels of bias in study designs and outcomes. Future literature should describe the source of patients and report the differences between participants and non-participants. Our next step is to categorize outcomes by duration of disease and compare within the same subtype as well as make recommendations on formulating a standard reporting format for future JIA research.

Disclosure of Interest
None declared

O055
Relationship between physical activity and characteristics of adolescents with Juvenile Idiopathic Arthritis (JIA): results from the German paediatric rheumatologic database
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Pediatric Rheumatology 2020, **18(Suppl 2):**O055

Introduction: Adolescence is a challenging period of life involving profound physiological and psychological changes. Developed health-related habits such as regular physical activity (PA) often persist into adulthood, influencing health prognosis and risk of noncommunicable diseases in later life. Adolescents with JIA experience a number of symptoms, which might be aggravated by insufficient PA. Considering the lower levels of PA reported in children with JIA and the presumed tendency for a precipitous decline in subsequent years [1], adolescent patients can be at high risk of missing out on the general health benefits of PA.
Objectives: Since factors influencing the amount of PA can help in understanding and designing targeted interventions, we aimed to i) quantify the weekly frequency of PA and ii) identify its associated characteristics in adolescents with JIA.
Methods: Data from JIA patients recorded in the German Paediatric Rheumatologic Database in the year 2018 were considered for the analyses. In accordance with the WHO definition, early (10-14 years) and mid-late adolescence (15-19 years) were classified. The fulfillment of the WHO recommendations on PA for health was determined on the basis of self-reported outcomes corresponding to the methodology used in the general population survey [2]. Patients met the WHO criteria if they stated to be physically active for at least 60 minutes per day. Analyses of covariance were used to identify factors related to the number of weekdays spent with at least 60 minutes in PA.
Results: In 2018, data of 2.501 patients aged 10 to 14 years (mean age 12.1 ± 1.4 years, female 65%, disease duration 5.3 ± 3.6 years, persistent oligoarthritis 37%) and 2.394 patients aged 15 to 19 years (mean age 16.6 ± 1.2 years, female 67%, disease duration 6.7 ± 4.8 years, persistent oligoarthritis 26%) were analyzed. The proportion of patients who met the recommended level of PA was 27% (10-14-year-olds) and 16% (15-19-year-olds), respectively. According to JADAS-based criteria [3], 11% of mid-late adolescents with inactive oligoarthritis and 10% with inactive polyarthritis stated to achieve the minimum amount of PA on at most 2 days per week. In patients aged 10 to 14 years, cJADAS-10 ($p = 0.027$, $\eta^2 = 0.005$), CHAQ ($P = 0.001$, $\eta^2 = 0.011$) and BMI ($P < 0.001$, $\eta^2 = 0.008$) were significantly associated with PA. In comparison, in 15-19-year-olds were sex ($P = 0.000$, $\eta^2 = 0.015$), CHAQ ($P = 0.001$, $\eta^2 = 0.013$) and BMI ($P = 0.003$, $\eta^2 = 0.006$) significantly related to PA.
Conclusion: About 80% of adolescence with JIA fail to meet the global recommendations on PA, partly despite of an inactive disease state. In order to promote activities of daily life and to implement adequate interventions, JADAS and CHAQ should be controlled. To clarify both the safety of PA and the health risks associated with inactivity, efforts are needed to improve the quality of information provided for parents, health professionals, teachers and patients.

Acknowledgements
The National Paediatric Rheumatological Database has been funded by the German Children Arthritis Foundation (Deutsche Kinder-Rheumastiftung), AbbVie, Pfizer, Chugai and Novartis.

Disclosure of Interest
None declared

O056
Influenza vaccine uptake among Juvenile Idiopathic Arthritis(JIA) patients: a multi-centre cross-sectional study
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Pediatric Rheumatology 2020, **18(Suppl 2):**O056

Introduction: While most countries provide safe&effective influenza vaccines for patients at risk,coverage among target groups like children with rheumatic disease remains uncertain.
Objectives: To assess the influenza vaccination rate in children with JIA,to investigate knowledge,perceptions& practices about influenza vaccine uptake among caregivers of children with JIA and to identify barriers and facilitators that could be used to increase it.
Methods: A multi-center cross-sectional study was performed across 7 countries.Participants completed a questionnaire about influenza vaccination uptake history including the current year(2019-2020),knowledge& perceptions regarding influenza vaccination and demographics and clinical data regarding JIA.Chi-Square and logistic regression models were used;significance level was set at $p \leq 0.05$.
Results: A total of 287 JIA caregivers were surveyed;mean age is 41.6years(SD=7.27), 75.6% females. 7 countries participated in the study(Table).The majority of the participants was employed(72%),married(82.5%) and had tertiary education(50.9%). The commonest diagnosis was oligoarticular JIA(28.9%), while 28.6% of caregivers did not know the child's diagnosis.The mean age of children is 10.5years(SD=4.8) with a median disease duration of 4years(IQR:2-7). Most patients are currently treated systemically(71.4%), mainly with MTX(47%). 13.3% reported previous vaccine side effects;82.2% were fully vaccinated according to national vaccination schedules while 40.9% had received influenza vaccine in the past.
A total of 87 children(30.3%) were vaccinated against influenza for this season and 89.7% of them had a stable disease during the immunization.Most of the participants were informed of the recommendation by attending pediatric rheumatologist(33.4%) or pediatrician(28.2%).The highest vaccine uptake was recorded in Greece(70.8%),followed by Israel(41.9%),while none of the JIA patients from Croatia and Slovakia was vaccinated($p < 0.05$).Compared to employed caregivers,unemployed ones were more likely to vaccinate their children(25.7%vs53.3%,$p < 0.05$).Children with sJIA had the highest vaccine uptake(65.4%) while caregivers who did not know the child's diagnosis reported the lowest one(12.2%)($p<0.05$).Those who were informed of influenza vaccine recommendations by medical staff and had vaccinated their children in the past were more likely to vaccinate the current season(both $p<0.05$).However,children who had previously experienced adverse vaccine-related events reported the lowest vaccine uptake($p<0.05$).
Among non-vaccinators,59.5% did not have the opportunity to discuss their concerns with a specialist.Major reasons for non-vaccination included unawareness of the need(39.7%),fear of side effects(28.4%) and fear of disease flare(17.1%). The decision for non-vaccination was driven mainly by personal beliefs(41.5%),while 17.5% reported it was a doctor's advice.Among suggestions to improve influenza vaccine uptake,"informing families in advance" was the most commonly cited recommendation(59.6%),followed by "campaigns"(32.4%).
Conclusion: Despite the variations among European countries,influenza vaccine uptake remains low among JIA patients.Those previously vaccinated and those aware of the recommendations were more likely to be vaccinated.Informing families,discussing their concerns and organizing campaigns that will address the fears and highlight the importance of the influenza vaccine for this JIA population at risk may increase vaccination rates in children with rheumatic diseases.

Disclosure of Interest
None declared

Table 1 (abstract O056). See text for description

Country	Participants N(%)	Vaccine uptake N(%)
Israel	62(21.6)	26(41.9)
Greece	65(22.6)	46(70.8)
Slovenia	43(15)	7(16.3)
Slovakia	46(16)	0
Turkey	16(5.6)	5(31.3)
Croatia	33(11.5)	0
Cyprus	22(7.7)	3(13.6)
Total	287	87(30.3)

O057

Predicting the individual risk of uveitis in children with juvenile idiopathic arthritis: an international multicenter cohort study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O057

Introduction: Uveitis is the most common comorbidity in patients with juvenile idiopathic arthritis (JIA) and can lead to sight-threatening complications if not diagnosed and subsequently treated in an early stage. The estimated prevalence of JIA-U varies up to 30%, but the individual risk of acquiring uveitis is unknown.
Objectives: To build a clinical prediction model for JIA associated uveitis (JIA-U) providing individual risk estimates that could be used to inform patients/parents and aid physicians in determining screening frequencies.
Methods: Data from the international observational Pharmachild registry were used. For every patient with a follow-up period of at least 4 years, occurrence of JIA-U was determined from retrospective and prospective records since registration into Pharmachild. Multivariable logistic regression analysis was used to determine significant risk factors for JIA-U after correcting for confounding variables and to build a prediction model. Risk factors and confounders concerned were identified based on the existing literature and consensus of the authors, these included: age at JIA onset, gender, JIA subtype, ANA positivity, RF positivity and HLA-B27 positivity. The prediction model was selected based on Akaike information criterion and bootstrap resampling with replacement (n = 200) was used for internal validation and to adjust for model optimism.
Results: JIA-U was observed in 1,108 of 5,535 eligible JIA patients (20.0%). After correcting for confounding variables, independent risk factors for JIA-U were ANA positivity (OR: 1.89, 95% CI: 1.55 – 2.32), HLA-B27 positivity (OR: 1.47, 95% CI: 1.11 – 1.94), undifferentiated arthritis (OR: 1.70, 95% CI: 1.17 – 2.43), oligoarthritis (OR: 1.56, 95% CI: 1.27 – 1.91) and enthesitis-related arthritis (OR: 1.49, 95% CI: 1.02 – 2.14). Older age at JIA onset (continuous variable) was an independent protective factor (OR: 0.84, 0.81 – 0.87). Of all variables considered, the combination of age at JIA onset (in years), JIA subtype and ANA status (1 = positive, 0 = negative) performed best in predicting JIA-U (Table 1). Following the model, ANA positive patients with a young age at JIA onset and enthesitis-related arthritis run the highest risk of acquiring JIA-U. The prediction model had good

discriminative power (AUC = 0.75, 95% CI: 074 – 0.77) and bootstrap resampling revealed little overfitting: optimism in the AUC estimate was 0.003. Based on this model, the individual risk of JIA-U can be calculated as: *p(uveitis) = 1/(1+EXP-(-0.55 + 0.68*ANA status – 0.17*age at JIA onset + JIA subtype coefficient))*

Conclusion: Here, we present a clinical prediction model for JIA-U based on data from the largest (international) registry of JIA patients, that could be of use in current clinical practice.

Disclosure of Interest
None declared

Table 1 (abstract O057). Coefficients table of prediction model for JIA-U (n = 5,207, optimism-corrected AUC = 0.75). Reference JIA subtype is undifferentiated arthritis (β = 0)

Predictor	OR (95% CI)	β	Optimism-corrected β
(Intercept)	0.59 (0.43 – 0.79)	-0.54	-0.55
ANA positive	2.02 (1.73 – 2.36)	0.70	0.68
Age at JIA onset	0.84 (0.82 – 0.86)	-0.17	-0.17
Oligoarthritis	0.90 (0.68 – 1.20)	-0.10	-0.10
Polyarthritis (RF negative)	0.50 (0.37 – 0.67)	-0.70	-0.68
Polyarthritis (RF positive)	0.06 (0.01 – 0.18)	-2.88	-2.80
Psoriatic arthritis	0.76 (0.48 – 1.20)	-0.27	-0.26
Enthesitis-related arthritis	1.38 (0.95 – 2.01)	0.32	0.31
Systemic arthritis	0.07 (0.04 – 0.13)	-2.63	-2.56

O058

Proposal for a damage and response index for ana-positive noninfectious anterior uveitis from the Multinational Interdisciplinary Working Group for Uveitis in Childhood Group (MIWGUC)

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Pediatric Rheumatology 2020, **18(Suppl 2):**O058

Introduction: Idiopathic chronic ANA-positive anterior non-infectious uveitis (CAU) has similar clinical characteristics as juvenile idiopathic arthritis related uveitis (JIAU), except for inflammatory arthritis. A damage and response index has already been developed by a European collaboration of pediatric rheumatologists and ophthalmologists for JIAU (MIWGUC)[1]. As innovative effective treatment options are emerging for pediatric uveitis, it is important to define a response and damage index to assess the effectivity of drugs in preventing ocular damage in children with idiopathic CAU.

Objectives: To develop a response and damage and response index to measure ocular damage in children with idiopathic CAU

Methods: MIWGUC already agreed on items to evaluate outcome [1] for JIAU. 6 paediatric rheumatologist and 6 uveitis specialized ophthalmologists were asked to score the items, which were derived from the JIAU response and damage index. Regarding relevance for response and damage in CAU (Table 1) the items were scored. Items with scores between 1-3 points were discarded, >7 were accepted, and 4-7 were further discussed in the group with nominal group technique. 80% agreement was required to keep the item.

Results: The MIWGUC group agreed in a consensus meeting in Barcelona, that idiopathic CAU and JIAU may be managed similarly. Tables one presents the result of the voting.

Conclusion: We propose items to assess response to treatment and ocular damage in children with CAU. Validation of these indices is required in clinical cohorts to assess effectivity of a given drug for treating activity and preventing eye damage. This proposal will be evaluated from the MIWGUC group in a prospective study.

Reference

1. Foeldvari I, Klotsche J, Simonini G, Edelsten C, Angeles-Han ST, Bangsgaard R, et al. Proposal for a definition for response to treatment, inactive disease and damage for JIA associated uveitis based on the validation of a uveitis related JIA outcome measures from the Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC). Pediatr Rheumatol Online J. 2019 Oct 1;17(1):66.

Disclosure of Interest
None declared

Table 1 (abstract O058). See text for description

Accepted outcome items for response and damage form the MIWGUC group 2015 for JIA associated uveitis	Accepted outcome measures for chronic non-infectious ANA-positive anterior uveitis	Voting for acceptance for outcome measures for chronic non-infectious ANA-positive anterior uveitis n=12 (6 ophthalmologists and 6 paediatric rheumatologists) Yes/no votes
New Item		
Global disease score	yes	12/0
Flare	discarded	12/0
Posterior synechiae	Yes	12/0
Cataract	Yes	12/0
Maculopathy	Yes	12/0
Opticopathy	discarded	
Decreased visual acuity	Yes	12/0
Ocular hypertony ≥21 mmHg	Yes	12/0
Ocular hypotony ≤6 mmHg	Yes	12/0
Glaucomatous field loss and /or glaucomatous optic atrophy	yes	12/0
Band-keratopathy	Yes	12/0
Epiretinal membrane formation	Yes	12/0
Visual deterioration – less than		
0.3 in any eye	Yes	12/0
Uveitis related disability VAS 0-	Yes	12/0
100 by ophthalmologist		
Uveitis related disability VAS 0-100 by pediatric rheumatologist	?	?

O059

Prospective observational study on Video Consultation (VC) in paediatric rheumatology - an experience from Mumbai, India

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Pediatric Rheumatology 2020, **18(Suppl 2):**O059

Introduction: VC, an offshoot of the communications technology boom has had a slow offtake in medical specialties in several countries due to legal, ethical and procedural concerns. An immense resource is thus spent to reach out to specialists. In the legitimized 'window of time' provided by lockdowns, we conducted a study on VC in pediatric rheumatology.
Objectives: To assess physician and care-giver (parent and referring doctor) satisfaction with VC in new and follow up patients across different age groups and diagnosis.
Methods: Following Indian Government Guidelines on Tele-medicine (25th March '20), we obtained ethics approval, informed referral network & patient database about VC. Bi-lingual instructions, disclaimers, consent for care, research and recording of VC were conveyed electronically. VC was carried out on subscribed platform observing security and privacy practices. Caregivers transmitted chronologic records, images (X-rays, rashes etc.) prior to VC. Referring physicians were encouraged to accompany new patients. After history, musculoskeletal examination was adapted with physician or parents eliciting signs under guidance. Three physicians attended each consult, graded their satisfaction on achievement of objective on a pre-defined 5-point Likert scale. Digital prescriptions were sent, explained telephonically. Referring physicians administered restricted-use drugs following written protocols. Counselling and educational inputs were offered to referring physicians & family members. Bi-lingual web-based feedback was obtained after VC.
Results: After excluding 10 poor quality VC, 186 VC were conducted over 41 days for patients world over but largely from a 700 km radius consulted. Age ranges (mean), physician-caregiver satisfaction with VC in differing age groups in new and old patients and their interobserver agreement is shown in Table 1. 6/7 new and 77/107 old patients and 9/9 physicians gave 5 star rating. 9/107 expressed dissatisfaction with physical examination on VC. Physicians expressed lacunae in the process, coordination and case presentation.
Conclusion: Benefits of VC as a resource saver is applicable to paediatric rheumatology, where perusal of records, meticulous history, and inspection stand crucial. Our study bears this out providing several highlights. However, lacunae like parents missing human connect, better elicitation of signs need to be addressed. VC provides excellent opportunity to partner with and educate referring physicians regarding diagnosis and management. Going forward VC can be proposed initially to selected follow-up patients >5years, alternating with in-person consultations. Educating caregivers on simple examination methods may make VC more conclusive. While structured in-person consultation remains the gold standard, VC can become viable alternative in difficult times or resource challenged situations. VC could plug the gaps in access to paediatric rheumatologists and open the concept of practice to a world without borders.

Disclosure of Interest
None declared

Table 1 (abstract O059). See text for description

Patients (n=167)	New (n=25)	Old (n=142)
Mean age (y)	9.81	11.09
Inter Observer Agreement in all patients 1.Satisfaction with VC 0.765; CRONBACH'S ALPHA =0.772		
2. Across various age groups: (p value < 0.001 moderate to good)	< 5 y (n=29)	O.778
	5- 12 y (n=82)	O.696
	>12 y (n=75)	0.807
3.Across diagnosis: (p value <0.0001)	Lupus	0.6860
	JIA	0.82

O060

Internet and smartphone-based ecological momentary assessment and Personalized Treatment Advice (PROFEEL) in adolescents with chronic conditions: a feasibility study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O060

Introduction: Growing up with a chronic disease comes with challenges, such as coping with fatigue. Many adolescents are severely fatigued, thugh its associated factors exhibit considerable interpersonal and longitudinal variation.
Objectives: We assessed whether PROfeel, a combination of a smartphone-based ecological momentary assessment (EMA) method using the internet, followed by (face-to-face) patient-tailored treatment advice based on a dynamic network analysis report, was feasible and useful.
Methods: Feasibility study in fatigued outpatient adolescents 12-18 years of age with an autoimmune disease, post-cancer treatment, or with medically unexplained fatigue. Participants were assessed at baseline to personalize EMA questions. EMA was conducted via smartphone notifications five times per day for approximately six weeks. Hereby, data was collected and stored via the internet. The EMA results were translated into a personalized report, discussed with the participant, and subsequently translated into a personalized treatment advice. Afterwards, semi-structured interviews on feasibility and usefulness were held.
Results: Fifty-seven adolescents were assessed (mean age 16.2y±1.6, 16% male). Adolescents deemed the smartphone-based EMA feasible, with the app being used for an average of 49 days. Forty-two percent of the notifications were answered and 85% of the participants would recommend the app to other adolescents. The personalized report was deemed useful and comprehensible and 95% recognized themselves in the personalized report, with 64% rating improved insight in their symptoms and subsequent steps towards treatment as good or very good.
Conclusion: PROfeel was found to be highly feasible and useful for fatigued adolescents with a chronic condition. This innovative method has clinical relevance through bringing a patient's daily life into the clinical conversation. Personalized treatment advices to cope with fatigue can boost motivation and treatment adherence, and may lead to improved self-management of symptoms, thereby decreasing the need for additional treatment.

Disclosure of Interest
None declared

O061

Evaluation of educational resources designed to facilitate access to care for children with musculoskeletal conditions

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Pediatric Rheumatology 2020, **18(Suppl 2):**O061

Introduction: Electronic educational resources (e-resources) have the potential to promote awareness and knowledge about paediatric musculoskeletal (paed MSK) conditions, but if they are to achieve this goal, it is important to understand if and how they may lead to change in clinical practice. This is important and timely, given the current expansion of e-learning within clinical education. Our research group has developed a suite of e-resources with the overall

goal of improving clinical skills and knowledge in healthcare professionals involved in paed MSK medicine.
Objectives: To develop an evaluative strategy, targeting healthcare professionals, focused on their use of our e-resources namely Paediatric Musculoskeletal Matters (PMM, www.pmmonline.org), paediatric Gait, Arms, Legs and Spine (pGALS) App (Google Play and Apple App Stores) and Newcastle University e-learning modules (ELM, https://cpd.ncl.ac.uk/courses).
Methods: Google Analytics and online survey with e-resource target audiences (PMM n=148, pGALS n=120, ELM n=111) to gather feedback on their design and usability; gain valuable insight into how they are used; and understand the drivers and barriers to their dissemination and uptake in order to bring about change. A random selection of PMM and ELM registered users were invited to complete the survey, in addition to purposive sampling using UK and international contacts within paediatrics, paed rheumatology and the global partners of PMM. Respondents were from 25 countries and comprised a range of roles within education and primary/community hospital care. Data was analysed using descriptive statistics and free-text comments using qualitative techniques. This study had ethical approval.
Results: To date the resources have wide international reach; (PMM: 627,275 hits, 246,515 users, 214 countries; pGALS App: 11,490 downloads; ELM: 152 users, 31 countries). Most survey respondents reported finding the e-resources useful or very useful (PMM 97%, pGALS App 98%, ELM 100%) and being able to use them for their required purpose quickly and easily (PMM 89% pGALS App 90%, ELM 90%). Most reported the e-resources have or could have an impact on the medical education of themselves or others (PMM 94%, pGALS App 90%, ELM 95%) and on their clinical or nursing practice (PMM 90%, pGALS App 83%, ELM 92%); reporting areas of impact that included: increased awareness and diagnostic capabilities, increased ease and capability in clinical examination, improved teaching, opportunity to view rare clinical cases, increased awareness in other healthcare providers, and the provision of resources and information to aid teaching and self review. Increased ratings of confidence in MSK medicine or examination were reported after use; 82% (PMM), 90% (pGALS App) and 87% (ELM) reported to be confident or very confident compared to 52%, 68% and 57% before. Suggestions to increase impact and use concerned increased awareness of resources, targeting a wider range of clinicians involved in the care of paed rheumatology patients, integration with local systems or curriculum, and linking in with professional organisations to increase visibility. Lack of awareness, time constraints, costs, potential language barriers and challenges in electronic access were reported as key barriers to use and impact.
Conclusion: E-resources have an increasingly key part to play in clinical education. Our findings suggest our e-resources are fulfilling their role in raising awareness and early recognition of MSK conditions in childhood. Future qualitative work will explore our findings in more depth in particular in relation to developing an evaluation strategy that may be applied to other e-resources.

Disclosure of Interest
None declared

O062

A realist approach to eliciting the initial programme theories for the self- and shared-management of juvenile idiopathic arthritis by children, young people, families and professionals involved in their care

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Pediatric Rheumatology 2020, **18(Suppl 2):**O062

Introduction: Enabling children and young people (CYP) with juvenile idiopathic arthritis (JIA) to adopt self-management behaviours early on is likely to benefit their health and wellbeing through childhood and into adulthood. However, there is limited evidence of interventions focused on supporting the self-management of JIA by CYP, and the shared-management by families, and the most appropriate manner in which to deliver such support. Therefore, there was a need to develop a theoretical basis to underpin future self- and shared-management support, across public, private and voluntary sectors, to support CYP living with JIA and their families across the life-course.
Objectives: To elicit initial programme theories (IPTs) as the first stage of a realist evaluation pertaining to the self- and shared-management of JIA by CYP, their families and professionals involved in their care.
Methods: A realist evaluation approach guided the theory elicitation stage of this study. Firstly, information was obtained from an integrative review of self- and shared-management interventions targeted at CYP and families living with long-term conditions. Secondly, a document review of long-term condition self- and shared-management evidence was undertaken. A pragmatic search of JIA self- and shared-management support then followed. A realist evaluation heuristic (context-mechanism-outcome [CMO]) was used to synthesise information from sources into IPTs and CMO configurations, using retroduction to link theory and causality.
Results: Seven IPTs pertaining to the self- and shared-management of JIA by CYP, their families, and professionals involved in their care were identified. Four IPTs (1-4) were elicited at the individual and interpersonal level, while three IPTs (5-7) were elicited at the institutional and infrastructural level (Table). The elicitation process reiterated the argument that causality is located at the individual and interpersonal level – amongst the actions CYP and families take, individually and collaboratively, in response to the resources made available to them through self- and shared-management support interventions.
Conclusion: The IPTs and the initial CMO configurations describe how and why JIA self- and shared-management support is expected to work. By qualitatively testing IPTs with key stakeholders using the realist evaluation approach, the IPTs can be refuted, refined, and consolidated into a refined theory of 'what works, for whom, in what circumstances and why' in the context of JIA self- and shared-management support.

Disclosure of Interest
None declared

Table 1 (abstract O062). See text for description

IPT number	IPT summary
1	Meaningful self-management support across the life course for CYP with JIA.
2	Meaningful shared-management support for families supporting CYP with JIA.
3	Individual healthcare plans as a shared management tool to aid other professionals in supporting the specific needs and preferences of CYP with JIA and their families.
4	Consistent recognition and approaches within the paediatric rheumatology multi-disciplinary team towards the value of self- and shared-management support for CYP with JIA and their families.
5	Self- and shared-management support services commissioned with statutory services as a component of routine care for CYP with JIA and their families.
6	Child, young person and family-centred holistic care across the life-course for those living with JIA.
7	Inclusive and proactive educational settings to enable CYP with JIA to secure equivalent educational attainment and social development to their peers.

O063

Patients perspectives on living with a systemic autoinflammatory disease: impact on quality of life

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Pediatric Rheumatology 2020, **18(Suppl 2):**O063

† K. Durrant and F. Dedeoglu on contributed equally to this work

Introduction: Systemic autoinflammatory diseases (SAIDs) encompass clinical entities in which spontaneous inflammation occurs due to dysregulation of the innate immune response. The variability in presentation and rarity frequently lead to a diagnostic delay with potential damage from uncontrolled inflammation and negative impact on quality of life (QOL).
Objectives: We aimed to investigate the patient-reported factors underlying this negative impact.
Methods: A self-reported 25 question online survey on QOL of patients with SAIDs was developed by the non-profit organizations, the Autoinflammatory Alliance, KAISZ/VAISZ, ENCA and sJIA Foundation in English and Dutch. Respondents were recruited by convenience sampling through online social media posts. Data on triggers, medications, family history, and correlation of symptoms with labs were collected in addition to detailed information on QOL both during and in between flares.
Results: Between 2017 and 2019, there were 365 responses (342 in English and 23 in Dutch; Demographics are in the table). The most common diagnosis was undifferentiated SAID (uSAID). Seventy percent was diagnosed by a rheumatologist. Delay in diagnosis was common (5-20 years for 40% of patients). Almost half of the respondents saw 3-8 specialists before receiving their final diagnosis. In addition to the common features such as fever (79%), rash (60%), abdominal pain (70%), and oral ulcers (50%), SAID patients often experienced pain (80%) and fatigue (87%).
Fifty percent of patients rated being "severely limited" during flares and "somewhat limited" in between flares. 80% reported negative affect on their studies, job, and career.
We categorized open-ended responses into different impact domains of: 1.Physical: lack of understanding of the disease amongst both the medical and lay community, delays in diagnosis, unpredictable symptomatology, unknown long term side effects of medications, 2. Emotional: feelings of anxiety, hopelessness and frustration, feeling doubted about disease severity, constant worry about flares, 3. Social: inability to make plans for vacations/social events due to unpredictability of symptoms, leading to isolation, dependence on others, 4. Financial: insurance not covering specialists/medications, inability to work.
Conclusion: Patient engagement in designing survey questions helps to capture the impact of a disease on all aspects of life. In addition to the well-known negative impact of chronic diseases on QOL, the unpredictable nature of the course of SAIDs magnifies the stress of daily living for patients and caretakers. More granular questionnaires paired with clinical and biomarker analyses are needed to identify specific vulnerabilities and risk factors so that preventive measures can be implemented to improve QOL of patients with SAIDs.

Disclosure of Interest

M. Marques: None declared, N. Tennermann: None declared, S. Angevare: None declared, R. Sinha: None declared, J. Tousseau: None declared, P. Readon: None declared, S. Lapidus: None declared, G. Schulert Consultant for: Novartis and SOBI, K. Durrant*: None declared, F. Dedeoglu* Consultant for: Novartis, UpToDate

Table 1 (abstract O063). See text for description

Demographics (n= 365)		Age at Diagnosis (n=365)		Diagnosis (n=365)	
Country of origin (n= 365)	n (%)	0-2 years old	30 (8%)	uSAID	92 (25%)
USA	236 (65%)	3-5 years old	65 (18%)	PFAPA	71 (19%)
UK	32 (9%)	5-10 years old	85 (23%)	CAPS	51 (14%)
Australia/ New Zealand/ Oceania	27 (7%)	11-19 years old	47 (13%)	FMF	41 (11%)
Canada	23 (6%)	20-30 years old	33 (9%)	HIDS/all MKD	23 (6%)
Netherlands	19 (5%)	31-40 years old	33 (9%)	TRAPS	21 (6%)
Rest of EU, Northern & Eastern Europe	20 (6%)	41-50 years old	41 (11%)	CRMO/CNO/ SAPHO	18 (5%)
Mexico, South America,	3 (1%)	51-60 years old	19 (5%)	Sweets	16 (4%)
Other, Asia, Middle East	5 (1%)	61+ years old	12 (3%)	Other	32 (9%)

O064

Cluster consortium champions, and the importance of patient and parent involvement and engagement in research consortiums

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Pediatric Rheumatology 2020, **18(Suppl 2):**O064

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Pediatric Rheumatology 2020, **18(Suppl 2):**O064

Introduction: Juvenile Idiopathic Arthritis (JIA) is the umbrella term for a group of childhood, chronic rheumatic arthritides affecting approximately 1 in 1000 children and young people. It is defined as persistence of arthritis for more than 6 weeks of unknown origin, in patients aged under 16 years (1). Whilst much research has been conducted into understanding prognosis and treatment of JIA, there is still much unknown regarding tools to predict outcome, select treatment, or predict response. The Childhood arthritis and its associated uveitis: stratification through endotypes and mechanism to deliver benefit (CLUSTER) Consortium aims to address these research priorities. The role of patient and parent involvement has been key in the creation of the Consortium. To provide two-way fully-integrated involvement and engagement within the programme, we developed a patient and parent working group entitled the CLUSTER Consortium Champions.
Objectives: To develop a patient and parent working group that feeds into all aspects of research and management within the Consortium. The goal is for CLUSTER Champions to collate and express the thoughts, interest and ideas of patients, parents and the public. This provides an integrated two-way system of benefit.
Methods: A concept document was developed, providing background information on the potential role of CLUSTER

Champions, along with expression of interest documents. The design was produced with local involvement and knowledge from NIHR INVOLVE standards (2). Building on previous success and the public launch of the CLUSTER Consortium (11th March 2019), a patient, parent and public day was developed and held on 21st June 2019. The concept of the CLUSTER Champions was presented at this event to acquire feedback and interest from those involved.

Results: The event hosted 22 family members (13 adults, 9 children aged <16 years old), 7 external volunteers and 5 charity representatives (excluding those also classified as parent/family members). Interest was overwhelmingly positive, with 16% of feedback focusing on methods of communication in the consortium and 32% of feedback around levels and degree of engagement for members. Upon launch of the scheme, six CLUSTER Champions have joined and are now fully integrated members.

Conclusion: Developing PPIE working groups within research allows for an exchange of ideas between researchers, families and the public. Our event showed that the public is generally enthusiastic and positive about involvement in research. PPIE working group provide an opportunity for researchers to understand public opinions and priorities and allows the public to gain insight into research methodology, governance and procedures. The Champions provide a link to the public for dissemination of papers, questionnaires, reports, as well as development and prioritisation of research ideas. Outside of the Consortium the CLUSTER Champions have provided expertise and dissemination of a COVID-19 risk algorithm developed at GOSH, and provided links to multiple families for dissemination of COVID-19 related information and help on research questionnaires and cohorts.

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Disclosure of Interest

F. Dekaj: None declared, L. Wedderburn Speaker Bureau of: Pfizer, Z. Wanstall: None declared, W. Thomson: None declared

O065

The perspective of parents/carers on vaccinations in children and young people with rheumatic and autoinflammatory diseases: results of an international survey

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Pediatric Rheumatology 2020, **18(Suppl 2):**O065

Introduction: Vaccination coverage in children and young people (CYP) with rheumatic and auto-inflammatory diseases is reported to be lower than healthy CYP. However, the reasons why vaccinations are declined by parents/carers remain unclear.

In September and November 2019 a survey was posted online. Awareness for this survey was raised through social media and patient organisations.

Main objective of the survey was to get more insight into the knowledge and awareness of patients with specific diseases (autoimmune and auto inflammatory) and their potential use of certain vaccinations.

Objectives: To understand the views of parents/carers regarding vaccinations in CYP with rheumatic and autoinflammatory diseases.

Methods: An electronic survey of parents/carers of CYP with rheumatic and autoinflammatory diseases was distributed in English using the national organisations representing parents/carers and CYP. The survey consisted of 60 questions, and was accessible between September and November 2019. Aside from demographics, we asked respondents for their views on the value of vaccinations, risk/benefit balance, available information/commentary on vaccinations and shared decision-making opportunities with health-care professionals (HCPs).

Results: A total of 463 responses were received (62% from Europe, 38% from non-European countries). We collected data on a variety of topics such as demographics, diseases, medications and vaccinations. While the majority of respondents recognised the importance of vaccinations (95%) and believed in the value of vaccination programmes (82%), 34% reported postponing vaccinations for personal reasons. Concerns were focussed more on short-term side effects (61%) than long-term side effects (48%); with 42% suggesting that they knew somebody else who had experienced a side effect. The most common vaccination concern was that a disease flare may be triggered. However, most were also concerned about vaccine-preventable diseases (62%). The top three reasons against vaccination were: risk of side effects, advice from HCPs (e.g. against live vaccines while on biologics) and poor information about vaccinations. The influence of media information about vaccinations was inconsistent. Most felt they were able to discuss vaccinations with HCPs (90%). Finally, several respondents called for an independent online resource about vaccinations for CYP with rheumatic and autoinflammatory diseases.

Conclusion: Parents/carers of CYP with rheumatic and autoinflammatory diseases generally recognise the importance and value of vaccinations. However, many are concerned about vaccinations triggering a disease flare, resulting in some parents/carers postponing vaccinations. It is clear that HCPs play an important role in discussing vaccinations with parents/carers as part of the shared decision-making process. An independent online resource about vaccinations, specifically for this population, may need to be developed to support evidence-informed decision-making.

Disclosure of Interest

None declared

O066

The covid-19 european patient registry: development of a patient-led rheumatology registry

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Pediatric Rheumatology 2020, **18(Suppl 2):**O066

Introduction: On 11 March 2020, the World Health Organisation characterised COVID-19 (coronavirus) as a pandemic. It quickly infected hundreds of thousands of people worldwide. Whilst many people with COVID-19 infection appeared to have mild or no symptoms, a significant proportion of patients became seriously ill.

In late March 2020, little was known about how patients with rheumatic diseases or autoimmune conditions, many of whom use immunosuppressive medications and drugs, are affected by the virus.

Objectives: To develop a patient-led, longitudinal survey to identify the potential risk-factors associated with COVID-19 infection in people with rheumatic, autoimmune and autoinflammatory conditions; to compare outcomes among these patients; and to characterise and understand how they may be differentially affected by COVID-19.
Methods: The COVID-19 European Patient Registry (EPR) was developed by parents of children and young people (CYP) representing ENCA, with support and involvement from individuals and organisations across Europe, including adult patients and the Paediatric Rheumatology European Society (PReS). As partners of the Global Rheumatology Alliance, the EPR was specifically created as a longitudinal survey tool. Development was very rapid, allowing data to be collected within 3 days from the start of the project, maximising the potential for capturing vital information through the web-based survey tools at www.jarproject.org/covid.
The EPR has two parts: paediatric (to be completed by parent/caregiver) and adult. It comprises an online survey asking about rheumatic conditions, general health, medication and underlying comorbidities. Each participant is sent a short follow-up survey, weekly, asking about exposure to COVID-19, preventative steps taken to avoid infection, symptoms, diagnosis and outcomes.
The EPR was launched on 24 March 2020 and is available in 13 languages. Individuals can join it at any time, on a rolling basis. Each week, data from the initial and follow-up surveys are downloaded, anonymised and combined to generate the longitudinal registry. Consent is provided when enrolling, and confirmed at each follow-up survey.
Results: As of 24 May 2020, 3,740 people (603 CYP and 3,137 adults) had joined the EPR. Among the CYP, only 5 reported a COVID-19 infection (0.8%). The follow-up response rate at week 1 was 52%. Table 1 provides a summary of CYP participants to 24 May 2020.
Conclusion: The COVID-19 EPR provides an opportunity to develop an understanding of how COVID-19 infection affects paediatric and adult rheumatology patients, to identify risk-factors for infection and/or disease severity. Currently, COVID-19 in CYP has low prevalence and mild outcomes. Updated results will be presented at the PRES Congress.

Acknowledgments
We are grateful to the team of volunteers who helped translate the surveys, as well as ENCA , PRES and representatives from the rheumatology community for their expertise and support.

Disclosure of Interest
None declared

Table 1 (abstract O066). Summary of participants as of 24 May 2020 (N=3,740)

Data included in the European Patient Registry (EPR)	*Children / Young People*	*Adults*
Participants (% female)	603 (67%)	3,137 (89%)
Number of countries represented	30	52
Number (%) diagnosed with COVID-19	5 (0.8%)	40 (1.4%)
Number hospitalised due to COVID-19 (% of those with diagnosis)	0 (0.0%)	3 (7.5%)

O067

Parenting stress in parents of children with Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O067

Introduction: Having a child with a chronic illness has been associated with increased levels of parenting stress across several health conditions. Parenting stress has not been examined in parents of children recently diagnosed with juvenile idiopathic arthritis (JIA). To help support parents, it is important to identify levels of parenting stress and to understand factors that may influence stress levels.
Objectives: To examine the relationship between the health status of children with JIA and illness-related parenting stress experienced by their parents.
Methods: Parents of children aged ≤12 years who had been recently diagnosed with JIA (≤6 months) were recruited during clinic appointments at tertiary paediatric rheumatology clinics in England. Participants were recruited to a multicentre randomised controlled trial of a website for parents of children with JIA. This abstract reports data collected prior to randomisation.
Parents completed the Pediatric Inventory for Parents (PIP) measure of childhood illness-related parenting stress. The PIP has two scales, measuring the frequency (PIP-F) and difficulty (PIP-D) of illness-related events that parents may face. Each scale provides a total score ranging from 42-210 with higher scores indicating greater stress. Child clinical data collected included: JIA subtype; time since diagnosis; medication; number of active and limited joints; erythrocyte sedimentation rate; Child Health Assessment Questionnaire; parent global rating; physician global rating; presence of co-morbid illness.
Multiple linear regressions were performed to analyse the relationship of child health status with PIP-F and PIP-D.
Results: Parents of 203 children participated; 166 mothers and 37 fathers are included in the analyses. Their mean age was 36.3 (6.5) years. Their children with JIA had an average age of 6.2 (3.4) years; most were female (n=136, 67%) and had oligoarticular (n=107, 52.7%) or polyarticular (n=65, 32.0%) JIA. Sixty-eight (33.5%) had been prescribed methotrexate.
Mean (SD) scores on the PIP-F and PIP-D were 108.6 (32.1) and 103.1 (32.6) respectively. This is similar to stress levels reported by parents of children with other health conditions, including type 1 diabetes and sickle cell disease.
Regression analysis explained 24% of the variance in PIP-F. Significant independent predictors of higher scores on the PIP-F, representing greater frequency of difficult events were: Female parent gender (B=12.72, p=0.018), systemic JIA subtype (B=26.30, p=0.038) and presence of a co-morbid illness (B=11.05, p=0.041).
Regression analysis explained 20% of the variance in PIP-D. Significant independent predictors of higher scores on the PIP-D, representing greater difficulty experienced were: systemic JIA subtype (B=43.26, p<0.001) and a poorer parent global rating score (B=2.089, p=0.037).
Conclusion: This research identified levels of parenting stress among parents of children recently diagnosed with JIA that are similar to those of parents of children with other serious health conditions. Parents in this study who were at an increased risk of high stress levels were those whose children have systemic JIA or co-morbid conditions and those who rate their child's overall wellbeing more poorly. The study findings have helped to identify parents who may be at increased need for support to help reduce parenting stress.

Trial registration identifying number: This abstract presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-1013-32005). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.
ISRCTN: 13159730

Disclosure of Interest
None declared

O068

Some aspects of the psychoemotional state of patients with Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O068

Introduction: Juvenile idiopathic arthritis (JIA) - combines a diverse group of chronic joint diseases and is one of the most common and disabling rheumatic diseases of childhood. The course of the disease leaves its mark on both the lifestyle and the psychoemotional status of a sick child, which may determine the risk of various psychological changes and disorders of the emotional and motivational sphere. The study of the psychoemotional status of patients with JIA is an urgent problem of our time, requiring study to form a set of measures of psychological support for a sick child.
Objectives: Assess the psychoemotional status of patients with a verified diagnosis of JIA.
Methods: The study involved 70 patients aged 3.9 years to 16.11 years (mean age 9.6 ± 4.1 years) with an established diagnosis of JIA according to ILAR criteria, no later than 6 months from the start of the study. In the study group there was the following distribution of patients — 20 children with a systemic variant of the disease and 50 children with the articular form of JIA (30 patients with an oligoarticular and 20 with a polyarticular variant of the course of JIA). The comparison group consisted of relatively healthy children (n = 20). Assessment of the psychoemotional status in the main and control groups was carried out using a set of standardized methods: Sachs-Levy test "Method of incomplete sentences" (SSCT method), test M. Kovach "Questionnaire for childhood depression" (CDI) for patients older than 7 years, test L.S. Slavina "Three wishes."
Results: Analysis of the Sachs-Levy test "The method of unfinished sentences" showed that almost 75% of the children of the main group had certain fears and concerns associated with the course of the underlying disease, but positive attitudes prevailed in 30.8% of patients in all spheres of life, while while 17.7% of children in the study group had negative attitudes that were not related to the course of the disease, in the control group this indicator was 12%. When analyzing the method of M. Kovach's "Questionnaire for Child Depression," the CDI score on the A scale showed that a general decrease in mood, a negative assessment of their own effectiveness, was generally observed in 45% of children in the study group and only 5% in the control group; on a scale B 19% of children in the main group identified themselves with the role of the bad, in the control group this indicator was 50%; on a scale of C, 27.5% of children showed a high level of conviction of inefficiency at school, in the control group, 2% of respondents; on a scale of D 35% of the respondents in the main group had a high level of exhaustion and a feeling of loneliness; on the E scale: a negative assessment of one's own inefficiency, the presence of suicidal thoughts was noted in 15% of the respondents in the main group and 1% of the control group. Evaluation of the results of the method L.S. Slavina's "Three Wishes" showed that in almost 90% of the children in the study group, at least one desire was associated with the course of the underlying disease, 15% had 2 wishes, and only one patient with a severe course of the systemic variant of JIA had all three wishes illnesses. An analysis of the data obtained indicated a narrowing of the motivational-consumer (MP) sphere in the study group.
Conclusion: A study of the psychoemotional status of patients suffering from JIA showed that, in general, more than half of the children showed changes in the emotional and motivational sphere of life compared with children from the control group. Thus, it is worth talking about the need for dynamic monitoring of the state of the psychoemotional sphere in rheumatological patients, and the need for psychological support, both at the stages of inpatient treatment and on an outpatient basis.

Disclosure of Interest
None declared

O069

Diagnosis of depressive disorders in children with Juvenal Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O069

Introduction: Depression is a common mental disorder, the leading cause of disability and makes a significant "contribution" to the global burden of diseases. Besides, depression is an associated condition in rheumatic diseases including arthritis even in childhood. The relevance of this problem is also due to the fact that in children, despite the presence of a chronic disease, high adaptive abilities of the psyche take place. Therefore, it is especially important to reliably determine the presence of the first signs of depressive conditions at earlier stages of the underlying disease.
Objectives: The aim of the study was to identify early signs of depressive states in children with juvenile idiopathic arthritis (JIA) and their relationship with the activity, duration and complex treatment.
Methods: This study included 16 children (8 girls and 8 boys) 6 - 17 years old (13.1±0.7) with JIA (poly- and oligoarticular variants according to ILAR classification, Edmonton, 2001), the average duration of the disease was 29.0±6.5 months. Disease activity according to the JADAS scale was 1 - 17 (4.4±1.1).
The main method of research was the Montgomery-Asberg scale (MADRS), which applies quickly assess the severity of depression. It contains 10 main subscales for assessing signs of depression on a 6-point scale. Interpretation of the results is carried out by arithmetic summation: from 0 to 6 points - no depressive episode; from 7 to 19 points - a small depressive episode; from 20 to 34 points - moderate depressive episode; more than 35 points - a major depressive episode. Results were analyzed using IBM SPSS Statistics for Windows with $p<0.05$ considered spastically significant.
Results: It was found that 9 children (56.25%; the MADRS indicator was 6.7±1.3) had no signs of emotional disturbances. 7 patients (43.75%) had manifestations of depressive states (the MADRS indicator was 22.5±3.4): 5 children had signs of a small depressive episode; 1 child - a moderate depressive episode, another child - a major depressive episode. Children with signs of depressive disorder had a longer duration of the disease (44.2±12.7 vs 20.6±6.2 mo., p=0.038), greater JADAS activity (7.7±2.4 vs 2.5±0.5, p=0.048) than children without positive MADRS scores. No reliable dependence of the scale indicators on the age (14.2±0.6 vs 12.4±1.0 years, p=0.054) and gender of patients (the MADRS indicator in girls 11.0±2.0 vs in boys 14.3±4.6, p=0.265), the inclusion of methotrexate in the treatment (the MADRS indicator with MTX 10.0±2.0 vs without MTX 14.2±3.7, p=0.169), was found. An analysis of the subscales used to assess the level of depression found that 68.0% of children had been depressed or in a bad mood for more than 3 days a week in the last month, looked depressed, but were quickly distracted from bad thoughts. 50.0% of children had problems falling asleep or short sleep, intermittent or restless sleep; 31.0% of patients noted difficulties with starting a new case; also 31.0% - difficulties in performing daily tasks that do not require much effort, 25.0% of children surveyed had sporadic thoughts about their own inferiority, failure in life and self-humiliation, and another 12.5% - thought it was better to die.
Conclusion: Mental health disorders are present in patients with JIA, starting in childhood. Their prevalence reaches almost half of teenage children, which requires additional diagnosis and rehabilitation measures.

Disclosure of Interest
None declared

O070

Rheumatic diseases in Mexican children and their psychosocial and economic impact on caregivers

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Introduction: Pediatric rheumatic diseases (PRD) are a heterogeneous group of disorders. PRD patients and their caregivers face a number of challenges, these include the consequences of the PRD in patients and the impact on multiple dimensions of the caregiver's daily life. Our group developed and validated the CAREGI VERS questionnaire to measure the impact on caregivers of children with PRD.
Objectives: The objective of this study was to measure the economic, psychological and social impact that PRD has on the caregivers of Mexican children and the factors associated with these impacts.
Methods: This is a cross-sectional study in which primary caregivers were prospectively included between April and November 2019 in four public hospitals of specialized care. Descriptive statistics used used to the sociodemographic characteristics of the participants and the patients' clinics, a univariate analysis was performed with the interview responses of the CAREGIVERS questionnaire and the sociodemographic, clinical, and health system variables using the Chi square, Mann-Whitney U, and Kruskal-Wallis tests ($p < 0.05$).
Results: 200 participants were included, women (84.5%) with median age of 38 years; 54.5% cared for patients with JIA, 14% with JDM and 31.5% with JSLE. Most of the caregivers felt concern (42.5%) when learning about the diagnosis, which then was modified by tranquility (44%) when the current feeling was questioned; however, 40 expressed sadness when sharing the patient's PRD (20%) and 39 do not like to do so (19.5%).The main cause of concern is pain (41.5%), followed by difficulty in movement (28.5%) and covering the costs of treatment (25%). Social impact: In 99 caregivers (49.5%), the use of their time changed a lot upon learning the PRD. Social life varied according to the PRD, in JSLE it had a significant change (39.6%), but it did not change in JIA (44%) and it slightly changed in JDM (53.5%, $p < 0.01$).Financial impact: the family financial situation worsened upon diagnosis of the patient in most cases (JIA 63 [57.8%], JSLE 19 [69.8%] and JDM 44 [67.8%], $p = 0.27$). Almost two thirds had had to borrow money, more frequently in JSLE (48 [76.1%] vs JIA 62 [56.8%] and JDM 19 [67.8%], $p = 0.03$); 63 stopped buying medicines due to lack of money (31.5%) and 86 received additional financial support for the treatment (43%).The emotional impact increased in caregivers of male patients. Social dimension showed significant differences regarding PRD, healthcare system, time to reach the center, presence of disability, active disease, cutaneous and systemic manifestations and treatment.
Conclusion: This study highlights a series of lessons learned and the most important is the need to improve opportunities for support, especially regarding financial support, for caregivers of patients with PRD. The study has shown that social status can be devastating in the impact that PRD can have on families. We feel confident that, although all the participants are Mexican, the findings can be generalized to populations with similar characteristics in other regions.

Disclosure of Interest
None declared

O071

Barriers and facilitators to physical activity in Juvenile Idiopathic Arthritis (JIA): a scoping review

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Pediatric Rheumatology 2020, **18(Suppl 2):**O071

Introduction: Physical activity is an important aspect in the management of JIA (Kuntze et al 2018). However physical activity levels are low in this population (Bos et al 2016). Limited research has been conducted to identify definitive barriers and facilitators to physical activity in children and adolescents who have JIA.
Objectives: The objective of this scoping review was to identify the common barriers and facilitators to physical activity in JIA.
Methods: Original studies, either quantitative or qualitative, including participants with a diagnosis of JIA, who were under 18 years of age were included. Two independent reviewers carried out a search of the literature and full text reviews of papers to determine eligibility for inclusion. The Critical Skills Appraisal Programme (CASP), Appraisal tool for Cross-Sectional Studies (AXIS) and Downs and Black critical appraisal tools were used to assess the quality of the included research articles.
Results:

Category	Quantitative studies (N)	Qualitative studies (N)
Barriers		
Physical barriers	N=13	N=4
Psychological barriers	N=7	N=5
Management barriers	N=5	N=3
Other barriers	N=7	N=0
Facilitators		
Physical facilitators	N=5	N=0
Psychological facilitators	N=6	N=6
Management facilitators	N=10	N=7
Other facilitators	N=4	N=0

Eighteen studies were included in the review. The included studies were of a variety of low, moderate and high quality. The synthesis of the data identified pain to be the most common barrier and the modification of physical activities to the need of the individual to be the most common facilitator to physical activity in JIA.
Conclusion: Identifying the most common barriers and facilitators to physical activity allows clinicians to apply better management strategies when treating an individual with JIA. Our findings demonstrate the need for further research in this area to assist increasing physical activity participation for children and adolescents who have JIA.

Disclosure of Interest
None declared

O072

Under detection of interstitial lung disease in Juvenile Systemic Sclerosis (JSSC) utilizing pulmonary function tests. Results from the juvenile scleroderma inception cohort.

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Pediatric Rheumatology 2020, **18(Suppl 2):**O072

Introduction: Juvenile systemic sclerosis (jSSc) has a prevalence in around 3 in a million children. Pulmonary involvement occurs in approximately 40 % in the international juvenile systemic scleroderma cohort (JSScC). Traditionally 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 interstitial lung disease (ILD) in children.
Objectives: To assess the sensitivity and specificity of FVC and DLCO assessment to detect ILD
Methods: The international juvenile systemic scleroderma cohort (JSScC) 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 jSScC, 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 DLCO (> 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 JSScC 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 Interest
None declared

O073

Cross-cultural adaptation and validation of the Localised Scleroderma Quality of Life Instrument (LOSQI) in JLS: a multicentre study of the PRES scleroderma working party in collaboration with members of the carra scleroderma working group

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Pediatric Rheumatology 2020, **18(Suppl 2):**O073

Introduction: ***Juvenile localised scleroderma (JLS)*** is characterised by chronic inflammation within the skin and tissues leading to fibrosis [1]. It is associated with significant complications including joint contractures, limb length discrepancy and facial atrophy that impact quality of life. Patient reported outcomes (PRO) are not well established within research settings and are not part of routine clinical care in many centres [2].
Several studies have measured health-related quality of life (HRQoL) in JLS, most commonly using the Children's Dermatology Life Quality Index[3-6]. This measure only captures impact of skin involvement and not HRQoL from extra-cutaneous manifestations. Psychometric analysis shows that it incompletely measures important concepts of HRQoL that are unique to JLS [7]. The Localised Scleroderma Quality of Life Instrument (LoSQI) has been developed in partnership with patients and families to capture aspects of disease which may not be well defined within generic HRQoL measures [8]. The initial development and validation process was iterative, patient-centred, and consistent with best practices in PRO development. Currently, the LoSQI is the only JLS-specific PRO, and the only PRO that includes both qualitative and quantitative validity evidence. It is currently being utilized within two large American scleroderma registries but will require cross-cultural adaptation for international use.
Objectives: to undertake cross-cultural adaptation and validation of the Localised Scleroderma Quality of Life Instrument (LoSQI) in juvenile localised scleroderma (JLS).
Methods: Workstream 1: cross-cultural adaptation of LoSQI via methods previously described by Guillemin et al, with pre-testing in selected study population. A single site in up to 35 PRINTO represented countries will take part.
Workstream 2: validation of the LoSQI via a multicentre prospective cohort study of 100 patients at 2 time points.
Results: This study was successful in obtaining funding from the **PRES 2025 / PRINTO Research Award** and is in study set up stage.
Conclusion: Collaboration between PRINTO centres, CARRA and PRES scleroderma working party members in partnership with patients and families will facilitate shared aims and this will be the first multinational study of a disease-specific patient-reported outcome (PRO) in JLS. To allow further validation work of outcome measures, this important step will allow cohorts from multiple countries to combine datasets and results with an overarching aim to embed PRO in routine clinical practice. This is invaluable for a rare disease population, where research is continuously limited by small samples sizes, large geographical dispersion of subjects, and lack of consensus in selection and use of outcome measures.

Disclosure of Interest
None declared

O074

Ischemic stroke in children with scleroderma en coupe de sabre

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Pediatric Rheumatology 2020, **18(Suppl 2):**O074

Introduction: Neurologic disturbances (ND) in children with localized scleroderma (LS) occur more frequent in linear scleroderma en coupe de sabre (ECDS). The frequency of Central nervous system involvement in pediatric craniofacial scleroderma is estimated to be 28–38%. Mostly epilepsy, headache, focal symptoms, neuropsychiatric disorders are described. Only several cases of stroke were recorded in adults with ECDS.
The origin of ND is still unclear. There is data for neurovasculitis hypothesis with endothelial cell injury, microthrombotic angiopathy. Other data suggests a prenatal malformation of one side of rostral neural tube resulting in hemiatrophy of facial tissue and underlying brain parenchyma.
Objectives: To analyze frequency of neurologic involvement ECDS in children, describe 3 cases ischemic stroke (IS).
Methods: Retrospective analysis of ND in ECDS childhood cases was done. All children carried out physical and neurologic examination, brain magnetic resonance imaging (MRI), electroencephalography (EEG), rheumatological observation (physical, instrumental and laboratory including homocystein serum level (Hcy), evaluation for genetic thrombophilia (GThr).
Results: We observed 115 children with ECDS, aged from 3 to 16 years, the mean age 12,4 years (M ±3,52), 63 girls and 52 boys (girls/boys = 1.2:1).

ND were found in 52 children (45%), among them: recent-onset headache in 25 patients (pts) (22%), seizures in 14 pts (12%), parasomnias in 5 pts (4,3%), IS in 3 pts (2,6%), cranial neuropathies in 3 pts (2,6%), hearing loss on the side of leisure in 2 pts (1,7%), paraplegic migraine in 1 pt. IS is a casuistic presentation of ECDS.
Clinical data on the IS patients is summarized in Table below.
2 of 3 presented cases (Pt.2 and 3) have neurologic signs, while typical skin scleroderma changes appeare in 8 and 12 months after IS. In another case (Pt.1) a patient suffered from LS for 2 years, before IS, received corticosteroids (CS) orally 0.5 mg/kg 10 weeks, methotrexate (MTX) 12 mg/b.sq. for 2 years with decrease of skin process activity. MRI showed local ischemic focus in the region of left middle cerebral artery. In cases of neurologic disease debut (Pt.2 and 3), focal neurologic deficit (hemiplegia, hemiparesis, aphasia, ataxia, and seizures) lasted for less than 24 hours. MRI showed ischemic foci in frontal and temporal brain regions. In both cases vascular brain anomalies were suspected. Pt.2 and 3 also had recurrent ischemic brain attacks. All pts showed mutations in MTHRF gene and elevated Hcy serum level. After the diagnosis of ECDS was clear in Pt.2 and 3, MTX 12 mg/b.sq. started, usage of CS was avoided. Pts received antithrombotic, neurotrophic and metabolic therapy, folic acid, and rehabilitation. Despite complex therapy, our pts have irrepressible changes of brain parenchyma revealed by MRI and serious neurologic sequelae in 2 -7 years follow up.
Conclusion: We speculate that IS in observed ECDS children was strongly associated with GThr and possible undiscovered brain vascular malformations, as addition to scleroderma vasculopathy. IS occurs in less than 3 % of ND in our cohort of ECDS children, but, it demands attention of rheumatologists due to life threatened consequences. Pts with ECDS have to be cheked for GThr, as a risk factor for stroke.

Disclosure of Interest
None declared

Table 1 (abstract O074). See text for description

Pt Sex/ age	LS onset (years)	IS onset (years)	Initial clinical display	Time span stroke – skin (months)	Facial atrophy side	MRI foci side	GThr	Follow up period (years)	Neurologic sequelae
1.M/ 13	7	9	skin	24	Left	Left	PAI-I, MTHR F	4	right hemiparesis
2.M/ 17	8	7	stroke	12	Left	Left	MTHR F	7	paresis n.facialis, anisoreflection
3 F./ 9	6	5	stroke	8	Right	Right	MTHR F	2	Paresis left hand, left side deviation of the tongue

O075

Raynaud's phenomenon in children: a survey of UK & Ireland practice

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Introduction: Raynaud's Phenomenon (RP) is an episodic response to cold or emotional stress which causes colour change and symptoms including numbness and pain in the extremities. Primary Raynaud's, due to functional changes in blood vessels, does not cause tissue damage. Secondary Raynaud's, associated and often the first sign of a rheumatological condition e.g. scleroderma or SLE, can cause tissue loss, digital ulcers and gangrene. It is characterised by nailfold capillaroscopic (NFC) abnormalities and autoantibody formation, which appear to be risk factors for CTD progression. Repeat autoantibody profile and NFC is important as they can progress over time.
The PRES scleroderma working group developed recommendations for assessment, monitoring and treatment of Paediatric RP in 2016, including ANA testing in all and the recommendation to screen for SSc-specific antibodies, anti-dsDNA and ENA in ANA positive patients. NFC should be performed in all and classified as 'normal', 'non-specific changes' or 'SSc pattern'.
Objectives: To describe UK & Ireland assessment, management and monitoring of paediatric RP, considering PRES working party recommendations.
Methods: Electronic Survey sent to Paediatric Rheumatology networks.
Results: There were 64 respondents. 60% were unaware of PRES working party recommendations.
Definition of primary RP varied. Most defined it as RP in the absence of a definitive/evolving CTD (48%) .
Most tested for ANA 'always' (62%) or 'sometimes' (34%) in a new patient. Clinical suspicion of evolving CTD and family history influenced decision.
ANA, if positive, was mostly repeated 'sometimes' (50%), rather than 'always' (23%) or 'not repeated' (27%). Titre, clinical condition and symptom evolution influenced decision to repeat. This was mostly done at 6-months (37%) or 12-months (21%).
SSc-specific antibodies were mostly measured 'sometimes' (41%) - particularly if scleroderma features. 29% tested these only if ANA positive, 13% never did. Other ENA (93%), Scl70/topoisomerase I (82%) and centromere (71%) were most often included.
Most performed NFC at diagnosis: 'Yes always' (58%) or 'Sometimes' (28%). Only 14% did not. Ophthalmoscope was most often used (68%), followed by dermatoscope (28%). 3% used a USB microscope. 9% referred to another centre for formal video-capillaroscopy. Half could not access formal video capillaroscopy. The other half could directly or elsewhere.
Only 12% of respondents had received formal NFC training, with most receiving informal training (62%) or none (25%). Confidence levels were mixed. 43% of trainees were 'fairly confident' and 50% 'fairly unconfident'. 41% of consultants were fairly confident, 28% confident, 24% neutral and 7% fairly unconfident. 88% used descriptive free text to describe NFC changes. 14% classified as 'normal', 'non-specific' or 'scleroderma-type'.
FU of a patient with no risk factors for CTD varied with most choosing not to follow-up (37%) or to follow-up 'sometimes' (22%). Frequency of follow-up (FU) was 'It depends' (45%), 6-monthly (22%) or annually (24%). At subsequent visits, most would perform neither ANA nor NFC (33%).
The vast majority (94%) would FU a patient with clinical and laboratory risk factors for CTD (3-monthly 19%, 6-monthly 28%, annually 12%, 'It depends' 41%). Most would do both ANA and NFC at subsequent visits (41%)
The commonest first-line treatment for primary RP was calcium channel blocker (76%), for RP with tissue damage IV prostinoid (34%) and calcium channel blocker (34%).
Conclusion: Among UK & Ireland clinicians, there is variation in definition, diagnosis, monitoring and management of paediatric RP. Access to imaging including NFC by video-capillaroscopy was poor. Our survey highlighted a NFC training need and un-warranted variation in practice from PRES working party recommendations.

Disclosure of Interest
None declared

O076

No disease progression after 36 months follow up in the juvenile systemic scleroderma inception cohort

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Pediatric Rheumatology 2020, **18(Suppl 2):**O076

Introduction: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. Longitudinal prospective follow up data of patients with jSSc is rare. In the international juvenile systemic scleroderma cohort (jSScC) patients are followed with a standardized assessment prospectively.
Objectives: To assess the progression of jSSc over 36 months in the jSScC
Methods: Patients diagnosed according the ACR 2013 criteria for systemic sclerosis were included, if they developed the first non-Raynaud symptom before the age of 16 and were under the age of 18 at the time of inclusion. Patients were followed prospectively every 6 months with a standardized assessment.
Results: 39 patients in the JSScC had 36 months follow up. 80% had a diffuse subtype. 95% of the patients were Caucasian origin. 31 of the patients were female (80%). Mean disease duration at time of inclusion was 3.5 years. Mean age onset of Raynaud's was 8.8 years and mean age of onset at the first non-Raynaud´s was 9.5 years. Around 30% of the patients were anti-Scl70 positive and none of them anti-centromere positive. The MRSS dropped from the time point of the inclusion into the cohort from 13.9 to 11.8 after 36 months. Pattern of organ involvement did not show any significant change, beside the increase of the nailfold capillary changes from 49% to 73% (p=0.037). No renal crisis occurred. No mortality was observed.
They were positive significant changes in the patient related outcomes. The physician global disease activity decreased from 40.0 to 22.1 assessed on a VAS scale of 0 to 100 (p <0.001).
Patients global disease activity decreased from 43.3 to 20.4 and patients global disease damage from 45.0 to 21.7 both assessed on a VAS scale of 0 to 100 (p<0.001).
Conclusion: After 36 months follow up, we could observe a significant improvement of patient related outcomes and only one significant change in organ pattern involvement. In a mostly diffuse subset patient population this is a very promising result regarding outcome.
Supported by the "Joachim Herz Stiftung"

Disclosure of Interest
None declared

O077

Lupus Low Disease Activity State (lldas) is associated with reduced flare frequency and damage accrual in children with juvenile-onset systemic lupus erythematosus

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Pediatric Rheumatology 2020, **18(Suppl 2):**O077

Introduction: Treat to target (T2T), in which treatment is adjusted or escalated until a specific target is achieved, is now part of routine clinical care in many areas of medicine. It has been proposed as a strategy to improve management of juvenile-onset systemic lupus erythematosus (JSLE), using existing treatments in a more structured way. The TARGET LUPUS research programme: 'Targeting disease, Agreeing Recommendations and reducing Glucocorticoids through Effective Treatment, in LUPUS' has been established in order to develop a JSLE T2T study. In adult SLE, Lupus Low Disease Activity State (LLDAS) is considered one of the most achievable and realistic targets. LLDAS is based on the principle of "tolerated" or "acceptable" levels of disease activity in a patient with a stable treatment and low dose of corticosteroids, with a low likelihood of adverse outcome. The achievability and impact of achieving LLDAS has not been explored in children to date.
Objectives: To evaluate if and when JSLE patients achieve LLDAS and how this impacts on disease flare and damage.
Methods: Participants of the UK JSLE Cohort Study (2006-2019), <18 years at the time of diagnosis, with ³4 ACR criteria for SLE, were eligible for inclusion. At each study visit achievement of LLDAS was assessed for. LLDAS was defined as per the Asia-Pacific Lupus Collaboration: SLEDAI-2K ≤4, without involvement of major organs (renal, central nervous system, cardiopulmonary, vasculitis or fever) nor haemolytic anemia or gastrointestinal involvement, and no new features of JSLE compared with previous assessment, together with a physicians global assessment ≤1, allowing the patient to be on treatment with ≤7.5mg/day of prednisolone and/or well tolerated standard doses of immunosuppressive drugs.
Recurrent events analysis was undertaken using Prentice-Williams-Petersen GAP models, to determine the impact of recurrent episodes of LLDAS on severe disease flare (defined as a BILAG score of A/B in any organ domain). A Cox proportional hazards model with time-varying covariates was used to assess impact of LLDAS on new damage accrual (defined as ≥1 in the SLICC SDI index).
Results: 348/432 (81%) of JSLE patients achieved a state of LLDAS when followed-up for a median of 46 months (IQR 18-63). LLDAS was first achieved 10.6 months (IQR 4-20) after diagnosis, with patients achieving this state for 32% (IQR 11-51%) of their total follow-up time. Within a multivariate model, the risk of severe flare was reduced in those: achieving LLDAS (HR 0.19, 95% CI 0.16,0.23, p<0.001), with a disease duration of >1 year (HR 0.85, 95% CI 0.81,0.89, p< 0.001) and of Asian (HR 0.82, 95% CI 0.69, 0.98, p=0.03) or white British ethnicity (HR 0.83, 95% CI 0.70, 0.97, p=0.02). The risk of new damage was also reduced in those achieving LLDAS, HR 0.73 (95% CI 0.58, 0.93, p=0.01).
Conclusion: To our knowledge this is the first paediatric study to evaluate the achievability and impact of LLDAS in JSLE in a national cohort. We have demonstrated that achieving a state of LLDAS is beneficial, reducing the risk of severe flare and damage. LLDAS should therefore be considered as a realistic treatment target for use within a future JSLE T2T study. Further studies evaluating alternative treatment targets (e.g. remission on/off treatment), comparing them also with LLDAS in children, are warranted.

Disclosure of Interest
None declared

O078

Developing a standardized corticosteroid dosing regimen in pediatric proliferative lupus nephritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O078

Introduction: Corticosteroids (CS) remain the mainstay of therapy for childhood-onset systemic lupus erythematosus (cSLE). However, widely accepted strategies for oral (PO) or intravenous (IV) CS dosing are lacking.
Objectives: 1) Develop a standardized CS dosing regimen (SSR) and 2) achieve consensus for this SSR among pediatric rheumatology and nephrology physicians treating cSLE, including lupus nephritis (LN).
Methods: Step(S)1: A Delphi questionnaire helped select covariates influencing CS dosing in LN. S2: Data from 147 children with proliferative LN were used to generate Patient Profiles (PP) describing cSLE course at 2 subsequent visits. S3: PP were sent to 142 physicians experienced in cSLE to rate the course of LN, extrarenal disease (ER), and propose CS dosage for PP. S4: SSR was developed using PP data. S5: SSR was refined using a focus group of experienced physicians; and S6: validated using PP describing disease course for ≤6 months after kidney biopsy. Consensus was defined by majority of PP ratings.
Results: In Steps 1/3, 103 physicians rated 353 PP. In Step 6, 18 physicians were asked to review 33 PP each resulting in 564 PP ratings of which 437 (77.5%) and 460 (81.6%) yielded consensus on PO and IV CS dosages respectively. CS doses depend on courses of

ER and LN. The latter is defined by 3 LN response variables (glomerular filtration rate, proteinuria, hematuria). PO CS ≥40mg are guided by LN course except in ER flares with organ damage. IV CS are used for disease courses that fail to respond to PO CS ≥40mg for up to 4 weeks (Table 1). Small decreases of PO CS occur with stable LN or ER. Complete renal remission (CRR) allows more pronounced reduction of PO CS. Six months after kidney biopsy CS dose is informed by partial renal remission (PRR) or CRR during induction therapy, the course of LN and ER (Table 1).

Conclusion: The proposed SSR for LN in cSLE may be useful for clinical care and to regulate background CS use in clinical trials of new medications for cSLE.

Disclosure of Interest
None declared

Table 1 (abstract O078). Corticosteroid (CS) use provided by the standardized CS dosing regimen (SSR)

INITIAL 4 WEEKS OF INDUCTION THERAPY	
PO CS	**IV CS**
Patients≥50kg→Prednisone 60mg/day (or CS equivalent) Patients<50kg→Prednisone 1.5mg/kg/day	Up to 3 doses (30mg/kg; max 1 gram)
Lowest dose at week 4→30mg/day for patients≥50kg	
WEEKS 5–26 OF INDUCTION THERAPY*	
LN course	***Much worse:*** Increase PO CS to 50-60mg/day; After 1-3 weeks, if response is (a) *Satisfactory→ No IV CS; (b) Non-satisfactory→ IV pulses +PO CS*
	Mild–moderately worse: Increase PO CS by 30% (if dose<40mg; max 60mg)
	Active stable: Stable PO CS dose (if dose< 40mg; else: slow decrease)
	Improved active or PRR[1]: Slow decrease; ***CRR[2]:*** More pronounced decrease of PO CS dose
Lowest PO CS dose at week 26	10mg/day
BEYOND 26 WEEKS POST KIDNEY BIOPSY*	
LN course	***Flare[3] after PRR/CRR:*** Prednisone≥40mg; After 1-3 weeks, if response is (a) *Satisfactory→ No IV CS; (b) Non-satisfactory→ IV pulses + PO CS*
	Worse after PRR/CRR: Increase PO CS dose FIRST
	PRR stable: Slow decrease; ***CRR or PRR improved:*** More pronounced decrease of CS dose

[1] PRR: >50% improvement of ≥2 LN response variables (LN-RVs) +remaining LN-RV NOT worse; [2] CRR: LN-RVs are NORMAL; [3]LN flare: ≥1 of the LN-RV changes is persistently present on ≥2 subsequent time points ≥1week apart; *(assumption stable ER)*

O079

Renal activity index for lupus nephritis distinguishes active renal disease among childhood systemic lupus erythematosus patients

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Pediatric Rheumatology 2020, **18(Suppl 2):**O079

Introduction: Renal involvement in childhood-onset systemic lupus erythematosus (cSLE) is a major cause of morbidity and mortality. Conventional tools to identify lupus nephritis (LN) fall short compared to renal biopsy. The renal activity index in lupus (RAIL) was developed using 6 urinary biomarkers to reflect disease activity(1).

Objectives: To test the usefulness of the RAIL in the clinical setting to identify children with active LN.

Methods: Urine samples were collected cross-sectionally from cSLE patients at the time of active LN or routine clinic visit. Patients were classified into active LN, inactive LN or non-LN SLE based on results of a renal biopsy and/or absence of LN determined by routine urinalysis. The following urine biomarkers are included in the RAIL score (neutrophil gelatinase-associated lipocalin, ceruloplasmin, monocyte chemoattractant protein-1, adiponectin, hemopexin, kidney injury molecule-1, urinary protein and creatinine). Analysis was done by Enzyme-linked immunosorbent assay (ELISA) and nephelometry. RAIL scores were calculated per the defined algorithm for each urine sample. Other data was collected (Table 1). The accuracy of the RAIL score was compared between groups.

Results: Among 117 cSLE patients, 37 had active LN, 30 had inactive LN and 50 had no LN. Clinical characteristics and distribution of RAIL scores are outlined in Table 1. RAIL scores of inactive LN and no-LN group largely overlapped so they were combined in one group (Group 2) and compared to active LN (Group 1). The RAIL score was significantly higher in Group 1 vs Group 2 (median 0.7 vs -1.1 respectively, $p<0.0001$). The RAIL score diagnostic accuracy was assessed in a multivariable regression model. Adjusting for patient's age and extra-renal SLE activity index (SLEDAI) score, the RAIL score was associated with odds ratio of 2.16 (95%CI 1.4-3.3, $p=0.001$) for active LN vs. inactive LN and non-LN SLE. A receiver operating curve for a RAIL cut-off score of 0.35 produced an area under the curve of 0.9 (sensitivity 86%, specificity 84%) for active LN. A RAIL score <0.35 had a negative likelihood ratio of 0.17. Further adjustment for urinary protein and creatinine did not significantly influence the results.

Conclusion: The RAIL score is highly accurate in distinguishing active LN identified by renal biopsy, from inactive LN and non-LN SLE. A score of 0.35 identifies cSLE patients who very likely have active LN.

Disclosure of Interest
None declared

Table 1 (abstract O079). Clinical characteristics and distribution of RAIL scores among Group 1 (active LN) and Group 2 (inactive LN + non-LN SLE) patients

	Group 1 Active LN N = 37	**Group 2 Inactive LN + Non-LN SLE N = 80**	***p*-value**
Age (y)	15 (13-17)	18 (16-21)	<0.0001
NIH-AI[¥]	9 (4-13)	0 (0-0)	<0.0001
NIH-CI[¥]	1 (0-2.75)	0 (0-0)	0.12
Extra-renal SLEDAI	9 (6-13)	2 (0-4)	<.0001
GFR	91 (60-129)	108 (98-126)	0.05
Urinary creatinine	92 (61-191)	134 (73-183)	0.32
Urinary protein	254 (98-404)	21 (11-50)	<.0001
Urinary microalbumin	254 (189-316)	15 (9-43)	<.0001
RAIL Score	0.7 (-0.1-1.6)	-1.1 (-2.5-0.3)	<.0001

Values represent median (interquantile range)
[¥] Includes active (N=24) and inactive LN (N=4) patients only. Only those who had renal biopsies within 30 days of urine collection are included

O080

Nailfold capillary abnormalities in a cross-sectional study in childhood-onset systemic lupus erythematosus compared with matched healthy controls

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Pediatric Rheumatology 2020, **18(Suppl 2):**O080

Introduction: Nailfold capillaroscopy (NFC), a noninvasive magnification method, is used to visualize the capillaries of the fingertips. NFC is a diagnostic instrument, used in patients with Raynaud's phenomenon: a capillary scleroderma pattern is associated with systemic sclerosis (SSc). Systemic Lupus Erythematosus (SLE) patients also show capillary abnormalities in NFC. As concluded in a recent review, adults with SLE show significantly higher number of tortuous capillaries, abnormal capillary morphology and capillary hemorrhages, when compared to healthy controls. Additionally, the capillary abnormalities also seem to correlate with disease activity. Studies on nailfold capillary findings in children with SLE are scarce and inconclusive. For systemic sclerosis (SSc), multiple studies have shown that capillary abnormalities (by qualitative description) can also be of use as a prognostic biomarker. For selection of high-risk SLE-patients it is necessary to obtain more indicators of disease severity that predict disease damage. Nailfold capillary abnormalities could be such an indicator or biomarker in SLE.
Objectives: The primary objective of this cross-sectional study is to describe capillary abnormalities in cSLE patients and compare them with healthy controls, matched for skin pigmentation, age and gender. These demographic variables have been described as confounding factors in healthy controls in interpreting capillary characteristics, such as density. The secondary objective is to correlate the observed capillary abnormalities with demographical variables in both cohorts and with disease-specific variables in cSLE patients.
Methods: Healthy controls were matched for ethnic background, age and gender. Quantitative and qualitative assessments of nailfold capillaroscopy images were performed according to the definitions of the EULAR study group on microcirculation in Rheumatic Diseases.
Results: Both groups (n=41 cSLE-patients and n=41 healthy controls) were comparable for ethnic background (p=0.317). Counted per mm, cSLE-patients showed significantly more 'giants' (p=0.032), 'abnormal capillary shapes' (p=0.003), 'large capillary hemorrhages' (p<0.001) and 'pericapillary extravasations' (p<0.001). Combined 'abnormal capillary shapes and pericapillary extravasations' (in the same finger) were detected in 78% (32/41 patients). 'Microangiopathy' was detected in 68.3% (28/41) and a 'scleroderma pattern' in 17.1% (7/41) of the cSLE-patients. The number of abnormal capillary shapes per mm was significantly correlated with treatment-naivety (p=0.022). The number of large pathological hemorrhages per mm was significantly correlated with disease score (p=0.002) and presence of nephritis (p=0.012). Compared to healthy controls, pericapillary extravasations were found in significantly higher numbers per mm (p<0.001), as well as in percentage of patients (p<0.001). Pericapillary extravasations were also significantly positively correlated with darker skin pigmentation in both study cohorts.
Conclusion: As in adult SLE-patients, our nailfold capillaroscopy study confirms the presence of significantly more giants, abnormal capillary morphology and hemorrhages in cSLE, when compared to healthy controls. Significant correlations were found between these capillary abnormalities and disease activity. A high frequency and total amount of "pericapillary extravasations" was observed in cSLE patients, possibly revealing a new subtype of capillary hemorrhage.

Trial registration identifying number: Dutch trial register registration no. NL60885.018.17

Disclosure of Interest
None declared

O081

Neuropsychiatric involvement in Juvenile-onset Systemic Lupus Erythematosus (JSLE): data from the UK JSLE cohort study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O081

Introduction: Juvenile-onset systemic lupus erythematosus (JSLE) is a rare autoimmune/inflammatory disease, accounting for up to 20% of SLE cases. Though clinically similar to adult-onset disease, it frequently follows a more severe course. Neuropsychiatric (NP) involvement in JSLE can be aggressive and significantly affect patients' quality of life as well as disease outcomes.
Objectives: The aim of this study was to describe the demographic characteristics, clinical and laboratory features of NP involvement in JSLE.
Methods: We analyzed data from JSLE patients enrolled in the UK JSLE Cohort Study between August 2006 and June 2019. Demographic (age, gender, ethnicity, family history), clinical (1997 ACR classification criteria, disease activity BILAG, SLICC, and damage index SLICC-SDI) and laboratory (ESR, CRP, CBC with diff, ANA, anti-ENA, anti-dsDNA, aCL, lipid profile, renal function, C3, C4, Ig levels, thyroid function, UA) data collected at disease onset and at last visit were analyzed.
Results: A total of 428 JSLE patients were included, with a female:male ratio of 5.4:1. The median age at diagnosis was 12.2 years (range: 0-17). A majority of JSLE patients were Caucasian (51.4%), followed by patients of South Asian (23.3%), Black African/Caribbean (16.7%), and East Asian (6.5%) descent. Patients with headaches as the only NP symptom were excluded here, because of the low specificity of this feature.
Overall, one quarter of JSLE patients (107/428, 25%) showed NP features; in 48.5% of these cases, NP symptoms were the presenting manifestation. The median age at disease onset and ethnic composition did not differ between sub-cohorts with vs without NP involvement. Most frequently recorded NP manifestations recorded included cognitive impairment (n=45, 42%), seizures (n=21, 20%), psychotic features (n=11, 10%), peripheral nerve involvement (n=9, 8%), cerebral vasculitis (n=10, 9%), and ischaemic stroke (n=7, 6%).

Headache was an accompanying manifestation in 74% of all NP SLE patients.
While no differences were recorded in autoantibody patterns and immune cell counts, lower platelet counts (<100.000/mmc) were found in patients with NP involvement at disease onset (p=0.02). Children with NP involvement showed both a higher number of ACR criteria (mean 4.9 *vs* 4.6, p=0.07) and higher SLICC scores (0.3 *vs* 0.2, p=0.029) at disease onset.
Conclusion: Approximately 25% of JSLE patients enrolled in the UK JSLE Cohort Study have NP involvement. Patients with NP involvement exhibit more disease-associated damage at the time of diagnosis when compared to patients without NP involvement and therefore represent a high-risk group.

Disclosure of Interest
None declared

O082

Utilization of anti-nuclear antibody analysis in tertiary pediatric clinic

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Pediatric Rheumatology 2020, **18(Suppl 2):**O082

Introduction: Anti-nuclear antibody (ANA) is a large group of auto-antibodies that occurred predominantly against cellular antigens found in the cell nucleus. It uses as the diagnosticmarker for systemic lupus erythematosus (SLE) and the other autoimmune diseases. ANA positivity can be detected in malignancy,infection as well as healthy population.
Objectives: We aimed that evaluation of how the ANA test was used in the clinical practice of a tertiary center.
Methods: Patients performed ANA test under the 18 year old were collected in period of 2013-2017 years. Demographic and clinical features, diagnosis, ANA result, titer, and staining pattern were obtained from the medical records The sensitivity and specificity of ANA titer at ≥1/100 and ≥1/1000 were evaluated based on the features of the patients at the time of autoimmun disease diagnosis.
Results: Total number of patients performed ANA tests were 3812. Of these patients, we achieved 3320 patients' medical records.
Anti-nuclear antibody was positive in 909 (27,4%) and negative in 2411 (72,6%) of the patients. Positiveness was more in females than males (respectively n= 617 (18,6%), n=292 (8,8%), p<0,0001). The most frequent clinical reason of patients performed ANA test was musculoskeletal findings (n=1355 (40,8%)).
The most common autoimmune disease was juvenile idiopathic arthritis (n=174, 20,2%) in patients with ANA positivity. Patients with SLE (n:52, 6%) followed the JIA. In patients diagnosed autoimmune diseases, for ANA titer up to 1/100 , positive predictive value (PPV) was 37,9%, negative predictive value (NPV) was 78,6%, sensitivity was 40,1%, specificity was 77,1%. For the titer of ANA≥1/1000, positive predictive value (PPV) was 43,4%, negative predictive value (NPV) was 77%, sensitivity was 24,1%, specificity was 89%.
Conclusion: Our results showed that performances of ANA test have low specificity and sensitivity to diagnosis of autoimmune diseases in clinical practices. Therefore clinical findings should be carefully evaluated before ANA test performed.

Disclosure of Interest
None declared

Table 1 (abstract O082). The clinical findings and diagnosis of patients performed ANA test and ANA results in patients with and without autoimmune diseases

Clinical findings	**n (%)**		
Musculoskeletal	1355 (40,8%)		
Neurologic	417 (12,6%)		
Enterohepatic	363 (10,9%)		
Skin lesions	284 (8,6%)		
Hematologic	247 (7,4%)		
Other	654 (19,6%)		
	ANA negative n (%)	**ANA positive n (%)**	
Rheumatic diseases			
Juvenile idiopathic arthritis	286 (33,2%)	174 (20,2%)	
Systemic lupus erythematosus	0	52 (6%)	
İdiopathic uveitis	37 (4,3%)	16 (1,9%)	
Psoriasis	5 (0,6%)	4 (0,5%)	
Systemic sclerosis	0	7 (0,8%)	
Localize scleroderma	8 (0,9%)	1 (0,1%)	
Mix connective tissue disease	2 (0,2)	4 (0,5%)	
Juvenile dermatomyositis	4 (0,5%)	3 (0,3%)	
Sjögren disease	0	3 (0,3%)	
Non-rheumatic diseases			
Autoimmune hepatitis	11 (%1,3)	20 (2,3%)	
Inflammatory bowel disease	4 (0,5%)	3 (0,3%)	
Celiac disease	19 (2,2%)	10 (1,2%)	
Immune thrombocytopenic purpura	44 (5,1 %)	12 (1,4%)	
Autoimmune hemolytic anemia	9 (1%)	4 (0,5%)	
Multiple sclerosis	17 (2%)	5 (0,6%)	
Optic neuritis	8 (2%)	1 (0,1%)	
Guillain-Barré syndrome	8 (0,9%)	2 (0,2%)	
Acute disseminated encephalomyelitis	4 (0,5%)	2 (0,2%)	
Chronic autoimmune urticaria	1 (0,1%)	4 (0,5%)	
Type 1 diabetes mellitus	6 (0,7%)	2 (0,2%)	
Tubulointerstitial nephritis	6 (0,7%)	0	
Other	36 (4,2%)	16 (1,9%)	
Total	**515 (59,9)**	**345 (40,1%)**	
ANA	**With autoimmune diseases n (%)**	**Without autoimmun diseases n (%)**	**Total (%)**
≥1/100 titer	345 (%10.4)		
Positive	515 (%15.5)	564 (%17)	909 (%27.4)
Negative		1896 (%57.1)	2411 (%72.6)
≥1/1000 titer	208 (6.3%)		
Positive	652 (19.6%)	270 (8.1%)	478 (14.4%)
Negative		2190 (66%)	2842 (85.6%)

O083

Medication utilization and renal biopsy patterns in childhood-onset lupus nephritis in the childhood arthritis and rheumatology research alliance registry

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Pediatric Rheumatology 2020, **18(Suppl 2):**O083

Introduction: Little is known regarding variation in care patterns within early management of pediatric lupus nephritis, which may be contributing to documented disparities in long-term renal outcomes.
Objectives: Our objective was to characterize sociodemographics, disease characteristics, and care utilization patterns from a large, multi-center North American cohort of cSLE patients with nephritis.
Methods: A cross-sectional analysis of the longitudinal, observational Childhood Arthritis and Rheumatology Research Alliance (CARRA) cSLE Registry was conducted on data prospectively collected from March 2017 to December 2019. Registry enrollment is ongoing with data collection every 6 months. Lupus nephritis was defined in patients with at least one renal biopsy date recorded and positive histopathologic classification by either 1995 World Health Organization (WHO) or 2003 International Society of Nephrology (ISN)/Renal Pathology Society (RPS) criteria. We abstracted the following variables: sex, race/ethnicity, insurance status, reported household income, reported parent education level, age at diagnosis, date of cSLE diagnosis, date of initial renal biopsy, WHO or ISN/RPS classification of initial renal biopsy, Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at enrollment, physician global assessment (PGA) of disease activity (0-10) at enrollment, and medications prescribed both prior to and following enrollment. Descriptive statistics were calculated using SAS v9.4.
Results: Out of 566 cSLE patients, we identified 220 with renal biopsy-positive lupus nephritis across 44 pediatric rheumatology centers. The cohort was 83% female, 31% Black, 25% White, and 24% Hispanic with a mean age of 13.6 years at cSLE diagnosis (Table 1). In 23% of patients, date of renal biopsy occurred > 90 days after date of cSLE diagnosis. On initial biopsy, 16% of patients had class I/II, 63% had class III/IV, 14% had class V, 6% had combined class III+V / IV+V, and 1 patient had class VI. Biopsies were classified using WHO criteria in 69% of patients, ISN/RPS in 43%, and both in 12%. Repeat biopsy was performed on 19 patients (9%) with a change in classification in 11 (58%). There was high ever-use of hydroxychloroquine (97%) and mycophenolate (84%) across the cohort, while cyclophosphamide (28%) and rituximab (25%) were more varied. In 15 centers with ≥ 5 patients with class III/IV proliferative disease, mycophenolate use ranged from 60-100%, cyclophosphamide use ranged from 0-100%, and rituximab use ranged from 0-100% of patients.
Conclusion: This initial study of patients with pediatric lupus nephritis in the CARRA Registry demonstrates a diverse cohort of patients with predominantly proliferative lupus nephritis. There is substantial variation medication utilization for proliferative nephritis between centers, as well as biopsy reporting practices across the cohort. Further study and implementation of optimal management for cSLE nephritis is needed to improve long-term outcomes.

Disclosure of Interest

E. Smitherman: None declared, R. Chahine: None declared, T. Beukelman Consultant for: Novartis, UCB, L. Lewandowski: None declared, A. Rahman: None declared, S. Wenderfer: None declared, J. Curtis: None declared, A. Hersh: None declared

Table 1 (abstract O083). Demographic and clinical characteristics of patients with renal biopsy-positive lupus nephritis

	Total Cohort (n = 220)
Minority race/ethnicity, n (%)	166 (75)
Non-private insurance status, n (%)	128 (58)
Household income <$75,000, n (%)	87 (40)
Parent education of high school or less, n (%)	71 (32)
SLEDAI-2K at enrollment, median (IQR)	4 (2-10)
Physician global assessment of disease activity at enrollment (0-10), median (IQR)	2.5 (1-4)
Time between cSLE diagnosis and renal biopsy, mean (SD) months	4.9 (13.8)

O084

How the covid-19 pandemic has influenced pediatric rheumatology practice: results of a global, cross-sectional, online survey

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Pediatric Rheumatology 2020, **18(Suppl 2):**O084

Introduction: The COVID-19 (coronavirus disease 2019) pandemic is a global health problem threatening millions of lives worldwide. As pediatric rheumatologists, we have a role in the multidisciplinary management of COVID-19. Our young patients with rheumatic diseases are a vulnerable population in this pandemic. Moreover, the drugs we use to treat rheumatic diseases are being tested for use against COVID-19.
Objectives: To analyze how the COVID-19 pandemic has affected pediatric rheumatology practice.
Methods: For this cross-sectional survey study, we developed an online, self-administered survey that included 18 questions regarding changes in pediatric rheumatology practice due to the COVID-19 pandemic. Results were analyzed using descriptive statistics.
Results: Worldwide, 271 pediatric rheumatologists (54% ≥45 years; 65.7% female) from 60 countries responded to the survey in May 2020. Almost 70% of the respondents were practicing in a university hospital. 221 (81.5%) had been in pediatric rheumatology practice for ≥5 years. Nearly two-thirds of the respondents disagreed that the COVID-19 pandemic had led to reduced prescription of nonsteroidal anti-inflammatory drugs, conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs), and biologic DMARDs. 220 (81.8%) did not change the management of patients who are using biologic DMARDs. Around 10% of the respondents were more inclined to prescribe hydroxychloroquine, while 237 (87.5%) did not report any change in their attitude towards prescribing this drug. Interestingly, 117 (43.2%) were more likely to taper corticosteroids faster. Most respondents reported that during the pandemic they hesitated to initiate treatment with cyclophosphamide (36.2%), followed by rituximab (25%). About half of the respondents cancelled scheduled appointments with established patients and shifted towards smartphone

applications for patient care, while 40% postponed clinic appointments with new patients and used video consultations instead.
Approximately one-third of respondents indicated that their patients had experienced a delay in the diagnosis of a rheumatic disease or in receiving an intraarticular steroid injection, while 56 (20.7%) stated that their patients experienced a flare due to delayed clinical appointments. 97 (35.8%) mentioned that their patients had difficulties in obtaining hydroxychloroquine due to shortages and 30 (11%) noted the same problem with tocilizumab. Almost half of the respondents (n=120; 44.3%) think that children on long-term corticosteroid treatment should avoid attending school, while 51 (18.9%) believe that children using biologic DMARDs should avoid school; especially those using rituximab (n=103; 38%).
The respondents indicated that they had seen increases in the numbers of patients with Kawasaki disease (25.5%), macrophage activation syndrome (13.3%), unusual vasculitic rashes (28%), and hyperinflammation (22.5%), since the beginning of the COVID-19 pandemic.
Conclusion: The COVID-19 pandemic has affected pediatric rheumatology practice extensively. Most changes arose from delays in clinic appointments, use of anti-rheumatic drugs in COVID-19 treatment/prophylaxis and concerns about the immunosuppressive effects of anti-rheumatic therapies. In addition, an increase in the use of virtual technologies for routine communication with patients was observed.

Disclosure of Interest
None declared

O085

Paediatric multi-system inflammatory syndrome temporally associated with SARS-COV-2 mimicking Kawasaki Disease (KAWA-COVID-19): a multicentre cohort

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Pediatric Rheumatology 2020, **18(Suppl 2):**O085

Introduction:
Current data suggest that COVID-19 is less frequent in children, with a milder course. However, over the past weeks, an increase in the number of children presenting to hospitals in the greater Paris region with a phenotype resembling Kawasaki disease (KD) has led to an alert by the French national health authorities.
Objectives: To describe paediatric multi-system inflammatory syndrome temporally associated with SARS-COV-2 mimicking Kawasaki disease ('Kawa-COVID-19') in Paris region since April 2020.
Methods: Multicentre compilation of patients with Kawa-COVID-19. A historical cohort of 'classical' KD served as comparator. Factors associated to a severe outcome were assessed.
Results: Sixteen patients were included (sex ratio=1, median age 10 years IQR [4·7-12.5]). SARS-COV-2 was detected in 11 cases (69%), whilst a further 5 cases had documented recent contact with a q-PCR-positive individual (31%). Cardiac involvement included myocarditis in 44% (n=7). Factors prognostic for the development of severe disease (i.e. requiring intensive care, n=7) were age over 5 years and ferritinemia >1400µg/L. Only 5 patients (31%) were successfully treated with a single intravenous immunoglobulin infusion (IgIV), whilst 10 patients (62%) required a second line of treatment. The Kawa-COVID-19 cohort differed from a comparator group of 'classical' KD by older age at onset 10 vs 2 years (p<0.0001), lower platelet count [188, vs 383 G/L (p< 0.0001)], a higher rate of myocarditis 7/16 vs 3/220 (p= 0.0001) and resistance to first IgIV treatment 10/16 vs 45/220 (p= 0.004).
Conclusion: Kawa-COVID-19 likely represents a new systemic inflammatory syndrome temporally associated with SARS-COV-2 infection in children. Further prospective international studies are necessary to confirm these findings and better understand the pathophysiology of Kawa-COVID-19.

Disclosure of Interest
None declared

O086

Absence of severe complications from SARS-COV-2 infection in children with rheumatic diseases treated with biologic drugs

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Pediatric Rheumatology 2020, **18(Suppl 2):**O086

Introduction: Children with SARS-COV-2 infection seem to develop a milder disease. A certain increasein infectious risk in children with autoimmune and autoinflammatory conditions is well known, and has beenattributed both to the intrinsic immune dysregulation, or to immunosuppressive therapy: this could begenerating reasonable concerns in pediatric rheumatologist and patients' families. Preliminary experience inadults treated with conventional disease-modifying antirheumatic drugs (cDMARDs) and biologic disease-modifying drugs (bDMARDs) seems to be reassuring
Objectives: To investigate the impact of SARS-COV-2 infection on pediatric patients with rheumaticdiseases treated with bDMARDs.
Methods: Survey evaluating patients' health conditions, direct exposure to subjects known to be affected byCOVID-19, modifications of ongoing DMARDs treatment and potential flares of underlying disease duringthe early weeks of Italian COVID-19 outbreak.
Results: Between February 25th and April 14th 2020, we collected data from 123 patient (83 F) treated with bDMARDs and followed in our unit. The survey was administered during outpatient clinic visits, or by telephone. Median age was 13 years (range 4-20), median disease duration ws 6 years. Diagnosis were: juvenile idiopathic arthritis (89), chronic uveitis (5), autoinflammatory disease (5), other (24). Therapy consisted in Anti-TNF (95), anakinra (7), tocilizumab (7), other (14); eighty-one patients were also on a cDMARD. None of them were confirmed cases of COVID-19 . Eight children presented mild respiratory symptoms; three of them were family members of adults with probable COVID-19 infection (i.e. with fever, cough, difficulty to breath but no confirmatory positive SARS-COV-2 Real-Time PCR . No patient stopped ongoing therapy nor needed hospitalization. All patients adopted a preventive strategy against COVID-19 based on social distancing and use of personal protective equipment, but usually only after the beginning of the outbreak.
Conclusion: No definitive conclusions about the incidence of SARS-CoV-2 infection in children with rheumatic diseases, nor on the overall outcome of immunocompromised patients affected by COVID-19 can be drawn from our study. However, in agreement with observations on adult rheumatology patients , our preliminary experience supports the idea that patients with chronic diseases treated with bDMARDs do not seem to be at increased risk of severe or life- threatening complications from SARS-COV-2 compared with the general population. A strict disease control may be of great importance since it is known that disease activity may be a risk factor for the development of infections.

Disclosure of Interest
None declared

O087

Covid-19 in pediatric rheumatology patients treated with biologic drugs: a cross-sectional, patient survey study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O087

Introduction: COVID-19 pandemic is a global health problem. Children are affected less compared to adults. Children with rheumatic diseases especially if treated with biologic drugs could constitute a vulnerable group in this pandemic. We lack data on the COVID-19 infection rate and disease course in pediatric rheumatology patients treated with biologic drugs.
Objectives: We aimed to analyze the frequency/severity of COVID-19 in pediatric patients with rheumatic diseases, treated with biologic drugs.
Methods: This is a cross-sectional survey study. We collected data about direct exposure to COVID-19 patients, presence of COVID-19 or symptoms associated with flu, and difficulties in obtaining biologic drugs they were using; starting from March 1st, 2020 when the first COVID-19 case was announced in Turkey. The survey was administered by telephone to all patients. In May 2020, we tried to reach to a total of 189 children with rheumatic diseases treated with biologic drugs who were being followed up in the Pediatric Rheumatology Unit of Hacettepe University, Ankara, Turkey. Results were analyzed using descriptive statistics.
Results: The final study population included 162 patients (48% female; mean age 13.2 ± 4.7 years). The underlying rheumatic diseases were as follows: Familial Mediterranean Fever (n=66), juvenile idiopathic arthritis (n=52), enthesitis related arthritis (n=16), cryopyrin-associated periodic syndrome (CAPS) (n=9), chronic recurrent multifocal osteomyelitis (CRMO) (n=6), ADA2 deficiency (DADA2) (n=4), Sting-associated vasculopathy with onset in infancy (SAVI) (n= 3), scleroderma (n=3), Takayasu arteritis (n=3), hyperimmunoglobulin D syndrome (HIDS) (n= 3), polyareritis nodosa (n=2), Behçet's disease (n=2). The patients were on these biologic drugs: canakinumab (n= 59), etanarcept (n=30), anakinra (n=26), adalimumab (n=18), tocilizumab (n=13), tofatisitinib (n=6), infliximab (n=4), rituximab (n= 3), secukinumab (n=2), barisitinib (n=1). Thirty patients had flu-associated symptoms and 14 of these were tested with RT-PCR for COVID-19. The results were negative in all. Thirteen (8%) patients reported that they had difficulty accessing their prescribed drugs.
Conclusion: None of our patients with rheumatic diseases treated with biologic drugs were diagnosed with COVID-19 nor had severe flu-associated complications. In our cohort, the pediatric rheumatology patients treated with biologic drugs did not seem to be at increased risk for COVID-19-associated severe complications compared to general population.

Disclosure of Interest
None declared

O088

Study of emapalumab, a fully human, anti-ifn gamma monoclonal antibody, in patients with MAS/SHLH on a background of sJIA and with inadequate response to high-dose glucocorticoids

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Pediatric Rheumatology 2020, **18(Suppl 2):**O088

Introduction: Macrophage activation syndrome (MAS) is a severe complication of rheumatic diseases and occurs most frequently in patients with systemic juvenile idiopathic arthritis (sJIA). Data from animal models and from observational studies in patients suggest that interferon gamma (IFNγ) is a driver of the hyperinflammation and hypercytokinemia observed in MAS/secondary hemophagocytic lymphohistiocytosis (sHLH).
Objectives: The purpose of this study is to assess the pharmacokinetics, efficacy, and safety of intravenous (IV) infusions of emapalumab, a fully human anti-IFNγ monoclonal antibody, in patients with MAS in the context of sJIA.
Methods: This ongoing, pilot, open-label, single-arm study (NCT03311854) includes patients with MAS (2016 ACR/EULAR criteria) on a background of confirmed, or high presumption of, sJIA, and with inadequate response to high-dose IV glucocorticoids. Twin study protocols are established in Europe and North America. Emapalumab is initiated at 6 mg/kg (1 dose) and continued at 3 mg/kg every 3 days for 2 weeks, and then twice weekly for a total of 4 weeks, or less upon achievement of complete response (CR). CR is defined as an absence of MAS clinical signs plus white blood cell and platelet counts above the lower limit of normal, LDH, AST and ALT <1.5 x upper limit of normal, fibrinogen >100 mg/dL, and ferritin decreased by ≥80% or to <2,000 ng/mL.
Results: We report preliminary data from the first 9 patients (median age [range] 11.6 [2.1-25.3] years) enrolled (7 in Europe and 2 in the USA). All patients had failed high-dose methylprednisolone, of which there were prior treatment failures from cyclosporin A (n=4) and from anakinra (n=4). Treatment with emapalumab resulted in rapid IFNγ neutralization, as demonstrated by a decrease in CXCL9 levels, and subsequent deactivation of T cells, as indicated by the decrease in sIL-2R levels (Table). CR was achieved in all patients after a median of 23 (12-56) days. A progressive improvement in all clinical and laboratory parameters of MAS was observed. Glucocorticoids were tapered in all patients (median tapering 92%; range 45% to 98% at Week 8). Emapalumab infusions were well tolerated by all patients, with no discontinuation. CMV reactivation was reported in 1 patient as a serious event possibly related to emapalumab and resolved with antiviral treatment.
Conclusion: Emapalumab administration led to rapid neutralization of IFNγ (rapid decrease in CXCL9 levels) and was efficacious in controlling MAS (all patients achieved complete response) and had a favorable safety profile. These results support the pathogenic role of IFNγ in MAS/sJIA and the therapeutic value of IFNγ neutralization in MAS patients who have failed high-dose glucocorticoid treatment.

Trial registration identifying number: NCT03311854

Disclosure of Interest
F. De Benedetti: None declared, P. Brogan Consultant for: Sobi, Novartis, Roche, UCB, C. Bracaglia: None declared, M. Pardeo: None declared, G. Marucci: None declared, E. Sacco: None declared, D. Eleftheriou Speaker Bureau of: Sobi, C. Papadopoulou: None declared, A. Grom Consultant for: Novartis, NovImmune, AB2Bio, P. Quartier Consultant for: Abbvie, Lilly, Novimmune, Novartis, Sobi, Speaker Bureau of: AbbVie, Lilly, Novartis, Sobi, R. Schneider Consultant for: Sobi, Novartis, P. Jacqmin Consultant for: Sobi, R. Frederiksen Employee of: Sobi, M. Ballabio Consultant for: Sobi, C. de Min Employee of: Sobi

Table 1 (abstract O088). See text for description

Parameters	Median baseline value (range)	Median days of treatment (range)
D-dimers to <1000 mg/L	12,480 (550-89,552)	15 (1-49)
sIL-2R to <2000 ng/L	4,596 (1,664-20,954)	21 (6-37)
Ferritin <500 mg/L	29,240 (716-192,584)	21 (9-42)
Physician visual analog scale of MAS activity ≤1	9.0 (2-10)	19 (9-56)
All MAS laboratory parameters within range of complete response	NA	21 (15-55)
All MAS parameters within range of complete response	NA	23 (12-56)
Glucocorticoid tapering at ≤1 mg/kg prednisolone equivalent	NA	42 (16-53)

O089

Risk score of macrophage activation syndrome in patients with systemic Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O089

Introduction: MAS is a severe, life-threatening, complication of sJIA with a significant mortality. A score that identify sJIA patients with high risk to develop MAS would be useful in clinical practice.

Objectives: To evaluate whether routine laboratory parameters at disease onset may predict the development of MAS in patients with sJIA. To define a risk score of MAS using these parameters and to validate the score in a second population.

Methods: Laboratory parameters of disease activity and severity were retrospectively evaluated in 99 sJIA patients referred to Bambino Gesù Hospital in the last 10 years with at least 2 years of follow-up. Laboratory parameters were evaluated during active sJIA, without MAS, at disease onset or disease flare, immediately before treatment for sJIA was started or modified. Patients were divided in sJIA patients without MAS in the 2 years of follow-up and sJIA patients with at least one MAS episode. To create the MAS risk score, laboratory parameters with a statistically significant difference between the 2 groups were selected.

Results: Thirty patients, that fulfilled the 2016 classification criteria for MAS at time of sampling, were excluded from the analysis. Therefore, we analysed laboratory parameters of 69 sJIA patients, 41 without MAS in the follow-up and 28 with at least one episode of MAS. Levels of ferritin, AST, LDH and triglycerides were significantly higher in patients with MAS during follow-up compared to those without. Their respective cut-off were computed by means of ROC curve analysis. A regression coefficient-based scoring system was used to assign weights to the risk index and the optimal score cut-off was defined by ROC curve analysis (Table1). A MAS risk score $\geq$5 identified 27 out of 28 sJIA patients with MAS during the follow-up and 8 out of 41 sJIA patients without MAS. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of the score are detailed in table 1. In order to validate the MAS risk score on a different population, we applied the score on 132 sJIA patients from other paediatric Rheumatologic centres, 100 without history of MAS and 32 with at least one episode of MAS. Se, Sp, PPV and NPV of the score are reported in table 1.

Conclusion: In conclusion we developed a MAS risk score based on routine laboratory parameters, available worldwide, that can help clinicians to identify early in the disease course sJIA patients with high risk to develop MAS.

Disclosure of Interest

S. Carbogno: None declared, D. Pires Marafon: None declared, G. Marucci: None declared, E. Sacco: None declared, M. Pardeo: None declared, H. Alsaleem: None declared, S. Fingerhutova: None declared, D. Ferhat: None declared, N. Čekada: None declared, M. Kostik: None declared, C. Kessel: None declared, O. Vougiouka: None declared, A. Gagro: None declared, J. Tibaldi: None declared, F. Minoia: None declared, I. Maccora: None declared, R. Schneider: None declared, P. Dolezalova: None declared, B. Sozeri: None declared, M. Jelusic: None declared, A. Insalaco: None declared, F. De Benedetti Consultant for: Grant Research Support from Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, C. Bracaglia: None declared

Table 1 (abstract O089). Laboratory parameters and cut-off used to create the MAS risk score in sJIA patients. Se, Sp, PPV and NPV in the construction and validation cohorts

Laboratory parameters	Cut-off	Score
Ferritin (ng/ml)	>750	3.5
LDH (UI/L)	>540	2.5
AST (UI/l)	>30	2
Triglycerides (mg/dl)	>100	1.5
	Construction cohort	**Validation cohort**
Sensitivity (Se)	96.4	81.3
Specificity (Sp)	80.5	60.0
Positive predictive value (PPV)	77.1	39.4
Negative predictive value (NPV)	97.1	90.9

O090

A patient with IFNAR2 deficiency causing dysregulation of nk cell functions and presenting with hemophagocytic lymphohistiocytosis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O090

Introduction: Hemophagocityc lymphohistiocytosis (HLH) is a life-threatening syndrome characterized by a hyperinflammatory state. HLH is typically caused by biallelic mutations in genes encoding proteins involved in the cytotoxic activity of T lymphocytes and natural killer (NK) cells (primary HLH), but it can also occur, in the absence of known genetic causes, in the context of malignancies, infections and rheumatic diseases (secondary HLH). A constitutive or transient defect in NK cell cytotoxicity is typically occurring in patients with, respectively, primary and secondary HLH and is believed to play a key role in the pathogenesis of the disease.

Objectives: HLH has also been reported in patients with inherited primary immunodeficiencies, including those caused by inborn errors of type I IFN-mediated immune responses. Here, we describe a 2 years boy with two previously undescribed frameshift mutations in the interferon (IFN)α/β receptor 2 (*IFNAR2*) gene presenting with HLH following measles-mumps-rubella (MMR) vaccination. The relation between HLH and defective type I IFN-mediated responses is to date unclear.

Methods: Clinical Exome, using a custom panel including 6920 genes known as associated to genetic diseases, was sequenced on NovaSeq6000® platform. *In silico* analysis was performed on the basis of the patient's clinical phenotype. Peripheral blood mononuclear cells (PBMCs) were isolated from the patient and his family and stimulated with IFNα or IFNγ; phosphorylation of STAT1 and type I and type II IFN signatures were analyzed by flow cytometric and RT-PCR analyses. NK cell degranulation and IFNγ production were analysed by flow cytometry.

Results: Here we report the case of a 2 year old Caucasian boy presenting with high fever and lethargy five days after inoculation of live-attenuated MMR vaccine. Laboratory parameters were suggestive for secondary HLH, with progressive decrease in cell blood count, hyperferritinemia, elevation of liver enzymes and lactate

dehydrogenase and hypofibrinogenemia. We identified two novel frameshift mutations c.234delT and c.555_559delAAAAG, in a compound heterozygous status, in *IFNAR2* gene (OMIM# 602376), resulting respectively in p.Leu79Ter and p.Ile185MetfsTer12 variants. Both mutations were predicted to be damaging by *in silico* tools, since they introduce premature stop codons leading to the putative complete lack of the protein. Functional analyses confirmed the absence of response to type I IFN in the patient's cells, as revealed by lack of phosphorylation of STAT1 and lack of induction of interferon-stimulated genes upon *ex vivo* stimulation with IFNα, and demonstrated that the response to IFNγ was not affected. In addition, consistent with data demonstrating that a direct action of type I IFN on NK cells is necessary for the innate immune defence against vaccinia viral infections, we showed that in patient's NK cells stimulated with IFNα the expected increase in degranulation and inhibition of IFNγ production were affected.
Conclusion: Our data support a role for NK cell function dysregulation and lack of inhibition of IFNγ production as contributors to the development of HLH in patients with impaired type I IFN signalling. Finally, from a clinical perspective, HLH episodes following administration of live-attenuated viral vaccine should be considered as suggestive of a defect in the type I IFN response.

Disclosure of Interest
None declared

O091

Traditional laboratory parameters and new biomarkers in Macrophage Activation Syndrome (MAS) and Secondary Hemophagocytic Lymphohistiocytosis (SHLH)

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Pediatric Rheumatology 2020, **18(Suppl 2):**O091

Introduction: MAS, and sHLH are hyperinflammatory conditions caused by a cytokine storm, in which IFNγ plays a pivotal role.
Objectives: To evaluate clinical characteristics and laboratory parameters of sHLH, MAS and systemic Juvenile Idiopathic Arthritis (sJIA) patients at disease onset. To compare laboratory parameters of hyperinflammation (platelet count, ferritin, AST, triglycerides, fibrinogen) with IFNγ related biomarkers in samples collected in three different time points: active disease (T0), 7-10 days from starting therapy (T1) and in clinical inactive disease (from 1 to 3 months from onset) (T2).
Methods: Routine laboratory parameters of disease activity and severity were collected from a cohort of 82 patients with sHLH (38), MAS in the context of sJIA (26) and sJIA (18) at T0, T1 and T2. Serum levels of the IFNγ related biomarkers (CXCL9, CXCL10, neopterin and IL-18) were measured at each time points by ELISA.
Results: A total of 306 samples were collected; laboratory characteristics at T0 are detailed in table 1. Fever was present in the majority of patients (95%), while splenomegaly was more frequent in MAS (65%) and sHLH (63%) compared to sJIA (17%).
Using the 2016 classification criteria for MAS, we found that platelet count is a specific parameter, no patient with sJIA had a value < $181x10^9$/liter; ferritin is sensitive, 94% of patients with MAS had ferritin >684 mg/ml.
CXCL9, CXCL10 and neopterin levels in T0 were significantly higher in MAS and in sHLH compared to sJIA, while IL-18 was significantly higher only in MAS group.
In MAS, CXCL9 and neopterin were significantly correlated to laboratory parameters of hyperinflammation as well as IL-18, that did not correlate only with ferritin. In sHLH, only neopterin was significantly correlated to platelet count and triglycerides.
The ROC curves performed for each biomarker showed a statistically significant AUCs ($p<0.05$) in MAS. Instead, in sHLH the AUCs were significant for CXCL9, CXCL10 and neopterin ($p<0.0001$), but not for IL-18 ($p= 0.9$). CXCL9, CXCL10, neopterin and IL-18 levels decreased progressively at T1 and normalized in T2. CXCL9 decreased faster compared to neopterin, with a similar trend to laboratory parameters.
Conclusion: Our results confirm that platelet counts and ferritin have high specificity and sensitivity, respectively, to diagnose MAS in the context of sJIA. Moreover, our results confirm that IFNγ related biomarkers are significantly high in patients with MAS and sHLH compared to sJIA and could be useful for diagnosis in addition to traditional laboratory parameters. As already known, IL-18 seems to be a specific biomarker for MAS. Moreover, these biomarkers seem to be also useful to monitor clinical evolution and treatment response.

Disclosure of Interest
None declared

Table 1 (abstract O091). Laboratory parameters and IFNg related biomarkers in T0. Data are reported as median (1^{st}-3^{rd} quartile)

N=number of samples (samples for IL-18)	sJIA N=22 (18)	MAS N=47 (35)	sHLH N= 45 (35)	MAS vs sJIA *p*	MAS vs sHLH *p*	sJIA vs sHLH *p*
Platelet (x10^9/liter)	455 (349-540)	237 (168-455)	95 (42-178)	**0.0010**	**< 0.0001**	**< 0.0001**
Ferritin (ng/ml)	458 (323-738)	3143 (1473-5573)	5215 (2220-17271)	**< 0.0001**	0.061	**< 0.0001**
AST (U/L)	28 (19-43)	64 (39-114)	136 (51-324)	**< 0.0001**	**0.003**	**< 0.0001**
Triglycerides (mg/dl)	84 (67-104)	166 (136-216)	222 (159-367)	**< 0.0001**	**0.037**	**< 0.0001**
Fibrinogen (mg/dl)	641 (492-696)	392 (251-583)	236 (137-317)	**0.0001**	**< 0.0001**	**< 0.0001**
CXCL9 (pg/ml)	300 (300-838)	1258 (300-6063)	4180 (1836-10038)	**0.015**	**0.011**	**0.0001**
CXCL10 (pg/ml)	150 (150-269)	452 (150-1161)	717 (198-3048)	**0.0017**	0.30	**0.0001**
Neopterin (ng/ml)	3.9 (2.7-4.9)	8.7 (4.8-14.4)	23.1 (8.6-35.0)	**0.0001**	**0.0013**	**< 0.0001**
IL-18 (pg/ml)	17924 (2171-36764)	150577 (60667-219466)	14429 (2635-103022)	**< 0.0001**	**< 0.0001**	0.75

O092

Macrophage activation syndrome in juvenile systemic lupus erythematosus: a single center study of nineteen patients

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Pediatric Rheumatology 2020, **18(Suppl 2):**O092

Introduction: Macrophage activation syndrome (MAS) is a severe complication of some pediatric rheumatic diseases (PRD), especially of systemic juvenile idiopathic arthritis (sJIA), which associated with high risks of the multiple organ failure and mortality. MAS can be observed in juvenile systemic lupus erythematosus (jSLE) with frequency about 0.9-4.6%, but compared to sJIA it is less studied and poorly recognized.
Objectives: To analyze the clinical and laboratory features of MAS as a complication of jSLE.
Methods: All patients (pts) with a history of MAS associated with jSLE from our whole database of 251 jSLE pts were included in retrospective study. Diagnosis of SLE was reviewed based on 2012

SLICC criteria. MAS was diagnosed according to preliminary diagnostic guidelines. SLEDAI 2K was used for disease activity assessment. Demographic data, clinical, hematological and immunological manifestations, SLEDAI-2K, and treatment were assessed.
Results: We studied 19 consecutive pts with jSLE who had the history of MAS, which was 7.6% of all pts with jSLE and 35.2% - with MAS cases (from total=54) observed in our center. 26.3% were boys, sex ratio F:M was 2.8:1, in compare to the group without episodes of MAS – 7.2:1. The median age at the onset was 11.8 y [8.6; 13.95], in the group without episodes of MAS – 13.7 y [11; 15.1]. The median disease duration at the time of jSLE verification was 5.5 months [3.5; 11.25]. Median disease activity by SLEDAI at the time of jSLE verification was 20.5 scores [15;25.5], in the group without episodes of MAS - 12 scores [8; 18]. In the group of pts with a history of MAS, statistically more often were observed: serositis (p=0.0028), mucosal ulcers (p<0.0001), neuropsychiatric disorders (p=0.0024), positive Coombs test (p=0.026). There was also a tendency towards a higher incidence of hypocomplementemia (52.5% and 33.2%, respectively, not statistically significant). A total of 20 episodes of MAS were recorded: 10 episodes of MAS developed at onset of jSLE, 8 – associated with flare of jSLE because of deviation of the treatment`s schedule. In 2 pts MAS developed just after infusion of rituximab (RTX). 1 patient had two episodes of MAS: at onset, on 6th years of disease (the 8th day after RTX - 1st infusion of 5th course,). First features of MAS were fever, sleepiness, lower platelet counts, increased transaminase level. Typical for MAS in sJIA bright rash with itching was not observed in jSLE. Lesions of the skin and mucous were mainly represented by point hemorrhages at an early stage. For the treatment of MAS all pts were received high dose of glucocorticoids (per os+iv), 5 pts (26.3%) - cyclophosphamide iv, 1 patient (5.2%) – cyclosporine per os, 6 pts (31.6%) - intravenous immunoglobulin, 2 pts (10.5%) - RTX. 5 pts (26.3%) died due to uncontrollable MAS (2 – at onset of jSLE).
Conclusion: In our study, it was found that pts with serositis, mucosal ulcers, neuropsychiatric disorders, and positive Coombs test are at higher risk to developing MAS. MAS may be more likely at the onset of jSLE, especially in pts an earlier age. MAS in jSLE should be suspected in pts with fever, CNS disorders, thrombocytopenia, and liver disorders. We observed a correlation between high jSLE activity at the onset of the disease, violation of the treatment protocol, and risk of MAS.

Disclosure of Interest
None declared

O093

Efficacy and safety of jak inhibitors in juvenile dermatomyositis: a retrospective monocentric study

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Pediatric Rheumatology 2020, **18(Suppl 2):**O093

Introduction: Juvenile dermatomyositis (JDM) is a rare juvenile idiopathic inflammatory myopathy. Janus kinases inhibitors (JAKi) have recently shown to improve skin, articular and lung involvement in adult patients with dermatomyositis but little is known for JDM, with only four patients reported to date.
Objectives: To assess the efficacy and safety of Janus kinases inhibitors (JAKi) in juvenile dermatomyositis (JDM).
Methods: Monocentric retrospective study of children with JDM treated with JAKi for at least 4 months. Response to JAKi was assessed by PRINTO 20 levels of improvement and the skin Disease Activity Score (DAS). Clinically inactive disease was defined according to PRINTO criteria and the skin Disease Activity Score. Serum interferon (IFN)-α concentration was measured by SIMOA digital ELISA assay (Quanterix Homebrew).
Results: Seven patients (6 female) received ruxolitinib (n=5) or baricitinib (n=2). Myositis specific antibodies (MSA) were present in 6/7 patients, including anti-MDA5 (n=2), anti-NXP2 (n=3) et anti-TIF1-g (N=1) antibodies. All received corticosteroids in combination with JAKi. The main indications for JAKi were refractory JDM (n=6/7) (time elapsed from diagnosis: 4-22 months) or new onset JDM (n=1). Three months after JAKi introduction, five JDM patients achieved response without relapse, all had withdrawn immunosuppressive drugs other than corticosteroids and JAKi, with median daily corticosteroids dose decreased from 1.3 to 0.4 mg/Kg. At the last follow-up (median follow-up time, 11 months, range, 4-30), 6/7 achieved a JDM PRINTO 20 and skin DAS improvement , and 4/7 had a clinically inactive disease (CID) (median time to CID since JAKi initiation 3 months, range 1,7-5,3). The only patient without MSA did not respond. Serum IFN-α concentrations were elevated in all patients at JAKi introduction (median 333 fg/ml, range 31-31328) and normalized (<10 fg/ml) in all 4 patients in with CID (range, 0,3-10 months). A muscle biopsy repeated 22 months after the initiation of JAKi in one patient showed a complete regression of severe muscle vasculopathy. Herpes zoster occurred in 3 patients. Skin abscess developed in 3 patients with ulcerations, complicated by psoas abscess in two of them.
Conclusion: PRINTO 20 levels of improvement and CID occurred in 6/7 and 4/7 patients with refractory or new-onset JDM respectively. The frequency of herpes zoster was high. Prospective studies are required to identify the subset of patients who will require JAKi as a first line treatment.

Disclosure of Interest
None declared

O094

Altered metabolism in Juvenile Dermatomyositis (JDM) monocytes: a new therapeutic focus in juvenile dermatomyositis

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Pediatric Rheumatology 2020, **18(Suppl 2):**O094

Introduction: JDM is a rare childhood autoimmune myositis that presents with proximal muscle weakness and associated skin changes. There is an unmet need to develop targeted treatments for JDM.
Objectives: This study aimed to identify dysregulated biological processes by RNA-sequencing in JDM and develop functional assays to confirm these pathways.

Methods: Peripheral blood samples were obtained from JDM patients and age/sex-matched child healthy controls (CHC). $CD4^+$, $CD8^+$, $CD14^+$ and $CD19^+$ cells were sorted by flow-cytometry from PBMC, and RNA was extracted and RNA-sequenced. Total PBMC were taken from JDM and CHC, sub-sets of the CD14+ cell population were analysed by flow cytometry. To measure cytokine expression; CD14+ monocytes were isolated by immunomagnetic positive selection from total PBMC populations from JDM and CHC samples. The monocytes were cultured overnight with and without LPS. Cytokine expression in the culture supernatant was measured by cytometric bead array (CBA). To investigate metabolic function, CD14+ monocytes were isolated by immunomagnetic positive selection from total PBMC populations from JDM and CHC samples. The monocytes were cultured in carbon-13 labeled glucose RPMI-media. Medium was sampled at hourly time points for 6hrs and then at 24hrs over a time course. The metabolism of the ^{13}C glucose into CO_2, lactate and ribulose-5-phosphate was measured by gas chromatography-mass spectrometry (GCMS).
Results: RNA-seq confirmed a strong IFN1 signature, and that genes involved in mitochondrial function were abnormally expressed in pre- and on-treatment CD14+ cells compared to CHC, indicating mitochondrial dysfunction not corrected by current treatment. A proportion of the JDM samples had a higher percentage of $CD14^{hi}CD16^{hi}$ intermediate monocytes (JDM median – 12.3 (25% percentile = 7.11, 75% percentile = 25.6); CHC median – 10.95 (25% percentile = 9.10, 75% percentile = 14.25), detected by flow cytometry. Linear regression showed a trend towards increased disease activity, reflected by a lower MMT8 score, with a higher percentage of intermediate monocytes, therefore, in samples from JDM patients naïve of treatment ($R = -0.57$, $p = 0.085$). Cytometric bead array (CBA) analysis showed that both pro-inflammatory and anti-inflammatory cytokines were down-regulated in monocytes from JDM compared to CHC (IL-6 ($p=0.0152$); IL-1β ($p=0.0152$); IL-10 ($p=0.0649$). Functionally, ^{13}C lactate concentration was significantly lower after monocytes had been cultured for 24hrs in ^{13}C glucose medium from JDM samples compared to CHC ($p=0.0063$). Ongoing work is being done to assess the expression of glucose transporters and uptake.
Conclusion: This study establishes that in JDM, monocyte metabolism and homeostasis is dysfunctional, identifying an exciting novel pathogenic mechanism. In the future a specific area to investigate is the mechanistic relationship between IFN1 driven inflammation and altered mitochondrial metabolism in monocytes, this has the potential to identify novel therapeutic targets.

Disclosure of Interest
None declared

O095

Biomarkers galectin-9 and CXCL10 are of additional value in the clinical decision-making in juvenile dermatomyositis

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Introduction: In patients with juvenile dermatomyositis (JDM) objective evaluation of disease activity is challenging but crucial for prevention of both over- and undertreatment. We recently validated galectin-9 and CXCL10 in a multi-center cohort study as sensitive and reliable biomarkers for disease activity in JDM, outperforming creatinine kinase (CK). Implementation of these biomarkers into clinical practice, as tools to monitor disease activity and guide treatment, might enable personalized treatment strategies for patients with JDM.
Objectives: We investigated the additional value of galectin-9 and CXCL10 in the clinical decision-making in JDM patients as assessed by pediatric rheumatologists.
Methods: Galectin-9 and CXCL10 serum levels as measured by multiplex immunoassay were implemented as routine tests in the diagnostic laboratory of a tertiary hospital in June 2017 and June 2018, respectively. Test results generally became available 1-2 weeks after sampling. Pediatric rheumatologists reported for all measurements performed in JDM patients between June 2017 and March 2020 whether, and if so, how the biomarker levels would have affected their clinical-decision making, had the results been available at time of consultation. In addition, they scored the additional value of the biomarker levels semi-quantitatively (*decisive, supportive, helpful, no added value (NAD), distracting* or *"other"*).
Results: Biomarker measurements from 184 consultations in a total of 39 JDM patients were included (175 galectin-9, 152 CXCL10). Median number of consultations per patient was 4 (range 1-17). In 154 consultations (84%) the galectin-9 and/or CXCL10 results were considered to be of additional value (8 *decisive*, 31 *helpful*, 115 *supportive*). Results were considered to be of *NAD*, *distracting* or "*other*" in 19, 7 and 4 consultations, respectively. Results were most often considered *decisive* or *helpful* when increased biomarker levels confirmed clinically active disease while CK remained low, when increased or rising levels indicated bad treatment response, or when low levels confirmed clinically inactive disease in cases with aspecific symptoms or increased CK. Results were most often considered *supportive* when low levels confirmed clinically inactive disease or when decreasing levels indicated good treatment response. Results were most often reported to be of *NAD* in patients in long-term drug-free clinical remission. Transient increases in biomarker levels during clinically inactive disease were considered *distracting*. Also, low levels in cases with evident clinical disease activity were scored as *distracting*. Interestingly, the latter was only reported in patients with skin but no muscle disease activity, indicating that the biomarkers do not reflect skin disease well. In 13% of consultations the galectin-9 and/or CXCL10 results would have led to changes in clinical decision making, mostly with regard to MRI requests and medication changes.
Conclusion: Galectin-9 and CXCL10 results were of additional value in the clinical decision-making in patients with JDM, as reported by pediatric rheumatologists. The biomarkers were particularly useful in monitoring treatment response and when CK was deemed unreliable. Also, their potential to guide personal treatment strategies and to reduce the use of expensive imaging modalities was shown. We are currently conducting a large prospective cohort study to further validate clinical implementation of these biomarkers, including their prognostic value and tissue specificity, and to develop recommendations for biomarker-guided treatment in JDM.

Disclosure of Interest
None declared

O096

Siglec-1 expression reflects the interferon signature in juvenile dermatomyositis and defines subclasses of patients with distinct inflammatory and clinical profiles

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Pediatric Rheumatology 2020, **18(Suppl 2):**O096

Introduction: Sialic acid-binding Ig-like lectin 1 (Siglec-1) is a strongly Interferon (IFN)-regulated marker expressed on CD14 positive monocytes in the blood. Since juvenile dermatomyositis (JDM) is a (partly) IFN-driven disease, Siglec-1 might be used as a surrogate marker in clinical practice.
Objectives: 1) To evaluate the relation between Siglec-1 expression, the IFN signature, inflammatory biomarkers and disease activity in JDM; 2) To demonstrate whether subgroups of JDM patients with different Siglec-1 expression and distinct inflammatory profiles at diagnosis can predict treatment response.
Methods: Forty-six JDM patients, 7 Duchenne muscular dystrophy (DMD) patients, and 15 healthy controls (6 children and 9 adults) were enrolled. Plasma samples (46 treatment-naïve JDM, 26 follow-up JDM during treatment ,and 7 DMD) were used to measure inflammatory biomarkers by Olink assay. PCR was used on PBMC to determine the expression levels of 5 type I IFN signature genes (MX-1, IFI44, IFI44L, Ly6E, and IFIT3) and Siglec-1 expression on CD14+ cells was assessed by flow cytometry. The IFN score was defined as the sum of relative expressions of the signature genes. JDM samples were classified into 3 groups based on clinical status; 1) onset (active disease before starting the treatment), 2) active on medication (active disease with medication), 3) remission on/off medication (clinically inactive with or without medication). The childhood myositis scale (CMAS; 0-52; 0-49 for age 4-5) was used to assess muscle disease activity and the physician's global assessment (PGA; 0-10) was used to determine overall disease activity, including skin.
Results: The Median fluorescent intensity (MFI) of Siglec-1 and the frequency of CD14+ Siglec-1+ cells were significantly higher in the onset group of JDM patients compared with DMD and healthy controls, and significantly decreased over time in longitudinal follow-up. The IFN score showed a similar pattern. Both Siglec-1 and the IFN score were significantly correlated with CMAS (r_s=-0.67, p<0.0001 and r_s=-0.60, p<0.0001) and PGA (r_s=0.71, p<0.0001 and r_s=0.75, p< 0.0001). JDM patients with high levels of Siglec-1 MFI at diagnosis had more severe muscle involvement and required more intense treatment within 3 months after diagnosis. Unsupervised clustering of inflammatory biomarkers at the onset of JDM patients revealed two distinct clusters: the larger cluster with high levels of CXCL-10, CX3CL1, MCP-1, MCP-2, MCP-3, and PD-L1 had significantly lower CMAS and higher PGA than the smaller cluster. In a Kaplan-Meier analysis, the larger cluster needed a longer time to achieve clinically inactive disease than the smaller cluster with statistical significance. Importantly, JDM patients in the larger cluster had a significantly higher Siglec-1 expression on CD14+ cells when compared to the other cluster, whereas no significant difference in IFN score between these 2 clusters was found.
Conclusion: Siglec-1 could be used as a surrogate biomarker reflecting IFN activity and monitoring disease activity in JDM. Siglec-1 expression at the onset of JDM patients might be a useful tool to define subgroups of JDM patients and identify patients at risk who may benefit from more aggressive treatment.

Disclosure of Interest
None declared

O097

Validation of the Eular/ACR 2017 idiopathic inflammatory myopathy classification criteria in JDM patients

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Introduction: Juvenile dermatomyositis (JDM) is the most common inflammatory myopathy of childhood. In 2017, a new set of criteria has been proposed by EULAR/ACR.
Objectives: We aimed to validate EULAR/ACR 2017 classification criteria[1]in JDM patients.
Methods: This study was held at Hacettepe University Department of Pediatrics, Divisions of Rheumatology, Neurology and Pediatric Pathology Unit. Control patients included inborn errors of metabolism presenting with myopathy and/or rhabdomyolysis (glutaric aciduria type 2 (n=8), carnitine-palmitoyl transferase II deficiency (n=2), LCHAD (n=1)), idiopathic rhabdomyolysis (n=3), dystrophinopathies (Duchenne/Becker muscular dystrophy (n=10)), neuromyotonia (n=1) and systemic rheumatological disorders (SLE (n=5), MCTD (n=4), interferonopathies (n=4), PAN (n=2)).
Results: 58 JDM patients (61.3% female) and 40 controls (32.5% female) were included in this study. Mean age at disease onset (JDM 8.1±4.3 vs control 8.7±5.4) and diagnosis (JDM 8.7±4.4 vs control 9.9±5.3) were comparable.
When the probability cut-off was set at 55% as recommended, the sensitivity/specificity of the new criteria to diagnose JDM were 96.5%/85% in the total cohort, 95.8%/84.6% without muscle biopsy data and 97%/85.7% with biopsy data (Table 1.) With the ROC curve analysis, the optimal probability cut-off for sensitivity and specificity was found >62% in our cohort; providing a sensitivity and specificity of 96.6% (95% CI: 88.1% to 99.6) and 90% (95% CI: 76.3% to 97.2%) respectively.
The new EULAR/ACR criteria[1] was the most sensitive however, the least specific compared to the Tanimoto[2] (sensitivity/specificity 64%/97.5%) and Bohan-Peter criteria[3,4] (sensitivity/ specificity 74.1%/92.5%). The specific skin rash as a mandatory criterion increased the specificity of Tanimoto and Bohan-Peter criteria which was not mandatory in the new EULAR/ACR criteria. Six control patients were misclassified as JDM with the new criteria. Muscle weakness parameters lowered the specificity and led to misclassification for three patients with inborn errors of metabolism; two patients with interferonopathy and one with mixed connective tissue disorder who presented with skin features. Although 75.5%(34/45) of our JDM patients who were checked for antibodies had at least one myositis-specific antibody, none of them had anti-Jo1 which causes a major drawback for the new criteria. Four out of 34 muscle biopsies did not met the new EULAR/ACR criteria, however, they had other features which were included in the previously validated muscle biopsy score tool[5,6] such as, overexpression of MHC-I, capillary drop-out and neonatal myosin positivity.
Conclusion: The new EULAR/ACR criteria performed favourably well in our JDM cohort especially with the probability cut-off of >62%. The yield of the criteria in childhood presentations may be improved by including the recently identified myositis-specific antibodies, validated muscle biopsy score tool parameters, and muscle magnetic resonance imaging data.

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Disclosure of Interest
None declared

Table 1 (abstract O097). Sensitivity and Specificity of Different Criteria for Classification of JDM

	Sensitivity (n=58)	Specificity (n=40)	Positive predictive value	Negative predictive value
EULAR/ACR criteria	96.5%	85%	90.1%	94.4%
- **Without biopsy**	- 95.8%	- 84.6%	- 85.1%	- 95.6%
- **With biopsy**	- 97%	- 85.7%	- 94.3%	- 92.3%
Bohan-Peter criteria	74.1%	92.5%	93.4%	71.1%
Tanimoto criteria	64%	97.5%	97.3%	65%

O098

Comparision of IVIG resistance predictive models in Kawasaki Disease

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Introduction: Intravenous immunoglobulin (IVIG) resistance may be observed in 10% to 20% of patients diagnosed with Kawasaki disease (KD). It is fundamental to define this group in early stages of the disease for improving prognosis and determining the need for additional treatment.
Objectives: We aimed to compare nine different prediction models (Kobayashi, Egami, Harada, Formosa, Sano, Piram et al, Wu et al, Yang et al, and Tan et al) and evaluate risk factors for IVIG resistance in Turkish children.
Methods: Patients who diagnosed with Kawasaki disease at the Hacettepe University between June 2007 and September 2019 were evaluated retrospectively. Complete or incomplete KD patients were included in the study.
Results: A total of 129 patients, 79 boys (61.2%), with a median age 36 (IQR 19.5-57.0) months were enrolled. Sixteen patients (12.4%) had IVIG resistance. The specificity of all scoring systems predicting IVIG resistance was higher than their sensitivity. Tan, Sano, and Egami predictive models had the highest specificity (97.3%, 89.4%, 86.7%, respectively). Almost all scoring systems distinguished the group of patients with low-risk for IVIG resistance but could not differentiate IVIG-resistant patients. High serum levels of total bilirubin, ALT, AST, GGT, and platelet count less than $300´10^9$/L were associated with IVIG resistance in univariate analysis. Five risk factors were re-evaluated with multivariate analysis; platelet count less than $300´10^9$/L and GGT serum levels were independent risk factors for IVIG resistance (OR: 3.896; 95%CI: 1.054-14.404; p=0.042 and OR: 1.008; 95%CI: 1.001-1.015; p=0.050).
Coronary artery involvement was detected in 44 of 129 patients (34.1%) which was more frequently observed in patients under the age of 1 year and in boys (p=0.01, p=0.02, respectively). The multivariate analysis identified male gender and young age (<1 year of age) as independent risk factors for coronary involvement (OR: 0.399; 95%CI: 0.175-0.908; p=0.029 and OR: 3.802; 95%CI: 1.248-11.582; p=0.019, respectively).
Conclusion: The adaptation of the current scoring systems is limited due to lack of sensitivity in our study population. Increased serum GGT levels and low platelet count were risk factors for predicting IVIG resistance.

Disclosure of Interest
None declared

O099

Kawanet-score for predicting resistance to first immunoglobulins in Kawasaki disease: confirmation of its good sensitivity and proposal to improve specificity.

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Pediatric Rheumatology 2020, **18(Suppl 2):**O099

Introduction: Kawasaki disease (KD) is the leading cause of acquired heart disease in childhood in developed countries. Early identification of these high-risk patients is critical to initiate aggressive therapies, but available scoring systems lack sensitivity in non-Asian populations. In their recent publication in Science Reports, Piram et al. proposed a new scoring system to predict the need for secondary treatment in non-Asian populations, the Kawanet score(-sensitivity 77%, specificity 60%).
Objectives: To validate the Kawanet score in an independent cohort.
Methods: We retrospectively analyzed clinical and epidemiological data from a registry including all successive KD patients followed in our French tertiary center from 2006 to 2019. After exclusion of patients who had participatedin the Kawanetstudy (n=20), 186 children were included in our study. Cardiac abnormalities at the first echocardiography were defined as presence of at least one abnormal echocardiography finding including coronary artery dilatation, aneurysm, zMax ≥2.0, perivascular coronary artery brightness, pericardial effusion, valvular dysfunction.
Results: In our cohort the Kawanet score had a sensitivity of 81,4% but a specificity of only 32,7%. Given the low specificity, we tried to implement other parameters to improve the Kawanet score performances. Abnormal findings at the initial echocardiography were observed in 61/186 (32.8%) patients. In multivariate regression analysis adjusted on the Kawanet score, initial cardiac abnormalities at the initial echocardiogram was significantly associated with a need of secondary treatment (OR 3.2, 95% CI [1.4; 7.6], p=0.0060). We built a "modified Kawanet score", including the Kawanet score variables plus cardiac abnormalities (one point per variable). The modified Kawanet score, with a cutoff at >=3, was associated with need for secondary treatment (OR of 3.4, 95% CI [1.4; 8.3], p= 0.0069). Combining the Kawanet score with information on abnormalities observed at the initial echocardiogram allowed to obtain a sensitivity of 71.4% and a specificity of 59.5%.
Conclusion: In conclusion, our observations confirm the good sensitivity of the Kawanet score to predict need for secondary treatments in European populations but point out a poor specificity. The specificity of this score can be substantially improved by adding initial echocardiography findings as an additional parameter.

Disclosure of Interest
None declared

O100

Different histological classifications for Henoch-Schönlein purpura nephritis - which one is the best predictor of disease outcome? pilot study of the PRES vasculitis working party

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Pediatric Rheumatology 2020, **18(Suppl 2):**O100

Introduction: Henoch-Schönlein purpura nephritis (HSPN) is the main and almost the only cause of morbidity and mortality among children suffering from this most common vasculitis in childhood. Several histological classifications are used in the analysis of renal biopsy findings in HSPN, but it remains unknown which one has the strongest association with the severity and outcome.
Objectives: The aim was to compare the four most commonly used histologic classifications for HSPN to determinate which one is the best predictor of disease outcome and to establish which variables

of each histological classification have the strongest association with unfavorable outcomes.
Methods: The cross-sectional study included 69 patients with HSPN (diagnosed by EULAR/PRES/PRINTO criteria) and available renal biopsy specimens for analysis using the four histological classifications for HSPN (the International Study of Kidney Disease in Children (ISKD C) classification, the Oxford classification, the Haas histologic classification of IgA nephropathy and the modified semi-quantitative classification (SQC), developed by Koskela *et al.*). The clinical outcome was defined through four categories, graded according to the modified classification of Counahan (physical examination, hematuria, proteinuria, urine albumin-to-creatinine ratio, hypertension and eGFR). The linear relationships between outcome and histological classifications were analysed using ordinal regressions using the first-order of polynomial orthogonal contrasts.
Results: The SQC classification proved to be the best, reducing the deviation (of the model-predicted outcome value from the observed value) by 9.5% (X^2_1=13,89, p < 0,001), followed by the Oxford classification with a deviation reduction of 8.0% (X^2_1=11,76, p = 0,001), then the ISKDC classification with a decrease in deviation of 3.3% (X^2_1=4,89, p = 0,027), and the worst was the Haas classification with a decrease in deviation of 2.1% (X^2_1=3,06, p = 0,080). Analysis of individual variables of Oxford and SQC classifications showed that with increasing values in the variables of interstitial fibrosis (t_{66} = 3,23, p = 0,002), tubular atrophy (t_{66} = 2,94, p = 0,005) and tubular dilatation (t_{66} = 2,40, p = 0,019) in the SQC classification, and endocapillary hypercellularity (t_{66} = 3,14, p = 0,003) and crescents (t_{66} = 2,07, p = 0,043) in the Oxford classification the outcome worsens.
Conclusion: The pilot study showed that the SQC classification, developed by Koskela *et al.*, has the strongest association with the severity and outcome of HSPN, followed by the Oxford classification, while other classifications are less related to the outcome of the disease. Although crescents on renal biopsy were considered the most important outcome indicators, this pilot study suggests that tubulointerstitial changes could be even more important as predictors of poor outcome. Histological changes in the interstitium and renal tubules of HSPN patients should be further explored in order to have an even better predictive value in terms of disease outcomes and to be incorporated into existing or new classifications, on the basis of which guidelines for the treatment of patients would be developed.
SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

Disclosure of Interest
None declared

O101

A pilot proteomic analysis of plasma biomarkers in IgA vasculitis

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Introduction: IgA vasculitis/ Henoch Schönlein Purpura (IgAV/HSP) is the most common vasculitis of childhood, characterized by the IgA1 immune deposits in the small vessels. Although it is very common, the understanding of its molecular pathogenesis is still very limited.
Objectives: We aimed to analyse plasma proteomes of IgAV/HSP patients using nano liquid chromatography – tandem mass spectrometry (nLC-MS/MS) to investigate the disease pathogenesis.
Methods: IgAV/HSP was diagnosed according to the Ankara criteria in 2008 (1). Five active IgAV/HSP patients and two age and gender-matched health controls were enrolled in this pilot study. Serum samples from subjects were collected on the same day of IgAV/HSP diagnosis and before steroid or other immunosuppressive treatment initiated. Sample preparation was carried out using PreOmics İST Kit. We investigated the alteration of serum proteome using the nano LC-MS/MS approach. Bruker raw files were analyzed using the proteomics software Max Quant (1.6.7.0). The human reference proteome set from UniProt was used to identify proteins. Proteomic data were analyzed with Perseus 1.6.7.0.
Results: The data file includes peptide and protein identification, accession numbers, protein and gene names, sequence coverage and label free quantification (LFQ) values of each sample. 345 proteins were reported per sample. Identifications from the reverse decoy database, identified by site only and known contaminants were excluded. Data were log transformed. Two sample T-test was performed between groups. We identified 23 significantly different expressed proteins. Mainly the differentially expressed proteins were in the innate immune system, Ig and complement pathway. The levels of Complement C3, Apolipoprotein E, Glyceraldehyde-3-phosphate dehydrogenase, Filamin-A, Alpha-1B-glycoprotein, Tubulin beta-1 chain, Lipopolysaccharide-binding protein, Ig mu chain C region were significantly higher in IgAV patients.
Conclusion: This pilot proteomic study may provide us a perspective in the pathogenesis of IgAV (HSP).
Grant Support: This work was supported by Hacettepe University Scientific Research Coordination Unit

Disclosure of Interest
None declared

P001

A fever lasting for four generations

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Introduction: Autoinflammatory diseases are clinical conditions characterized by recurrent episodes of fever, associated with symptoms such as skin rash, abdominal pain, chest pain, lymphadenopathy, arthritis and elevation of inflammatory markers. Cryopyrin-associated periodic syndromes (CAPS) are autoinflammatory disorders caused by mutations of the gene NLRP3 (NOD-like receptor 3), with autosomal dominant transmission. It encodes a protein called cryopyrin, connected to the activation of proinflammatory interleukin-1 (IL-1). Different point mutations in this gene promote an inappropriate, excessive IL-1 production, responsible for the clinical features of different CAPS. These are: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome and chronic infantile neurological cutaneous articular syndrome (CINCA) also called neonatal-onset multisystem inflammatory disease (NOMID). FCAS is the mildest form. Symptoms usually appear during the first year of life and include urticarial rash, arthralgias, conjunctival injection and fever spikes of short duration (usually 24 hours), induced by the exposure to generalized cold.
Objectives: To present the peculiar characteristics of FCAS, through a case report that includes four generations of the same family. To stress the importance of familial history, that together with clinical features, can lead to the hypothesis formulation and to the request of a genetic assessment that will confirm the diagnosis.
Methods: We describe a case of FCAS in a 2-years-old child, who came for the first time to our rheumatology clinic because of a history of recurrent fever episodes, associated with urticarial rash and elevations in acute phase reactants, beginning at 6-7 months of life.
Both father and paternal grandmother were in follow up for hives rash and arthritis since childhood, diagnosed as seronegative polyarthritis. In addition, father presented conjunctivitis. The episodes of urticarial eruption and fever appeared to be induced by cold exposition. Paternal great-grandmother was reported to have the same clinical situation. The medical and familial history were suggestive for an autoinflammatory disease, therefore genetic analysis was performed and the family was referred to the Autoinflammatory Diseases Centre of the IRCCS Gaslini in Genova. Written informed consent to publication of the case report was obtained by parents.

Results: The genetic analysis found a point mutation on the gene NLRP3 (Ala439Val), thus confirming the diagnosis of FCAS. The same mutation was found on blood samples of father and paternal grandmother, while great-grandmother is still being analyzed. Treatment with Anakinra was promptly initiated in both child and relatives.
Conclusion: Cryopyrin-associated periodic syndromes are rare disorders with relatively aspecific manifestations. An infant presenting with recurrent episodes of fever and urticarial rash exacerbated by generalized cold exposure, should be investigated for FCAS. Early diagnosis and rapid initiation of IL-1 inhibition control the inflammation and prevent organ damage with rapid resolution of clinical symptoms. Anti-interleukin-1 treatment with anakinra, rilonacept or canakinumab induces in most cases complete remission and normalization of inflammatory markers.

Disclosure of Interest
None declared

P002

Attention and thinking functions in children with monogenic auto-inflammatory diseases

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Pediatric Rheumatology 2020, **18(Suppl 2):**P002

Introduction: Monogenic auto-inflammatory diseases (mAID) are a group of severe chronic multisystemic diseases with recurring episodes of fever and other manifestations that significantly affect the patients' life quality. Moreover, the hyper expression of pro-inflammatory cytokines (IL1β, etc.) observed in these patients may have a negative effect on the central nervous system.
Objectives: to study the state of the functions of attention and thinkingin children suffering from monogenic auto-inflammatory diseases.
Methods: there were examined 22 children at the age of 7 to 17 years old diagnosed with CAPS-9, TRAPS-8, FMF-5. Among them there were 12 boys and 10 girls. The diagnosis in all the patients was confirmed through detection of pathogenic mutations in the NLRP3, TNFRSF1A and MEFV genes. The following methods were used: a clinical conversation; attention diagnostics (Schulte tables); thinking diagnostics (establishing a sequence of events, "four is a crwod", simple analogies, interpretation of proverbs).
Results: Tabl. №1
The functions of attention of children suffering from monogenic auto-inflammatory diseases.
In the majority of patients with TRAPS and CAPS, indicators of the operational side of thinking were normal (87.5% and 55.5%, respectively).The majority of the examined patients with FMF (80%) had a non-severe violation of establishing causal relationships. Inertia of thinking was more often registered in patients with TRAPS (37.5%). Violations in the motivational sphere of thinking were not detected in any group.
Conclusion: Impaired attention functions were observed in the majority of patients with TRAPS and were expressed in them to the maximum extent. Most patients with CAPS and FMF had impaired attention distribution, and all other attention functions were not impaired in most of these patients. Non-rough thinking disorders were registered in the majority of patients with FMF. In the majority of patients with CAPS and TRAPS, indicators of thinking function were within the normal range . In patients with TRAPS, more often than in patients with CAPS and FMF, inertia of thinking was observed.

Disclosure of Interest
None declared

Table 1 (abstract P002). The functions of attention of children suffering from monogenic auto-inflammatory diseases

Attention processes	TRAPS N=8		CAPS N=9		FMF N=5	
	Normal	Disturbance	Normal	Disturbance	Normal	Disturbance
Concentration	3(37,5%)	5(62,5%)	4(44,4%)	5(55,5%)	3(60%)	2(40%)
Distribution of attention	0	8(100%)	2(22,2%)	7(77,8%)	2(40%)	3(60%)
Exhaustion	2(25%)	6(75%)	6(66,7)%	3(33,3%)	3(60%)	2(40%)
Efficiency	2(25%)	6(75%)	4(44,4%)	5(55,5%)	3(60%)	2(40%)
Degree of workability	3(37,5%)	5(62,5%)	4(44,4%)	5(55,5%)	3(60%)	2(40%)
Sustainability	3(37,5%)	62,5%	8(88,9%)	1(11,1%)	1(20%)	4(80%)

P003

Immunological evaluation of the patients with CAPS

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Pediatric Rheumatology 2020, **18(Suppl 2):**P003

Introduction: Cryopyrin-associated periodic syndrome is a group of rare, heterogeneous autoinflammatory disease characterized by interleukin 1β-mediated systemic inflammation and clinical symptoms involving skin, joints, central nervous system, and eyes. There are three clinical subtypes; familial cold autoinflammatory syndrome (FCAS), Muckle-Wells Syndrome (MWS) and, neonatal-onset multisystem inflammatory disease (NOMID)/ chronic infantile neurological cutaneous and articular syndrome (CINCA), which share several overlapping clinical features.
Objectives: In this study, we aimed to evaluate the status of the adaptive immune system in our patients with CAPS.
Methods: Nine patients who were diagnosed with CAPS were included in the study. The data were obtained retrospectively from the hospital records.
Results:

	Median	Minimum	Maximum
Absolute lymphocyte count (/mm^3)	2280	1190	3530
CD3 /mm^3), (%)	1740.33, (77.3)	952, (68.5)	2534.54, (84.4)
CD4 /mm^3, (%)	1120.22, (51.5)	685.45, (37.6)	1736.76, (63.2)
CD8 /mm^3, (%)	523.75, (23.7	215.4, (14)	893.34, (31.5)
CD19 /mm^3, (%)	289.56, (11.6)	138.04, (8.2)	528.8, (18.6)
CD3-CD16/56 /mm^3, (%)	154.65, (7.1)	57.12, (4)	582.45, (17.9)
Ig G (mg/dl)	1060	931	1870
Ig M (mg/dl)	131	84	223
Ig A (mg/dl)	296	110	393

Conclusion: CAPS is classified as a subgroup of innate immune deficiencies by the International Union of Immunological Societies in 2017. In this study, we disclosed that there was no adaptive immune system deficiency in CAPS patients.

Disclosure of Interest
None declared

P004

Pyrin associated autoinflammation with neutrophilic dermatosis: a rare cause of leucocytoclastic vasculitis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P004

Introduction: We describe a case of a six year old girl who presented with episodes of recurrent abdominal pain and petechial and purpuric rashes affecting the lower limbs. The clinical picture resembled Henoch Schonlein Purpura but following her third episode, we requested additional investigations including genetic analysis and found a homozygous mutation in an exon 2 of gene MEFV, which is associated with a recently reported disease of Pyrin associated autoinflammation with neutrophilic dermatosis (PAAND).
Objectives: To describe the clinical presentation of a child who was found to be homozygous for the MEFV variant c.623G>C.
Methods: A six year old girl presented with recurring stereotyped episodes of abdominal pain, joint pain and petechial and purpuric rashes to the lower limbs resembling Henoch-Schönlein purpura. The typical episode lasted for six-eight weeks and resolved spontaneously. She remained systemically well on each occasion with normal urinalysis and vital signs. On the third presentation she was noted to have a petechial rash to the extensor surfaces of her lower limbs and a swollen left ankle. The physical examination was otherwise unremarkable with no organomegaly or lymphadenopathy. She had no history of fever, weight loss or fatigue. She was of Pakistani ethnicity and her parents were consanguineous. There was no family history of note. She attended a mainstream school, there were no developmental concerns. Abdominal ultrasound was normal. Her blood tests showed a mild normocytic anaemia and a mild eosinophilia with maximum 0.82. The rest of the full blood count was unremarkable. She had normal renal and liver function. Her inflammatory markers were mildly elevated with maximum erythrocyte sedimentation rate (ESR) 87 mm/h, CRP 59 mg/L, serum amyloid 13.0 mg/L. Complement factors C3 and C4 were normal. Antinuclear antibody (ANA) and anti C1q antibodies were negative. Atypical p-ANCA antibodies were detected with negative specific ANCA PR3 and MPO antibodies. Skin biopsy showed small vessel leucocytoclastic vasculitis. She was kept under follow up and following her fifth presentation with similar picture, we requested genetic testing focusing on autoinflammatory diseases and she was found to be homozygous for the MEFV mutation c623G>C.
Results: MEFV is a gene associated with recessive Familial Mediterranean Fever (FMF). This specific mutation is known to be associated with a phenotype of Pyrin associated autoinflammatory disease. Another three patients of Pakistani consanguineous background carrying the same mutation have already been described. All patients share a remitting–relapsing course of disease, characterized by raised inflammatory markers, eosinophilia, oral ulceration, intestinal inflammation and lymphadenopathy [1]. Following her fourth flare of rash and joint pain, our patient commenced a short course of oral prednisolone with good response. She remains under regular follow up with a plan to trial colchicine in case of further flare
Conclusion: FMF is the most frequent autoinflammatory disease caused by mutations in MEFV gene. Pyrin associated autoinflammation with neutrophilic dermatosis is a recently described condition associated with mutations in exon 2 of the MEFV gene [2, 3].

Disclosure of Interest
None declared

P005

The diagnostic challenge of PAMI syndrome: a case report

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Pediatric Rheumatology 2020, **18(Suppl 2):**P005

Introduction: Mutations in PSTPIP1 gene, encoding for proline–serine–threonine phosphatase-interactive protein 1, are associated to an autosomal dominant autoinflammatory syndrome called PAPA (sterile pyogenic arthritis, pyoderma gangrenous and cystic acne) and to pyoderma gangrenous, acne and suppurative hydrosadenitis with or without pyogenic arthritis syndromes (PASH and PAPASH). Recently, two PSTPIP1 mutations (p.E250K and p.E257K) have been described in a disease characterized by pancytopenia, hepatosplenomegaly, acne and gangrenous pyoderma, known as PSTPIP1-associated myeloid-related protein inflammatory (PAMI) syndrome, a distinct autoinflammatory disorder with its own clinical and biochemicals features.
Objectives: To describe the clinical course of PAMI syndrome in a 15-year-old girl.
Methods: Case report.
Results: The patient, a 15-year-old girl, suffered from migrant and recurrent arthralgias, hepatosplenomegaly and elevation of inflammatory markers since the first year of life. She firstly came to our attention at the age of 20 months for upper and lower limb pain episodes, mostly nocturnal and associated with functional impotence. At past medical history, left shoulder arthralgia appeared 10 days after a Roseola Infantum infection was reported at the age of 14 months, in association with anemia, neutropenia and inflammatory markers and lactate dehydrogenase (LDH) increase.
At admission, clinical examination showed hepatosplenomegaly and enlarged neck and submandibular lymph nodes, but joint assessment was normal. At laboratory investigation, anemia and neutropenia were confirmed and LDH was persistently high. Immunological and autoimmune screening were normal, including the neutrophilic degranulation test. Bone marrow aspiration was negative too. A total-body X-ray was negative while abdomen ultrasound confirmed hepatosplenomegaly.
During the following years, the patient presented arthralgias in several districts, responsive to short courses of nonsteroidal anti-inflammatory therapy. Joint symptomatology progressively improved during the growth until complete remission after puberty. Since the age of 6 years, she had presented recurrent blepharitis and chalazion episodes, treated first with antibiotic therapy and then with surgery, and a mild form of psoriasis. A relapsing abscess of median cyst of the neck was treated with oral antibiotic therapy. Periodic blood exams showed neutropenia and raised LDH, c-reactive protein and erythrocyte sedimentation rate.
Suspecting an autoinflammatory syndrome, in 2008 and 2016 she underwent genetic investigations (Sanger technique) resulted normal. In August 2018, a new genetic study performed with Next Generation Sequencing highlighted the *de novo* genomic variant p.E250K (c.748G>A) in heterozygosity of the PSTPIP1 gene, described as a pathogenetic variant associated to PAMI syndrome. The diagnosis was confirmed after the evaluation of serum zinc levels resulted elevated (538 ug/dl).
Conclusion: PAMI syndrome is a rare auto-inflammatory disease, genetically determined, with early onset, incomplete penetrance and variable expression. Our patient presented a mild phenotype of PAMI syndrome, since some typical features of the disease, such as poor growth, skin inflammation, thrombocytopenia and arthritis, were absent. PAMI syndrome should be considered in the differential diagnosis of patients with neutropenia and undefined systemic inflammation, even if other clinical manifestations are absent; the dosage of serum zinc may be a useful tool in the differential diagnosis in these cases because high serum zinc values can lead the clinician towards an early diagnosis.

Disclosure of Interest
None declared

P006

The peculiarities of the course of familial mediterranean fever among patients of the crimean tatar nationality: preliminary results of a retrospective study.

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Pediatric Rheumatology 2020, **18(Suppl 2):**P006

Introduction: Familial Mediterranean fever (FMF) is the most common monogenic auto-inflammatory disease with peculiar ethnic predisposition. The disease occurs frequently among Mediterranean populations like Turks, Jews, Armenians, and Arabs. It was not until 2016, the Crimean Tatars, people of Turk origin, became first considered as the population with prominent incidence of FMF.
Objectives: the study examines the clinical and genetic features of FMF among children of Crimean Tatar nationality and studied the distribution of exon 10 MEFV alleles in healthy adults.
Methods: the retrospective study included data from case histories of 16 children aged 5 to 18 years. Diagnosis of FMF was based on Eurofever/PRINTO 2019 criteria. In each patient clinical characteristics including administered colchicine dose, tolerance, side effects, and biologics therapy were evaluated. All patients underwent direct Sanger sequencing of exon 10 of the MEFV gene. For population study we included 127 healthy unrelated adults without FMF and any periodic fever, whome exon 10 of the MEFV gene were analyzed.
Results: The mean age of FMF diagnosis was 9.5 (4.0; 14.2), the mean time from the first symptoms to the diagnosis was 5.5 (2.0; 9.3) years. The main clinical manifestations were fever (100%), arthritis (100%), peritonitis (50%), pleuritis (7%), and erysipeloid rash (57%). Most commonly involved joints were knee (100%) and hip (25%); in 13% of patients both joints were affected during the attack. Patients were at first diagnosed as having acute respiratory infection (n=14) or juvenile idiopathic arthritis (n=2). Genetic analysis revealed well-known pathogenic alleles of MEFV, p.M694V (88%), p.M680I (6%) and p.V726A (6%). The most common p.M694M mutation was found in heterozygous/homozygous state in 81% and 19%, respectively. Parents of 8 patients (50%) were consanguineous. Colchicine intolerance was observed in 13%, and colchicine resistance in 25% of the patients. 6 patients (38%) received biologic treatment: canakinumab - 4 (25%), and tocilizumab - 2 (13%). Colchicine treatment and biologics were effective in 100% of patients. In healthy adults from Crimean Tatar origin 13/127 (10.2%) had pathogenic exon 10 mutations: V726A (n=2, 1.6%), M694V (n=9, 7.1%), M680I (n=2, 1.6%)
Conclusion: MEFV mutations are frequent in Crimean Tatars probably due to founder effect. The main clinical features observed in the FMF patients were fever and arthritis. A high proportion of patients receives biologic therapy. Further investigations required to evaluate the characteristics of FMF in the Crimean Tatars population.

Trial registration identifying number: This work was supported by the Russian Foundation for Basic Research (grant № 18-515-57001).

Disclosure of Interest
None declared

P007

Multiplex long-range PCR for routine genotyping of up to nine autoinflammatory gene in a single analytical run by next generation sequencing

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Pediatric Rheumatology 2020, **18(Suppl 2):**P007

Introduction: During the last decade, remarkable progress with massive sequencing has been made in the identification of disease-associated genes for AIDs using the next generation sequencing technologies (NGS). International group of experts described the ideal genetic screening method which should give information about SNVs, InDels, Copy Number Variations (CNVs), GC rich regions.
Objectives: Our aim was to develop and validate molecular diagnostic method in conjunction with NGS platform as an inexpensive, extended and uniform coverage and fast screening tool which consist of nine genes known to be associated with various AIDs.
Methods: To validation of four and nine gene containing panels, long range multiplex models were setup on 9 healthy sample without any known variations for MEFV, MVK, TNFRSF1A, NLRP3, PSTPIP1, IL1RN, NOD2, NLRP12 and LPIN2 genes. Ten patients with AIDs who had already known causative genes were sequenced for analytical validation. As a last step, multiplex models validated on 46 patients with pre-diagnosis of AIDs. All sequencing steps were performed on Illumina NGS platform. Validity steps included the selection of related candidate genes, primer design, development of screening methods, validation and verification of the product. GDPE (Gentera) bioinformatics pipeline was followed.
Results: Although there was no non-synonymous variation in 9 healthy samples, 127 synonymous variant alleles and some intronic and UTR variants were detected. In 10 patients who underwent analytical validation, beside the 11 known non-synonymous variant alleles, 9 additional non-synonymous variant alleles and a total of 110 exonic variant alleles were found. In clinical validation phase, 46 patients sequenced with multiplex panels, genetic and clinical findings were combined for diagnosis.
Conclusion: In this study, we described the development and validation of NGS-based multiplex array enables the "long-amplicon" approach for targeted sequencing of nine AIDs genes. This screening tool is less expensive and more comprehensive compared to other methods and more informative than traditional sequencing. Our panels have a great advantage compared to WES or hybridization probe equivalents in terms of CNV analysis, high sensitivity and uniformity, GC-rich region sequencing, InDel detection and intron covering.

Disclosure of Interest
None declared

P008

Adherence to colchicine treatment and colchicine resistance in a multicentric FMF national cohort

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Pediatric Rheumatology 2020, **18(Suppl 2):**P008

Introduction: Colchicine is the standard treatment for Familiar Mediterranean Fever (FMF), however about 5% of patients (pts) experience colchicine resistance. There is no standard definition of colchicine resistance. Recently a panel of experts elaborated a new definition based on a Delphi consensus approach.
Objectives: We aim to describe main features of the disease and clinical outcome of a cohort of FMF pts with particular interest on the colchicine resistance and tolerability according to the definitions proposed by the recent consensus.
Methods: Since November 2009, 425 Italian pediatric and adult FMF pts from 13 centers were enrolled in a national longitudinal cohort study, using the EUROFEVER registry. Demographic, genetic and clinical data, including response to treatment, were analyzed. Supplementary information on quality of life and treatment adherence was also collected by a specific questionnaire.
Results: Complete information were available in 341 pts (M/F 189/152, 211 children and 120 adults). The median age at disease onset was 5.0 years (range 0.1-59); the median diagnostic delay was 8.7 years (0-61). The median age at enrollment was 12.1 years (0.4-82). The MEFV genotype was the following: 103 (30.2%) pts carried biallelic pathogenic (P) variants; 59 (17.3%) one P variants and one variants of unknown significance (VOUS)/likely benign (LB) variant; 27 (7.9%) had biallelic VOUS/LB variants; 97 (28.45%) were heterozygous

for P variants; 30 (8.8%) were heterozygous for VOUS/LB, 25 (7.33%) were genetically negative.
Colchicine treatment was used in 280 patients; during treatment, biologic treatment (anti-IL1) in 22 patients. 61 patients received NSAI D or steroid on demand.
We analyzed the behavior of the pts treated with colchicine according to the statements on resistance/intolerance defined by Ozen (1) (Table 1).
Conclusion: Almost 46% of FMF pts display some disease activity despite colchicine treatment. The treatment is generally under-dosed, especially in children. The adherence and the compliance to the treatment is generally good.

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Aknowlegments This research was financially supported by Novartis AG

Disclosure of Interest
R. Gallizzi: None declared, M. Bustaffa: None declared, F. Mazza: None declared, D. Sutera: None declared, G. Fabio: None declared, L. Obici: None declared, M. Alessio: None declared, D. Rigante: None declared, L. Cantarini: None declared, A. Insalaco: None declared, M. Cattalini: None declared, M. C. Maggio: None declared, G. Simonini: None declared, A. Olivieri: None declared, S. Pastori: None declared, M. Lancieri: None declared, F. Calzantini: None declared, N. Ruperto: None declared, M. Gattorno Consultant for: Novartis, Sobi, Speaker Bureau of: Novartis, Sobi

Table 1 (abstract P008). See text for description

Adherence	62% displayed a total adherence (> 90% of prescription); 10.8% a good adherence (50-89% of prescriptions); 1.9% poor adherence (< 50% of prescriptions); 0.9% no adherence
Dose adjustment criteria/ Recommended maximum colchicine dose	Mean colchicine dose:
	Pts <5 years: 0.57mg/de (std. dev. 0.18)
	5-10 year: 0.77mg/die (std. dev. 0.23)
	10-18 years: 1.1mg/die (std. dev. 0.39)
	Adults : 1.16 mg/die (std. dev. 0.37)
	Pts with a dose equal or lower to the recommended starting dose:
	5-10 years: 35.3%
	10-18 years: 58.9%
	Adults: 67.6%
Resistance to Colchicine	Resistance was be defined as persistence of fever attacks, despite optimal treatment.
	54% pts had a complete disease control
	46% pts had some disease activity:
	- 30.4% pts had < 1 episode/ month for 3 months
	- 7.8 % had ≥1 episode/month for 3 months
	- 7,3% frequency not known
Inclusion of secondary amyloidosis in the definition of colchicine resistance	5 adult pts (1.5%) displayed amyloidosis
Colchicine intolerance	11 pts (3.2%) withdraw colchicine because of drug intolerance
Patient quality of life and patient-reported outcomes	20.7% of pts experience fatigue or chronic pain, 16.9% limitations in daily activities, and 16.9% have lost school/ work days.

P009

Efficacy of anakinra treatment in pediatric rheumatic diseases; a single-center experience

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Pediatric Rheumatology 2020, **18(Suppl 2):**P009

Introduction: Anakinra, a recombinant IL-1 receptorantagonist, is a treatment option that acts byblocking the biological activity of IL-1 in autoinflammatory conditions. The diseases that the IL-1 was over expressed are the potential conditions for this treatment. Such as familial Mediterranean fever (FMF), cryopyrin-associated periodic syndrome (CAPS), and hyperimmunglobulin D syndrome (HIDS) with monogenic inheritance, and systemic juvenile idiopathic arthritis (SoJIA) or idiopathic recurrent pericarditis as non-Mendelian polygenic diseases, can be listed as examples of these diseases.
Objectives: We aim to report our experiences of pediatric rheumatic diseases treated with anakinra.
Methods: The study group consisted of children with pediatric rheumatic diseases followed up in the Pediatric Rheumatology Department of University of Health Sciences and treated with anakinra (anti-IL 1) for at least one month, between 1 July 2016 and 1 January 2020. The data of these patients were collected retrospectively. The disease activity of the patients at 3rd month and 12th month after the treatment were assessed.
Results: There were 28 patients treated with anakinra for the different pediatric rheumatic diseases. The diagnoses of these patients were as follows; eight were macrophage activation syndrome (MAS) complicating SoJIA, six were HIDS, four were CAPS, four were FMF, four were idiopathic recurrent pericarditis, one was deficiency of interleukin-36 receptor antagonist (DITRA), and one was undefined systemic autoinflammatory disease. 46.4% of the patients were male and 53.6% were female. The median age of diagnosis of the patients was 6.5 ((interquartile range (IQR): 4-12.7) years. The median follow-up duration of the patients was 14 (IQR: 3.7-28) months. The patients median anakinra treatment duration was 3 (IQR: 1-4) months. Fever reduced and C-reactive protein normalized within median 2 (IQR: 1-3) and 5 (IQR: 5-7) days, respectively. In the 3rd month after treatment; It was observed that 53.6% of patients achieved a complete remission (no attack was seen or MAS was improved). The frequency of attacks were decreased more than 50% in 35.7% of patients and less than 50% in 7.1%. 3.6% of patients were unresponsive to treatment. In the 12th month assessment after the initiation of treatment, it was observed that 28.6% of patients were still under anakinra treatment and in remission, 10.7% of them were in remission without anakinra treatment. In 60.7% of patients, anakinra was switch to other biological treatments for different reasons (35.7% partial response or unresponsiveness, 17.8% injection site reactions and 7.1% daily-injection difficulty). Biologic drug switch to canakinumab and tocilizumab was observed in 88.2% and 11.8% of patients , respectively. One patient developed recurrent MAS episodes when the anakinra dose was tapered, and one another patient was unresponsive to the anakinra and dead due to secondary to MAS.
Conclusion: Anakinra seems to be a successful treatment to achieve inactive disease in a significant portion of patients in the early period. The recurrence of disease attacks while drug tapering and injection site reactions were appears the main causes of treatment switch or discontinuation.

Trial registration identifying number: None

Disclosure of Interest
None declared

P010

Majeed syndrome and FMF in a lebanese patient: a case report

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Pediatric Rheumatology 2020, **18(Suppl 2):**P010

Introduction: Familial Mediterranean Fever (FMF) and Majeed syndrome are both rare autosomal recessive periodic fever syndromes that are most prevalent in the Eastern Mediterranean population(1). Majeed syndrome is extremely rare and caused by mutations in the LPIN2 gene which encodes phosphatidate phosphatase LPIN2 (Lipin-2), that controls excessive production of pro-Interleukin-1 beta(pro–IL-1β) during inflamasome priming(2). This syndrome associates recurrent fever, congenital dyserythropoetic anemia, chronic recurrent multifocal osteomyelitis (CRMO) and neutrophilic dermatosis and it has a poor long-term outcome(2).
Objectives: We report the association of these 2 rare autoinflammatory diseases in a Lebanese child and the dramatic clinical and biological improvement with IL-1 blockade.
Methods: A now 8-year-old girl born to consanguineous parents, presented with severe anemia since the age of 3 months (Hb=4g/dL). Intermittent high LDH and low neutrophils counts were seen. Repeated Bone Marrow Aspiration (BMA) and bone marrow biopsy came in favor of myelofibrosis with signs of dysmyelopoiesis. The child was successfully treated with long duration oral steroids.
She came to our attention at the age of 3 years for intermittent fever and mild arthritis in both ankles with no other abnormality. Her family history was notable for JIA in a paternal cousin. Biology showed normal CRP, WBC, platelets with Hb at 10g/dL. ANA, antiDNA, antiENA, RF and anti-CCP were negative. C3, C4, C1q inhib and C1q were normal. X-rays of ankles showed bilateral unspecific diaphysal and metaphysal osteocendensation.
She received NSAID with Methotrexate; ankles normalized but anemia worsened motivating re-use of glucocorticoids.
History was then marked with repeated episodes of fever for 3 days with abdominal pain. Genetic testing for FMF showed compound heterozygous mutations (M694I/E148V). Methotrexate was stopped and colchicine was started.
The patient was then lost to follow-up and took colchicine inconsistently due to digestive intolerance. Fever recurred daily and ankle pain was intermittent. Seen again at the age of 7 years, we noted growth delay with normal physical exam. Biology showed anemia(Hb=8.3g/dL) with increased inflammatory markers (CRP=125mg/L, SAA 877mg/L). X-ray of ankles was normal.
Results: Given the atypical association of FMF to probable autoinflammatory myelofibrosis and the atypical osteoarticular findings, genetic testing was performed and revealed a homozygous mutation in LPIN2(c.362delC) confirming the diagnosis of Majeed syndrome. Anakinra treatment was then started. Fever and arthralgia resolved. After 9 months of biotherapy, the patient was still asymptomatic with normal biology and catch-up growth.
Conclusion: Majeed syndrome is an extremely rare disease with only few recent reports in literature(3). This is the first report of a Lebanese patient. To the best of our knowledge, there was no previous association of Majeed syndrome and FMF.
Based on this clinical presentation, other genetic inflammatory diseases should be considered in case of atypical symptoms or resistant FMF.
In this patient who received steroid therapy for years, IL-1 blockade with Anakinra was attempted and showed sustained control of inflammation with correction of anemia and complete resolution of symptoms.

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Disclosure of Interest

None declared

P011

Musculoskeletal symptoms and their impact on health-related quality of life in chronic nonbacterial osteomyelitis patients

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Pediatric Rheumatology 2020, **18(Suppl 2):**P011

Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare, non-infection-related inflammatory disorder that affects children and teens (1). Clinical manifestations of CNO range widely from moderate, time-limited, monofocal inflammation of the bone to extreme multifocal or chronically active inflammation of the bone (2). Patients are increasingly complaining of bone and joint pain, sometimes very crippling (3).
Objectives: The main aim of this study was to explore the correlation between musculoskeletal (MSK) symptoms and health-related quality of life (HRQoL) in patients with CNO.
Methods: Children and adults with CNO and their parents were asked to answer a web-based survey .The survey consisted of multiple questions centered around demographic, clinical and therapeutic data , MSK discomfort form based on the Nordic MSK Questionnaire and HRQoL based on Pediatric Quality of Life Inventory-4 (PedsQL-4) and PedsQL rheumatology module. The inclusion criteria included diagnosis of CNO before the age of 18. Patients who had malignancies or any chronic rheumatic, MSK, neurological disease were excluded.
Results: There were a total of 68 participants, mostly females (66.2 %), with median age 14 years and median disease duration 4.75 years. The median number of bones affected by CNO was 5 and ranged from 1 to 24 bones. Among the studied patients, 45 patients (66.2%) had musculoskeletal manifestations at the last month. The most commonly affected part was ankle and feet (26.5%). Regarding HRQoL, patients with MSK manifestations had lower scores than did patients without in PedsQL-4 ($p<.001$) including domains of physical functioning ($p<.001$), emotional functioning ($p=.033$), social functioning ($p<.001$) and school functioning ($p=.007$) in addition to lower scores in PedsQL rheumatology module ($p<.001$) including domains of pain and hurt ($p<.001$), daily activities ($p<.001$), treatment ($p=.035$), worry ($p=.001$) and communication ($p<.001$).
Conclusion: MSK manifestations have a negative impact on HRQoL in CNO patients. So, early identification and treatment are highly recommended.

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Disclosure of Interest

None declared

P012

NLRP1-Associated Autoinflammation with Arthritis and Dyskeratosis (NAIAD Syndrome) in a 3-year-old boy

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Introduction: NLRP1-associated auto-inflammation with arthritis and dyskeratosis (NAIAD) is a rare, genetic auto-inflammatory and autoimmune disease in childhood. It was first reported in 2016 in three patients from two families with dyskeratosis, arthritis, recurrent fever and increased inflammatory markers.
Objectives: To report a case of a 3-years-old Turkish boy who presented with some clinical features of NAIAD syndrome.
Methods: Presentation of clinical and genetic finding of a patient with NAIAD.
Results: A 3-years-old boy attended our clinic with progressive joint swelling and limping lasted for six months. In the physical examination; generalized polyarticular joint involvement, mild dyskeratotic lesions of the limbs and trunk, and nail dystrophy on his foot were detected. The level of acute phase reactants was high. He received pulse steroid and IVIG treatment due to severe autoimmune hemolytic anemia (hemoglobin=3.9 g/dl, direct coombs=4+, reticulocytes=11%) when he was two years old. The family reported that he had dyskeratotic lesions on his limbs and trunk, and nail dystrophy on his foot since he was two months old and these lesions regressed following the steroid treatment. The patient was scanned in terms of metabolic diseases due to skeletal dysplasia and polyarthralgia. Skeletal radiographs revealed abnormal features such as overgrowth and osteopenia in the epiphysis and metaphysis of distal femoral and proximal tibias. Ultrasonography detected intraarticular effusion and synovitis in hands, feet, knees, ankle and wrists, and these findings were confirmed with magnetic resonance imaging. ANA and rheumatoid factor were negative. C3 and C4 were normal. No signs of uveitis were detected. Subcutaneous methotrexate and oral steroid (2mg/kg/day) were administered due to an initial diagnosis of polyarticular juvenile idiopathic arthritis. Despite the improvements, steroid could not been tapered. Recurrent episodes of unprovoked fever and systemic inflammation associated with elevated levels of CRP and ESR occurred. Persistent arthritis, presence of skin lesions, history of autoimmune hemolytic anemia, and abnormal features in the skeletal radiographs suggested autoinflammatory diseases. Anti-TNF inhibitor (etanercept) was added to treatment. However, no clinical response was achieved at 6 months. A heterozygous mutation in NLRP1 c.1887 C>A, p. Phe629Leu was detected in the patient. Anti-TNF treatment was ceased and IL-1B inhibitor (canakinumab) and steroid (2mg/kg/day) were administered. The arthritis dramatically improved. However, steroid treatment could not be reduced below 1mg/kg/day. Eventually, IL-1 inhibitor was ceased and IL-6 inhibitor was started. The patient is currently well under the tocilizumab treatment once in a two week for 6 months.
Conclusion: Only four patients with NAIAD were reported worldwide so far. The NLRP1 mutation of the present patient (c.1887 C>A, p. Phe629Leu) was predicted as "probably damaging" according to PolyPhen-2 database. To the best of our knowledge, this patient is the first NAIAD case presenting this mutation.

Disclosure of Interest
None declared

P013

Assessment of blood ferritin levels in patients with monogenic auto-inflammatory diseases and systemic juvenile arthritis.

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Introduction: Auto-inflammatory diseases (AIDs) are a group of monogenic and polygenic diseases caused by violations of the functioning of the innate immune system. The development of such a life-threatening complication as macrophage activation syndrome, which is significantly less common in monogenic AIDs, is characteristic of systemic juvenile arthritis(sJA). The main laboratory marker of macrophage activation syndrome is an increase in ferritin.
Objectives: to evaluate serum ferritin levels in children and adults with various monogenic AIDs and sJA.
Methods: ferritin was detected in 85 samples of blood serum of 74 patients(pts): in 30 children with sJA (female 16, male 14). 17 samples from 13 FMF pts (children -10, adults - 3, male -6, female-7). In 4 pts, the study was performed in dynamics before and past the appointment of therapy(in 2 colchicine, in 2 colchicine with biologic (and etanercept). 25 samples of serums were from 22 pts with CAPS pts(children -11, adults - 11, male -9, female-13); in 4 pts, the study was performed in dynamics before and past the appointment of canakinumab therapy. 13 serums from 10 pts with TNF-receptor-associated periodic syndrome (TRAPS): (children -9, adults - 1, male -5, female-5, including 3 pts in dynamics on the background of canakinumab therapy. Ferritin was determined by enzyme immunoassay with a set of reagents ORGENTEC. The normal value for ferritin varies between 20 and 150 μg/L. Diagnoses of monogenic AIDs (FMF, CAPS, TRAPS) were confirmed by the detection of pathogenic mutations of causal genes. The diagnosis of sJA was based on ILAR criteria. Statistical analysis was performed using standard indicators: median, 25th and 75th quartiles, and the difference between the groups according to the Mann-Whitney criterion. In all patients the same sera values of CRP and SAA were determined using the nephelometric method.
Results: Tabl.1
Ferritin levels in serum of patients with monogenic AIDs and systemic juvenile arthritis.

	Median μg/L	Min μg/L	Max μg/L	Lower quartile μg/L	Upper quartile μg/L
sJA	61.09	0.73	1 500	22.03	385.76
FMF	57.22	3.36	174.22	21.36	133,52
CAPS	28.88	0.98	183.57	8.13	118
TRAPS	16.52	2.42	930.1	5.42	67.27

In patients with sJA the normal ferritin values were found in 12 (41%) pts; in FMF the normal values were found in 100% of pts; in pts with CAPS normal values in 8 (32%) sera semples; in pts with TRAPS normal values were found in 9 (90%) pts, and only 1 pt showed an increase in ferritin despite treatment with canakinumab. A statistically significant difference was obtained between the groups of sJA and CAPS ($p<0.001$), sJA and TRAPS ($p=0.03$). The correlation between the level of CRP and ferritin was maximal for pts with CAPS: $r=0.64$($p<0.001$) and with sJA: $r=0.6$ ($p<0.001$). There was no significant correlation between the level of CRP and ferritin in patients with FMF. The correlation of SAA and ferritin levels was maximal in pts with TRAPS: $r=0.7$($p=0.0072$) and CAPS: $r=0.54$ ($p=0.0051$). There was no significant correlation between SAA and ferritin levels in patients with FMF.
Conclusion: the maximum sera values of ferritin were observed in pts with sJA, their value was statistically significantly higher than in the CAPS and TRAPS groups. Among pts with mAIDs, the most frequent increase in ferritin was observed in patients with CAPS. In patients with FMF, no elevated ferritin levels were detected; in a patient with TRAPS, a persistent increase in ferritin in dynamics was observed in 1 patient whose phenotype had the similarity to sJA. Ferritin may be used as an additional laboratory differential diagnostic sign between patients with sJA and mAIDs.

Disclosure of Interest
None declared

P014

Genetics of chronic nonbacterial osteomyelitis in the irish population: no evidence of a role for FBLIM1 variants

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare inflammatory disease affecting bone predominantly affecting the paediatric population. CNO is frequently associated with other inflammatory conditions including psoriasis, synovitis and pustulosis, and the typically adult-onset disease SAPHO syndrome is considered to be part of the same disease spectrum. The *FBLIM1* gene has been implicated in the pathogenesis of CNO with rare variants identified in 2 patients of South East Asian descent, enrichment of a nonsynonymous variant rs114077715 in European population and also in an Italian cohort. However, there was no association of *FBLIM1* variants in a European SAPHO population. The Irish paediatric CNO population has a high frequency of extraosseous involvement, particularly cutaneous involvement.
Objectives: To ascertain the frequency of variants in *FBLIM1* in an Irish cohort of patients with CNO and compared to the gnomAD non-Finnish European (gnomAD NFE) population.
Methods: 43 Irish children and adolescents currently attending paediatric rheumatology services with CNO were recruited; all met the Bristol criteria for diagnosis of CNO. Whole exome sequencing was performed using Agilent SureSelect XT Human All Exon V6 kits and Illumina HiSeq 3000 with 150bp paired-end reads. Reads were aligned to the hg19 reference genome using BWA software, duplicates removed using Picard tools and GATK software used to realign indels and call variants. The resulting VCF files were annotated using wAnnovar. Rarer variants (gnomAD NFE </= 0.05) were hard filtered for mapping quality (MQ > 40) and depth of coverage (QD > 2)[GW1] . A MAF of <0.05 was selected in order to include previously published candidate variants. Statistical analysis was performed in RStudio (version 1.1.456).
Results: Five individuals had variants in FBLIM1 with MAF <0.05, all were heterozygous. Four carried the nonsynonymous minor allele rs114077715 indicating a MAF in this population of 0.0465 with no significant enrichment (gnomAD NFE MAF=0.0264, OR 1.79, p= 0.29). One carried the synonymous minor allele rs140170023 indicating a similar MAF to that reported in gnomAD (NFE MAF= 0.017). No variants were present with a MAF between 0.03 and 0.05.
Conclusion: Variants in *FBLIM1* do not occur at a significantly higher frequency than expected in the Irish paediatric population with CNO compared to gnomAD non-Finnish European allele frequencies. This may be a reflection the clinical heterogeneity of CNO in different populations.

Disclosure of Interest
None declared

P015

Towards a combined pediatric rheumatology-dermatology clinic: one-year experiences

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Introduction: Dermatological findings may be the sole complaints of diseases in pediatric rheumatology practice. It is well-known that evaluating patients with a multi-disciplinary approach may facilitate access to an accurate diagnosis.
Objectives: Herein, we reported our one-year experiences of collaborative pediatric rheumatology-dermatology.
Methods: Patients were initially evaluated separately in pediatric rheumatology-dermatology outpatient clinics. Subsequently, once a week, final diagnoses of patients with suspected skin rash were collaboratively discussed by two pediatric rheumatologists and a dermatologist.
Results: A hundred and one patients were included to the study. Of these patients, 65 attended initially to dermatology outpatient clinic while the remaining 36 applied to pediatric rheumatology outpatient clinic. The most common mucocutaneous finding was squamous lesions in 30 patients, followed by erythematous lesions in 28 and mucosal ulcers in 14. Finally, 69 patients were diagnosed with a rheumatic disease while 32 had differential diagnoses apart from rheumatic diseases.
Conclusion: Patients with rheumatologic diseases frequently present with only mucocutaneous findings. So a detailed examination of the mucosa, skin and its attachments is of paramount importance in rheumatology practice. We suggest that a close interaction between pediatric rheumatology-dermatology and formation of consensus clinics are going to assist clinicians to make easier and accurate diagnoses.

Disclosure of Interest
None declared

Table 1 (abstract P015). Demographic and clinical characteristics of the patients

	Psoriasis (n=30)	BH (n= 14)	SLE (n=13)	Scleroderma (n=7)	JDM (n=2)	DADA2 (n=3)	Non-rheumatologic conditions (n= 32)
Gender (F/M)	20/10	10/4	10/3	6/1	0/2	2/1	20/12
Age, median (min-max)	10.7 (1.8-16.9)	15.1 (10.2-17.8)	13.6 (8.1-16.7)	9.8 (3.-17.5)	11.1/ 11.5	15.2 (8.2-15.6	11.5 (3.1-17.5)
Type of skin lesion	Papulosquamous lesions	Oral aphthous	Malar rash (n=12) and lupus pernio (n= 1)	Sclerotic lesion	Gottron papule	Livedoid rash	Erythematous lesions, hyperpigmented lesion, xerosis
Arthralgia, n	22	8	4	2	0	3	31
Arthritis, n	13	2	8	1	0	1	7

BH, Behçet's disease; DADA2, deficiency of adenosine deaminase 2; F, female; M, male; max, maximum; min, minimum; n, number of patients; SLE, systemic lupus erythematosus

P016

The musculoskeletal system manifestations in children with familial mediterranean fever

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Introduction: Familial Mediterranean fever (FMF) is a monogenic inherited periodic fever syndrome presenting with episodes of self-limiting fever and inflammation of serosal membranes. The attacks emerge with arthritis were defined as one of the major diagnostic criteria besides involvement of serosal membranes. Non-specific musculoskeletal findings such as myalgia, arthralgia, transient synovitis, and more rare manifestations like protracted febrile myalgia can also be seen in FMF patients attacks
Objectives: We aim to reveal the frequency and genotype association of musculoskeletal manifestations in children with FMF.
Methods: The patients diagnosed with FMF between January 1, 2017 and June 1, 2019, and followed for at least 6 months in our pediatric rheumatology clinic were included in the study. Musculoskeletal manifestations of patients were enrolled. The patients were grouped according to the "Mediterranean Fever" (MEFV) gene variants. Musculoskeletal manifestations of the patients were compared between the groups
Results: The study group included 634 children with FMF (336 female and 298 male, F/M: 1.13/1). The clinical manifestations of patients in attack period were as follows: 99% of the patients had fever, 87.3% had abdominal pain, 20.7% had chest pain, 11.3% had

vomiting, 10.7% had erysipelas like erythema, and 9.3% had headache. The musculoskeletal symptoms were accompanied by 58.6% (n: 372) of the patients during the attack period. The most common musculoskeletal manifestation was found as arthralgia (32.6%, n: 206). Also, the other musculosceletal manifestations were found as follows during attacks; arthritis in 23.7% (n: 150), myalgia in 20.5% (n: 130), exertional calf pain in 6.5% (n: 41), and protracted febrile myalgia in 1% (n: 7) of the patients. It was observed that the musculoskeletal manifestations were significantly higher in patients with homozygous M694V variant in exon-10 (p=0.017). Also, it was found that the musculoskeletal manifestations are more common in the attack periods of patients carrying the M694V variant in at least one allele (p = 0.019).
Conclusion: We found that the musculoskeletal manifestations were accompanied in more than half of FMF patients. M694V variant found as a risk factor for emerge of musculoskeletal manifestations.

Trial registration identifying number: (Approval No/Date: B.10.1.TKH.4.34.H.GP.0.01/233 / 18.12.2019)

Disclosure of Interest
None declared

P017

An italian cohort of patients with chronic recurrent multifocal osteomyelitis

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Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO) is a rare disease characterized by sterile bone inflammation with many unclear aspects in terms of diagnosis, treatment and follow-up.
Objectives: To evaluate demographic, clinical, laboratory, imaging, histopathological characteristics, and treatment responses of pediatric CRMO patients.
Methods: The clinical records of patients with CRMO diagnosed between 2006 and 2019 at three tertiary centers in Italy were reviewed. The diagnosis was based on clinical findings, radiological images and histopathological studies.
Results: We identified 50 patients (62% female) with a median age at onset of 10.00 yrs. Median follow up time was 27 months (range 5-156) and median delay in diagnosis was 7 months (range 1-62). Bone pain was the most common presenting symptom (98%) followed by functional impairment (76.6%). Swelling and fever occurred in 40.4% and 24% of the cases respectively. Median number of affected sites was 3 (range 1-17). Multifocal bone lesions were described in 86% of the patients. Long bones (66%) and vertebrae (52%) were the most commonly affected sites. Increased inflammatory markers (ESR or CRP) at presentation were detected in 32 (64%) patients. Biopsy from bone lesions was performed in 66% of patients. All of the biopsy samples showed evidence of mixed inflammatory infiltration and sclerosis and no infectious agents were found. Whole-body magnetic resonance imaging (MRI) was used as a diagnostic tool in 68% of patients and always was abnormal revealing marrow edema (97.8%), soft tissue edema (85.1%), osteolytic lesions (76.1%), asymptomatic lesions (59.1%), sclerosis (39.1%), joint involvement (23.4%), hyperostosis (15.2%). Other autoimmune diagnosis were associated with 30% of patients (SAPHO n=2, Crohn's disease n=2, autoimmune thyroiditis n=2, JIA n=1, pulmonary fibrosis n=1, coeliac disease=1) although no association with psoriasis. The medications and treatment response are summarized in Table 1. At the last visit, disease status was considered to be in remission in 31 of 50 patients, of whom 43.5% (n=20) without medication and 32.6% (n=15) still on therapy.
Conclusion: MRI is a very sensitive technique for detecting bone lesions in CRMO and can be used for monitoring the disease course. Methotrexate, bisphosphonates, corticosteroid and anti-TNF seem more effective than NSAIDs in treating CRMO, but there is no consensus yet about the management of this rare condition. Rarity and unclear pathophysiology leads to challenges in conducting randomized controlled trials with sufficient power to provide a definitive outcome.

Disclosure of Interest
None declared

Table 1 (abstract P017). Medications and treatment response according to physician assessment

	Full response	Partial response	No response
NSAIDs (n=39)	12 (30.8%)	7 (17.9%)	20 (51.3%)
Corticosteroid (n=10)	5 (50.0%)	3 (30.0%)	2 (20%)
Methotrexate (n=17)	9 (52.9%)	4 (23.5%)	4 (23.5%)
Infliximab (n=11)	5 (45.5%)	4 (36.4%)	2 (18.2%)
Neridronate (n=15)	8 (53.3%)	4 (26.7%)	3 (20%)
Pamidronate (n=11)	5 (45.5%)	4 (36.4%)	2 (18.2%)

P018

Presence of R202Q mutation of the mefv gene defines an atypical subtype of pfapa which benefits from colchicine treatment

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Pediatric Rheumatology 2020, **18(Suppl 2):**P018

Introduction: PFAPA syndrome (periodic fevers, aphthous stomatitis, pharyngitis and cervical adenitis) is the most common autoinflammatory disorder in childhood but its pathophysiology is still unknown. In patients with PFAPA, variants of the MEFV gene including R202Q alteration, have been reported. Furthermore, the role of R202Q is still unclear. The first studies described R202Q as a benign polymorphism. However, further studies suggest that R202Q may play a role as a disease-causing mutation associated with a mild phenotype of Familial Mediterranean Fever (FMF).
Objectives: To compare the clinical features of patients with clinical diagnosis of PFAPA and R202Q alteration of the MEFV gene in both heterozygosity and homozygosity (atypical PFAPA, aPFAPA) to patients affected by typical PFAPA (tPFAPA). The second objective was to compare the clinical phenotype of patients with heterozygous R202Q to patients with homozygous R202Q alteration and to evaluate the efficacy of colchicine treatment in both groups.
Methods: We reviewed the demographic and the clinical characteristics of consecutive patients with clinical diagnosis of PFAP A. Data were analyzed using SPSS version 18.0 Chi-square and Mann-Whitney tests.
Results: 91 patients, 41 with aPFAPA and 50 with tPFAPA, entered the study. The average age at disease onset was higher in aPFAPA than in tPFAPA (4.5 vs 2.1 years; $p = 0.004$). aPFAPA had significantly higher rates of irregular interval between febrile attacks (19.5% vs 2.0%, $p=0.010$), abdominal pain (56.1% vs 30.0%, $p=0.012$), vomiting (22.0% vs 2.0%, $p=0.004$), diarrhea (19.5% vs 4.0%, $p=0.039$) and arthralgias (53.7% vs 30.0%, $p=0.022$). Conversely, pharyngitis and apthous stomatitis were significantly less frequent in aPFAPA than in tPFAPA (75.6% vs 100%, $p<0,005$, and 36.6% vs 58.0%, $p=0,042$,

respectively). There were no significant statistical differences between the two groups based on family history for recurrent fevers, presence of cervical adenitis, chest pain, arthritis or skin lesions during febrile attacks.
As for the second objective, we found no significant differences in the phenotype of patients with heterozygous and homozygous R202Q mutation. Colchicine was administered to 48.1% of patients with heterozygous and 63.6% of patients with homozygous R202Q. Both groups had a notable clinical improvement with colchicine treatment although it was significantly higher in patients with homozygous R202Q mutation (100% vs 46.2%; $p = 0.049$). 63.6% of the patients with homozygous R202Q mutation had a complete resolution of the symptoms whereas 36.4% had a partial clinical improvement. Colchicine-related side effects lead to a withdrawal of the therapy in 30.8% of the patients, all from heterozygous R202Q group.
Conclusion: R202Q alteration of the MEFV gene is associated with atypical PFAPA, overlapping some clinical features of FMF, characterized by older age at onset, less regular interval between febrile attacks and more frequent abdominal pain, vomiting, diarrhea and arthralgias, as compared to typical PFAPA phenotype. We have demontrated that patients with R202Q mutation, particularly in homozygosity, may benefit from colchicine treatment.

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Comak E, Akman S, Koyun M, et al. Clinical evaluation of R202Q alteration of MEFV genes in Turkish children. *Clin Rheumatol.* 2014 Dec;33(12):1765-71.

Disclosure of Interest

None declared

P019

Ocular inflammatory diseases in children with familial mediterranean fever: a true association or a coincidence?

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Introduction: Familial Mediterranean fever (FMF) is typically described as an autoinflammatory disease that can involve joints, skin, muscles, and kidneys. A variety of different clinical entities have been associated with FMF over time [1]. Ocular inflammatory diseases (OIDs) are one of the uncommon entities reported with FMF [2].
Objectives: We aimed to describe the characteristics of OIDs observed in children with FMF and to criticize possible relations between these two inflammatory entities.
Methods: Demographic and clinical data were extracted from the electronic medical records of FMF patients followed in the Department of Pediatric Rheumatology of Ankara University School of Medicine. The diagnosis of FMF was based on Yalcinkaya criteria [3]. OIDs were diagnosed and treated in collaboration with the Department of Ophthalmology.
Results: Among 512 pediatric patients with FMF, five patients were found to have OIDs: chronic bilateral panuveitis in two patients, one patient for each of recurrent orbital myositis (ROM), recurrent optic neuritis (RON), and acquired Brown's syndrome. All patients had at least one M694V mutation and received a diagnosis of OIDs during the follow-up while on colchicine. None had any other concomitant disease. Serum biochemistry, urinalysis, an infectious screen, autoantibodies, HLA testing, serum angiotensin-converting enzyme level, a chest X-ray, and in addition to these, in patients with ROM, RON, and Brown's syndrome cranial and orbital magnetic resonance imaging were carried out to exclude other secondary causes of OIDs. All these investigations were within normal limits for all patients. Colchicine and steroids were used in all patients and methotrexate and biologics were added according to the course of OID. The demographic and clinical characteristics of patients are presented in Table 1.
Conclusion: Although uveitis and optic neuritis have been reported in patients with FMF before, to the best of our knowledge, the first cases of ROM and acquired Brown's syndrome have been introduced. As the presence of M694V mutations creates a pro-inflammatory state, FMF may be a susceptibility factor for various inflammatory diseases like OIDs. Identification of pathogenic pathways linking FMF to OIDs warrants further investigations.

Ethics approval: Parental informed consent and institutional ethical approval were obtained.

Disclosure of Interest

None declared

Table 1 (abstract P019). Demographic and Clinical Characteristics of Patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gender	Female	Male	Female	Male	Male
Age at FMF onset	6 months	Neonatal	4 years	18 months	18 months
Age at FMF diagnosis	1 year	6 years	5 years	3 years	6 years
Clinical findings of FMF	Recurrent fever, abdominal pain, joint pain	Recurrent fever, abdominal pain, joint pain	Recurrent fever, chest pain, abdominal pain	Recurrent fever, chest pain, joint pain, abdominal pain	Recurrent fever, chest pain, joint pain, arthritis, abdominal pain
MEFV gene mutation	M694V/M680I	M694V/M694V	M694V/M680I	M694V/M694V	M694V/M694V
A family history of FMF	+	+	+	+	+
Age at OID onset	6 years	8 years	12 years	5.5 years	8 years
Type of OID	Bilateral panuveitis	Bilateral panuveitis	Recurrent bilateral orbital myositis	Recurrent bilateral orbital neuritis	Unilateral acquired Brown's syndrome
Treatment	Colchicine, topical and systemic steroids, methotrexate, cyclosporine A, adalimumab, infliximab	Colchicine, topical steroids, methotrexate, adalimumab	Colchicine, systemic steroid	Colchicine (dose increased), systemic steroid, anakinra	Colchicine (dose increased), systemic steroid, anakinra

FMF: Familial Mediterranean Fever, MEFV: MEditerranean FeVer, OID: Ocular Inflammatory Disease

P020

Molecular and clinical findings in children with undifferentiated periodic fever syndromes

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Pediatric Rheumatology 2020, **18(Suppl 2):**P020

Introduction: Periodic fever syndromes (PFS) are genetically determined disorders which appear with episodes of unprovoked inflammation. It should be noted that a range of conditions including autoinflammatory disorders (AID), primary immune deficiency syndromes (PIDS), rheumatic diseases, infections and malignancy may manifest themselves by periodic fevers. The main diagnostic difficulties are related to differentiation between AID and PIDS due to similar clinical signs and inflammatory profile. Some PFS such as familial mediterranean fever (FMF) or cryopyrin-associated periodic fever syndromes can be reliably diagnosed on clinical grounds while others may be revealed only by genetic testing. Finding causative genes may drastically improve patient's quality of life allowing earlier diagnosis and proper treatment.
Objectives:
To evaluate the role of next generation sequence in the diagnosis of PFS.
Methods:
41 unrelated patients with PFS and clinical suspicion of AID were included in the study. Clinical and laboratory findings of these patients were evaluated. DNA samples were subjected to targeted next-generation sequencing (MiSeq, Illumina) with enrichment for coding sequences of 344 PID-associated genes including 27 of those associated with autoinflammatory diseases.
Results: The following clinical symptoms were presented: periodic fever (n=17, 42%), persistent fever (n=17, 42%), peripheral lymphadenopathy (n=18; 44%), rash of different types (n=22; 54%), arthritis (n=27; 66%), vasculitis (n=13; 32%), and serositis (n=13; 32%).
Laboratory findings included high ESR, CRP and WBCs and were presented in all patients. Genetic testing allowed us to divide patients into 3 groups:
I - patients with mutations in the typical AID genes: TNFRSF1A (n=5), TNFAIP3 (n=2), NLRP12 (n=4.), MEFV (n=5), MVK (n=1). Mutations in these genes are associated with tumor necrosis factor receptor-associated periodic syndrome (TRAPS), Bechet-like syndrome, Muckle–Wells syndrome, FMF, and HIDS.
II - patients with mutations in PIDS - associated genes (n=4), such as WAS, CTLA4, NFKB2 and MBL2. Mutations in these are associated with Wiscott-Alrdrich syndrome, autoimmune proliferative syndrome, common variable immunodeficiency with adrenal insufficiency and insufficiency of complement activation.
III - patients (n=20) in which we failed to find variants in known periodic-fever associated genes.
We have not found any significant difference between patients with AID (group I) and without AID (groups II+III) in terms of onset age, clinical and laboratory findings, except ESR: 58 (40; 68) vs 28 (18; 53) mm/h ($p = 0.005$) and hepatomegaly 73% vs 36% ($p = 0.002$).
Conclusion: Targeted sequencing is a helpful tool for obtaining genetic diagnosis in patients with PFS. Considering somewhat similar clinical presentation of autoinflammatory diseases and primary immunodeficiencies, genetic testing is sometimes the only way to distinguish one from the other.

Trial registration identifying number: This work was supported by the Rssian Foundation for Basic Research (grant № 18-515-57001).

Disclosure of Interest
None declared

P021

Broadening the genetic and clinical spectrum of a20 haploinsufficiency

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Pediatric Rheumatology 2020, **18(Suppl 2):**P021

Introduction: Heterozygous mutations in TNFAIP3 gene werefound to cause a systemic autoinflammatory disease known as A20 haploinsufficiency (HA20) that resembles Behcet's disease. The protein A20 encoded by TNFAIP3 is structurally divided into two types of domains, OTU domain and C-terminal domain. It is involved in the negative regulation of nuclear factor-kB (NF-Kb). Dysregulation of A20, due to mutations in both domains, leads to constitutive NF-kB activation and development of inflammation. Patients with HA20 can also show an autoimmune phenotype
Objectives: To describe a novel mutation in TNFAIP3 gene leading to a novel phenotype in four patients from an Italian family
Methods: Clinical data of the patients were reviewed. Clinical Exome was sequenced on Illumina NovaSeq6000® platform. *In silico* analysis was performed on the basis of the patient's clinical phenotype. We took into account only variants with an allelic frequency in global population lower than 1%, according with GnomAD database. Production of pro-inflammatory cytokines following *ex vivo* stimulation of PBMCs with lipopolysaccharides (LPS) was analysed by ELISA. B and T cell phenotyping were performed. Moreover, B and T cells stimulation were done to follow the ability of the cells to respond to stimuli and the ability to proliferate
Results: Patient (Pt) 1 was referred to our hospital because of a severe relapsing remitting form of haemolytic anaemia that was treated with immunoglobulin, glucocorticoids and a course of rituximab. From the age of 5 she suffered from autoimmune thyroiditis. In addition, at 9 years she developed an antinuclear-antibody (ANA) negative polyarthritis, treated with intra-articular glucocorticoids and methotrexate. Her mother (Pt2) presented with autoimmune thyroiditis and oral aphtosis. Her elder sister (Pt 3) suffered from type I diabetes and autoimmune thyroiditis; at 20 years, she presented with wrist arthritis and tenosynovitis that required subcutaneous treatment with methotrexate and etanercept. Her younger sister (Pt4) suffered from recurrent febrile episodes associated with cervical lymphoadenopathy not related to infections until the age of 7. All of them were evaluated for short stature; Pt 2 was treated for one year with growth hormone therapy that was dismissed due to inefficacy. Sequencing analysis revealed the heterozygous c.1723_1724insC variant, not described previously in human genetic database. This variant leads to a premature stop codon causing a putative truncation of the protein and segregates with phenotype in the family. Western blot analysis, that could demonstrate the truncation of the protein, is still ongoing. PBMCs obtained from Pt1-4 were stimulated ex vivo with several concentration of LPS releasing significantly higher levels of the pro-inflammatory cytokines IL-1b and IL-6 compared to healthy subjects. Pt1 immunological assay revealed a marked reduction of memory and transitional B cells. The few switched memory B cells present did not express IgG and IgA on the surface. Table 1 shows the clinical features of patients
Conclusion: We identified, in four patients of an Italian family, a novel mutation of TNFAIP3 gene that, based on our functional data, seems to be pathogenic. The majority of the patients (3/4) showed autoimmune rather than autoinflammatory features. This study confirms that HA20 is characterized by different phenotypes even among members of the same family carrying the same mutation. Our results expand the phenotype and genotype spectrum of A20 haploinsufficiency.

Disclosure of Interest
None declared

P022

Pericardial effusion after cardiac surgery: retrospective study in a pediatric cohort

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Pediatric Rheumatology 2020, **18(Suppl 2):**P022

Introduction: Post pericardiotomy syndrome (PPS) is an inflammatory process involving the pericardium, pleura or both. PPS is a common complication of any cardiac surgery with an incidence

ranging from 1 to 40%. Atrial septal defect (ASD) surgical correction is associated with the highest incidence of PPS.
Objectives: To evaluate the incidence and predictive risk factor for PPS after surgical ASD closure.
Methods: We collected patients followed at Bambino Gesù Hospital (Rome) between January 2015 and September 2019 who underwent cardiac surgery for ASD closure. Statistical analysis: chi-square (or Fisher's exact test as appropriate) and Mann-Whitney U test.
Results: A total of 203 patients (124 female) with different ASD type (secundum-type ASD, primum-type ASD [partial atrioventricular canal defects], sinus venosus-type ASD and coronary sinus-type ASD) were included. Median age at cardiac surgery was 4.4 years (IQR 2.7-7.3). Patients were divided in two groups: group 1 including 38/203 patients (18.7%) who developed pericardial effusion (PE) and group 2 including 165/203 (81.3%) patients without PE. The incidence of PPS after surgical ASD closure in our cohort was consistent with that reported in the literature No significative differences were noted between the two groups with regards to gender or age at the surgery, Moreover there were no significant differences between the two groups regarding duration of surgery and/or presence of comorbidities. The median time for the development of pericardial effusion in group 1 was 15 days after surgical correction (IQR 6–20). Incidence of fever after surgey was significantly higher in group 1 as compared to group 2 (23.7% vs 2.4%; p<0.0001). Furthermore, the eletcrocardiogram performed routinely at the time of hospital discharge showed significantly ST segment elevation in children who subsequently developed PPS (24.3% vs 1.8%; p<0.0001). We further subdivided patients with PPS in two subgroups on the basis of the severity of PE: 1) slight PE (<7mm; n=33) and 2) moderate/severe PE (≥7 mm; n=5). Patients with moderate/severe PE underwent surgery at an older age than the others and, they tend to have an higher body mass index (BMI) values (median 18 [IQR 17.4-21.1] vs 15.6 [13.5-16.5]; p=0.013). BMI percentile (72 [71-84] vs 23 [1-57]; p=0.017) confirmed this trend. Among the 38 patients with PE, only three patients did not required any therapy, 27 were treated only with ibuprofen and 8 with a combination of ibuprofen and colchicine.
Conclusion: In this study we evaluated the incidence of PPS in a large pediatric cohort of 203 cases and the presence of predictive risk factors associated to the development of PPS. Analyzing the two groups (with or without PPS) no differences were noted in terms of gender, duration of intervention or presence of comorbidities. An older age at the moment of surgery and an higher BMI seem to be associated to an higher risk of development of clinically significant pericardial effusion. The presence of fever and ST segment elevation at ECG following surgery can be predictive for a later development of PPS requiring a closer follow-up of these patients after discharge.

Disclosure of Interest
None declared

P023

Long-term efficacy and safety of canakinumab in patients with autoinflammatory periodic fever syndromes – first interim analysis of the FMF/TRAPS/HIDS subgroup

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Pediatric Rheumatology 2020, **18(Suppl 2):**P023

Introduction: Autoinflammatory periodic fever syndromes characterized by excessive interleukin(IL)-1ß release and severe systemic and organ inflammation have been successfully treated with the anti-IL-1ß inhibitor canakinumab (CAN). In clinical trial situations and real life, rapid remission of symptoms and normalization of laboratory parameters were observed in most patients.
Objectives: The present study explores long-term effectiveness and safety of CAN under routine clinical practice conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndromes), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).
Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up period. Pediatric (age ≥2 years) and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD that routinely receive CAN are enrolled in order to evaluate effectiveness and safety of CAN under standard clinical practice conditions. Evaluation of disease activity and fatigue by patients' assessment, days absent from school/work due to study indication, inflammatory markers and physician global assessment (PGA) was performed at baseline and will be further assessed at 6-monthly intervals within the 3-year observation period of the study.
Results: This first interim analysis of a patient subset diagnosed with FMF, HIDS and TRAPS includes baseline data of 41 patients (29 FMF, 10 TRAPS, 2 HIDS) as well as preliminary 6-month data of the FMF subset (N=16).
Preliminary results of a first subset of N=16 patients diagnosed with FMF indicate stable remission and disease control upon long-term CAN treatment. Within the first study interval, no major changes were observed regarding the analyzed parameters (table 1). Physician Global assessments of disease activity (% none-mild/moderate-severe) were for FMF patients at baseline 35-28-7 and 38-44-0 at month 6, for TRAPS patients at baseline 11-67-0 and for HIDS/MKD patients at baseline 100-0-0. Serious adverse events were reported for 2 patients including tonsillectomy and arthritis.
Conclusion: Baseline characteristics of the FMF/TRAPS/HIDS-subgroup and first interim data of FMF patients are available from the RELIANCE study, the longest running real-life CAN registry. Further interval data will be analysed to assess efficacy and safety of long-term CAN-treatment in patients with autoinflammatory periodic fever syndromes.

Disclosure of Interest
K. Tilmann Speaker Bureau of: SOBI, Roche, CSL, Novartis, N. Blank Speaker Bureau of: Novartis and SOBI, M. Borte: None declared, I. Foeldvari Consultant for: Novartis, J. Henes Speaker Bureau of: Novartis, Roche-Chugai, G. Horneff Speaker Bureau of: Abbvie, Chugai, Roche, Novartis, Pfizer, MSD, Bayer, M. Hufnagel: None declared, B. Kortus-Götze Speaker Bureau of: Novartis, C. Schuetz: None declared, F. Weller-Heinemann: None declared, J. Weber-Arden Employee of: Novartis, J. Kuemmerle-Deschner Speaker Bureau of: Novartis, AbbVie, SOBI

Table 1 (abstract P023). See text for description

	FMF			TRAPS	HIDS
	Baseline	Baseline*	6 Months	Baseline	Baseline
Number of patients, N	29	16	16	10	2
Mean age, years (SD)	26 (5; 56)	16 (5; 47)	16 (5; 47)	22 (4; 43)	11 (5; 18)
Mean duration of prior CAN treatment, years (min; max)	2.2 (0; 6)	2.2 (0; 6)	2.2 (0; 6)	1 (0; 2)	3 (2; 4)
Patient's assessment of disease activity 0-10, mean (min; max)	3 (0; 10)	2.8 (0; 8)	2.2 (0; 7)	2.1 (0; 5)	0 (0; 0)
Patient's assessment of fatigue 0-10	4.4 (0; 9)	4.6 (0; 9)	3.9 (0; 8)	3.4 (0; 8)	0 (0; 0)
Number (%) of patients with days absent from school/work due to study indication during last 6 months	5 (17)	2 (13)	5 (31)	4 (44)	2 (100)
CRP, mean (mg/dL)	0.9	0.5	0.6	2.0	0.1
SAA, mean (mg/dL)	5.3	2.4	2.4	7.9	0.6

P024

a pediatric case of familial chilblain lupus with R152H homozygous mutation in TREX-1 gene

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Pediatric Rheumatology 2020, **18(Suppl 2):**P024

Introduction: Familial chilblain lupus (FCL) is a rare form of monogenic systemic SLE that typically develops in early childhood with chilblain-like skin involvement. It presents with autosomal dominant inheritance (1). Typical clinical findings are painful and ulcerated erythematous plaques that occur after cold contact on the acral faces (2).
Objectives: Here, we present a case of FCL who was followed with the diagnosis of lupus pernio since infancy and diagnosed with FCL after show up homozygous mutation in the TREX1 gene.
Methods: Written consent form was taken from our patient and his family.
Results: A 13 year-old male patient presented with the complaint of painful wounds on his ears, cheeks and toes. It was reported that similar complaints developed in the ears and cheeks, since nine-year-old. There was no additional rheumatologic complaint in the history. Skin biopsy of erythematous lesions on the soles of the feet performed in infancy was found consistent with lupus pernio. Physical examination of the patient shown painful and in places ulcerated erythematous plaque lesions on the both ears helix, on both cheeks and dorsal faces of bilateral toes. All laboratory parameters were found in normal range. Brain MRI and echocardiography were performed and found normal. FCL was considered as a preliminary diagnosis in the patient with chilblain-like lesions onset at an early age and triggered by cold. Genetic panel analysis was performed. Homozygous R152H mutation was shown in TREX-1 gene. The patient was diagnosed as FCL due to the presence of just chilblain lesions. Hydroxychloroquine, prednisolone and tofacitinib treatment were started, respectively. All chilblain lesions healed, leaving hyperpigmentation. During the follow-up, prednisolone was tapered and discontinued. The 23-year-old sister of the index patient, who had arthritis and chilblain lesions, had also the same TREX-1 mutation and was diagnosed with FCL.
Conclusion: Familial chilblain lupus should consider in differential diagnosis in patients with chilblain lesions beginning at early age and with a similar family history.

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Acknowledgments

We thank our patient and his family

Trial registration identifying number: According to the legal status in our country, ethics committee approval is not required for case reports. It is adequate to obtain informed patient consent.

Disclosure of Interest

None declared

P025

From smart working to smart co-working in the covid-19 era: a pilot program of cooperation around autoinflammatory diseases

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Pediatric Rheumatology 2020, **18(Suppl 2):**P025

Introduction: The last time was signed by the pandemic diffusion of COVID-19, with an emergency area COVID-19 dedicated and the need to minimize the inflow of children and adolescents affected by chronic diseases into the hospitals. Otherwise, paediatricians had to limit visits and to consider a new setting for febrile children.
Objectives: Patients affected by autoinflammatory diseases were assisted by telephonic consultations guaranteed by the paediatricians of free choice and by the paediatric rheumatologists.
However, the patients frequently needed a direct clinical approach and a specialistic evaluation in the case of flares and/or abnormal laboratory parameters and adverse reactions to drugs.
Another frequent question was the differential diagnosis of febrile episodes, to distinguish a recurrent fever, linked to autoinflammation, from an infectious disease.
Methods: we proposed to paediatricians of free choice in west-Sicily a questionnaire about difficulties met in the follow-up of children with autoinflammatory syndromes; needs of scientific or bibliographic support, number of patients with these diseases and treated with biological drugs.
Results: 55 questionnaires were collected: the most frequent recorded conditions were PFAPA and Familial Mediterranean Fever (FMF); a lower percentage followed CAPS; MVK, TRAPS.
The most frequent treatment in PFAPA was steroids on demand; in FMF was colchicine. A low percentage (10%) was treated with anti-IL-1 drugs, needing the access to the hospital to receive the therapy.
All the paediatricians needed specialistic support to adequately control flares, especially in FMF, CAPS, TRAPS and MVK. PFAPA patients were almost individually controlled by paediatricians.
Conclusion: Patients and paediatricians needed a specialistic help to organize the follow-up of these patients and to guarantee a good compliance to treatment.
This period characterized by smart working, telemedicine, strategies to monitor remotely the patients, can find the winning strategy in the approach of the "Co-working", a new cooperation between hospital and paediatricians of free choice, in the global follow-up of autoinflammatory diseases.

Disclosure of Interest

None declared

P026

Juvenile Idiopathic Arthritis with NOD2/CARD5 gene mutation or blau syndrome with arthritis and uveitis: lessons from familial case report

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Pediatric Rheumatology 2020, **18(Suppl 2):**P026

Introduction: Blau syndrome (BS) is systemic autoinflammatory disease characterized by an early onset granulomatous arthritis, uveitis and skin rash, caused by a mutation in the NOD2/CARD5 gene. In real practice an extremely rare monogenic disease like BS is difficult to recognize and it's initially diagnosed as Juvenile idiopathic arthritis (JIA) due to phenotypically similar symptoms.
Objectives: To analyze the diagnosis pathway and results of biologics therapy in a family case of two siblings with BS.
Methods: Case report of 2 brothers with BS genetically confirmed by NOD2/CARD5 gene mutation.
Results: Two brothers of 15 and 3 years old were examined in our clinic. The elder brother presented arthritis of both wrist joints at the age of 2 years. The appearance of a scaly erythematous maculopapular rash on the trunk and extremities preceded the development of onset of arthritis. 3 years later he developed polyarthritis involved knees, ankles and three PIF joints of the left hand. There was no significant improvement after treatment with NSAID, methotrexate (MTX) and cyclosporine A in regional hospital, so etanercept was added since 2012 with variable result. Despite of

biologic and MTX therapy the disease has not been gone into remission. Intra-articular glucocorticosteroids injections were required from 4 to 10 times a year. On admission in our clinic in November 2019 he had high degree of activity polyarthritis. Also, during the examination uveitis de novo as a well-known "paradoxical effects" after 7 years of using etanercept was detected. At the same time the second patient (his younger brother 3 y.o.) was admitted to our clinic with recently appeared polyarthritis with «boggy-like» synovitis and tenosynovitis of wrists, ankles and knees. Anterior uveitis of both eyes was identified. In previous months he developed a small-spotted rash with desquamation that was preceded the onset of arthritis. Blood examination didn't show increased inflammatory activity in both sibs throughout the disease. Because of clinical picture in younger brother we revised the initial diagnosis (JIA) and suggested the Blau syndrome. Molecular genetic testing of the NOD2/CARD15 gene in both brothers showed the same mutation of c.1001G>A (p. Arg334Gln). Because of inefficacy of etanercept therapy and active uveitis in older brother we decided to switch etanercept to golimumab with success. Younger brother showed an excellent initial response to methotrexate and adalimumab for arthritis and uveitis. This history seems to be usual for a lot JIA pts without any other conditions. So we have two pts from one family with typical for BS gene mutation and clinical picture of arthritis and uveitis which responded to TNF-monoclonal antibodies and MTX. It should be noted that the eldest brother (20 years old) has been suffering from arthritis of large joints since his early childhood and inflammatory back pain at present time. We are also going to perform a molecular genetic test for him and extended study for the whole family.

Conclusion: our case report shown that there are now certain answer for the question: Is BS the separate disease or NOD2/CARD15 gene mutation just determines clinical features of JIA. One of the most fascinating aspects of this clinical case is the presence of BS in two (or 3?) children of the family. The further study is needed.

Disclosure of Interest
None declared

P027

Systemic autoinflammatory disease resembling very early onset inflammatory bowel disease: a familial case report

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Pediatric Rheumatology 2020, **18(Suppl 2):**P027

Introduction: Systemic autoinflammatory diseases (SAIDs) are characterized by the presence of chronic or recurrent inflammation secondary to an abnormal activation of innate immunity, generally due to mutation of genes encoding proteins with a key role in regulating inflammatory response.
Objectives: To report a familial case of an autoinflammatory disorder in order to improve our knowledge of genetic patterns associated to SAIDs.
Methods: Case reports.
Results: P1 was an 8-month-old male child. Since five months of life, he presented recurrent episodes of fever, perianal abscess and bloody diarrhea associated to raised inflammatory markers, elevated calprotectin level and anemia. Family history revealed death of older brother at the age of 2 years, suffering from an undefined syndrome characterized by persistent fever, diarrhea, perianal abscesses, anemia, arthritis and severe growth retardation. An older sister (9 years old) (P2) presented recurrent episodes of fever associated to exudative pharyngotonsillitis, enlarged neck lymph nodes and elevation of inflammation indexes, with good response to steroids, since the 6 months of life. Skin rash, diarrhea, arthritis and abdominal pain were not reported during the first years of illness. Suspecting PFAPA, she underwent tonsillectomy, without benefit. Over time, abdominal pain appeared during fever episodes.
At laboratory investigation, P1 presented C-reactive protein (167.2 mg/L) and serum amyloid A (215 mg/L) elevation, calprotectin increase (405 mg/kg), neutrophilic leukocytosis, non-hemolytic anemia (Hb 7.8 g/dl). No signs of infection were detected. Immunological and autoimmune profiles were normal. Bone marrow aspiration was normal. Suspecting very early-onset inflammatory bowel disease (VEO-IBD), ileocolonoscopy was performed. Macroscopic findings resulted normal but a chronic inflammatory infiltrate of the lamina propria was found. Next Generation Sequencing for VEO-IBD, including Mevalonate kinase gene (MVK), was performed. The presence of two heterozygous variants, c.803T> C and c.1129G> A in the MVK gene in exon 9 and 11, causing the variants p.Ile268Thr and p.Val377Ile, was detected. Both these mutations are described as rare and pathogenetic. Due to the family and personal history, clinical and laboratory findings, a SAID was suspected, and genetic investigation was also performed in P2, revealing the same two heterozygous MVK mutations. The variant of uncertain significance c.586G> A in the MEFV gene in heterozygosity was also detected in P1. Although MVK mutations were present in heterozygosity, given the highly suggestive clinical picture and the death of a brother with similar clinical characteristics, Canakinumab was started, with clinical resolution and laboratory normalization in both patients. Parents genetic analysis is ongoing.
Conclusion: Even though MKV deficiency is inherited in an autosomal recessive pattern, both these siblings presented an autoinflammatory phenotype, responsive to anti-IL1 therapy. Allegedly, also the other brother died from an unidentified SAID. These SAID familial cases show how clinical features of autoinflammatory disorders can vary even among relatives who share common mutations: while milder clinical features resembling PFAPA were described in P2, P1 presented a phenotype compatible with a VEO-IBD. Indeed, since chronic intestinal inflammatory disease has been described in association of SAIDs, it is important to consider SAIDs in the differential diagnosis of VEO-IBD.

Disclosure of Interest
None declared

P028

The long and winding road to the diagnosis in a patient with early-onset sarcoidosis and multiple organ involvement

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Pediatric Rheumatology 2020, **18(Suppl 2):**P028

Introduction: Early-onset sarcoidosis (EOS) is a sporadic form of a rare granulomatous autoinflammatory disease associated with mutations in the NOD2 gene. It usually presents in infancy and is characterized by the triad of rash, arthritis and uveitis. However, anterior uveitis and arthritis in the absence of typical skin lesions in a patient with EOS may be misdiagnosed as juvenile idiopathic arthritis (JIA). Therefore, proper diagnosis may be delayed, depending on other EOS-related conditions, e.g. panuveitis, fever, hypercalcaemia (HC), or involvement of spleen, liver, lymph nodes, lung, kidneys, and nervous system. In addition, other causes of such symptoms should always be considered. Regarding the therapy, basic principles are fortunately similar for JIA and EOS.
Objectives: To demonstrate the sequential development of EOS multiple symptoms in association with changes in medication strategy in a boy initially diagnosed with JIA.
Methods: A case report of a patient diagnosed and treated at a paediatric rheumatology centre.
Results: A 23-month-old boy with no familial history of rheumatic diseases, presented with polyarthritis, accompanied by bilateral chronic anterior uveitis with multiple posterior synechiae of iris. At that time, he had no systemic symptoms, not even a rash. The laboratory tests showed elevated CRP, ESR, mild anaemia and negative autoantibodies (AB). Due to the initial diagnosis of JIA with uveitis,

the patient was treated with local corticosteroids (CS), methotrexate (MTX), along with systemic CS; after 3 months, CS were changed to adalimumab (ADA). Several mild relapses during a 30-month treatment period were followed by a significant arthritis and uveitis flare, leading to increase in ADA dose of 20 mg from q2w to qw. Six weeks later, full neurological examination was performed because of 2 brief, mild episodes of dysarthria, qualitative consciousness alteration and slight motor deficit. Brain MRI revealed multiple demyelinating lesions and CSF analysis detected pleocytosis, elevated protein and positive oligoclonal bands. No infection was found, AB were negative. MTX and ADA were withdrawn owing to their potential association with the condition, particularly ADA-induced demyelination was suspected. Instead, high-dose systemic CS were introduced with a positive effect on overall status. Unfortunately, decreasing the CS dose resulted in relapse of eye and joint disease; moreover, a transient macular rash (not indicated for biopsy) occurred, followed by fevers, unilateral peripheral facial nerve palsy, HC and nephropathy with elevated serum 1,25-dihydroxy vitamin D and chitotriosidase (ChT) activity, while ACE level was normal. The kidney biopsy revealed granulomatous interstitial nephritis and the EOS diagnosis was confirmed by genetic testing showing heterozygous R334Q mutation in NOD2 gene. CS were escalated and tocilizumab plus MTX were added. The skin, ocular, neurological, and kidney symptoms seem to be well controlled at present. Nevertheless, in correlation with serum ChT levels, especially arthritis control still requires higher CS doses.

Conclusion: High-dose (off-label) ADA was administered to our patient with putative JIA and uveitis resistant to conventional ADA and MTX doses. Subsequently, the change to single CS therapy due to the neurological complications may have contributed to manifestation of new symptoms including HC and nephritis leading to final diagnosis on the histological and genetic basis. Serum ChT unlike ACE was useful for the diagnosis and activity assessment in our case, as also reported by other authors.

Disclosure of Interest
None declared

P029

Baricitinib-induced remission in PRAAS/Candle Syndrome: a case report

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Pediatric Rheumatology 2020, **18(Suppl 2):**P029

Introduction: PRAAS/CANDLE is a rare genetically defined autoinflammatory interferonopathy caused by mutations in genes that code for proteasome components[1]. At present, less than 100 cases have been reported worldwide.

Objectives: To describe the therapeutic effect of the JAK1/2-inhibitor, baricitinib, on the inhibition of the type I interferon (IFN) inflammatory pathway in a patient with PRAAS/CANDLE.

Methods: n.a.

Results: A one-year-old girl presented with an erythematous and nodular rash on the upper and lower extremities, mostly pretibial. At first, an erythema nodosum was suspected. Two weeks later, she developed pyrexia, hand and feet swelling, arthralgia in her ankles and myalgia. Her echocardiography revealed pericardial and bilateral pleural effusions. She was treated with steroids and non-steroidal anti-inflammatory drugs (NSAIDs), upon which she became afebrile and her symptoms partially improved. Steroid tapering was followed by fever reappearance and deteriorating of the patient´s conditions with abdominal pain, loss of appetite, weight loss and muscle atrophy. Laboratory investigations revealed ongoing severe systemic acute phase responses and hypochromic anemia. Her abdominal MRI revealed a mesenteric panniculitis. Escalation of treatment with etanercept only achieved a ten-day sustained defervescence. She developed progressive lipodystrophy, hypertriglyceridemia and increased liver function tests. A combination therapy with anakinra, steroids and NSAIDs led temporarily to milder symptoms, but did not influence disease progression. She developed lipoatrophy (mostly in the face), finger swelling, prominent abdomen, growth arrest, hypertrichosis, lymphadenopathy and hepatosplenomegaly, which led to the clinical diagnosis of PRAAS/CANDLE. RNA-sequencing revealed a type I IFN signature with evident up-regulation of IFN-inducible genes, which confirmed the diagnosis. No mutation was found in *PSMB8*, the results of the Whole Exome sequencing (WES) are pending. The patient was treated *off-label* with baricitinib 4 mg daily. Within days, she was fever-free and CRP-, ESR-, CK- and transaminase levels dropped. Anemia improved, the weight normalized, lymphadenopathy and mesenteric panniculitis were not further seen, and myalgia and arthralgia subsided, allowing her to walk again and attend preschool.

Conclusion: PRAAS/CANDLE is considered a type I interferonopathy. The genetic background is heterogeneous. Besides mutations in *PSMB8*, mutations in a number of other proteasome-associated genes are described[1]. Interferon signature and Whole Exome sequencing serve as key diagnostic tools in autoinflammatory disorders. Therapeutically, JAK1/2 blockage through baricitinib proved to be very effective in down-regulating type I IFN pathway sustained activation

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Disclosure of Interest
None declared

P030

Contribution of the next generation sequencing technique in the management of familial mediterranean fever patients

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Pediatric Rheumatology 2020, **18(Suppl 2):**P030

Introduction: Familial Mediterranean Fever (FMF), the autoinflammatory inherited prototype with a autosomal recessive mode, is mainly diagnosed by clinical criteria and supported by genotyping, especially in atypical phenotypes. Genotyping however is not covered by public insurance in many countries.

Objectives: Primary objective: To depict the FMF genotype of Greek pts (patients) and investigate the contribution of Next Generation Sequencing technique (NGS) beyond the contemporary technique (PCR & hybridization) Secondary objective: To unravel any associations between the mutated genes with the disease course and response to treatment.

Methods: This is a single center, retrospective study including young and adult pts with an established clinical diagnosis according to Tel-Hashomer or Livneh diagnostic criteria. FMF pts with non-confirmative genetic analysis based on PCR & hybridization technique underwent NGS testing during the 15-mo period March 2015 to July 2017.

Results: Overall 31 pts, 12 male and 19 female with a mean age of 18.69 ± 10.14 years participated in the study.

PCR and hybridization technique detected ≥1 mutation in 25/31 pts (80.7%), most frequently p.Met694Val (29%), p.Met680Ile (16.1%), p.

Arg202Gln (12.9%). The majority of the pts were heterozygous (20/25, 64.5%), 2/25 (6.5%) homozygous and 3/25 (9.7%) compound heterozygous, respectively. None of the pts had a complex genotype. NGS analysis detected mutations in 26/31 (83.9%), most frequently, p. Arg202Gln (61.3%), p.Met694Val (48.4%), p.Met680Ile (19.4%). 9 pts (34.6%) were compound heterozygous, 5 (19.2%) heterozygous, 1 (3.8%) homozygous and 11 (42.3%) had a complex genotype.
Noteworthy, the application of NGS revealed that 4 genotypes among 8 pts remained unchanged and 17/25 pts were carriers of other mutations. Two siblings with a former negative PCR genotype but a classical phenotype turned out to have a complex genotype (M694V/R761H/R202Q).
Among the 17 pts who were characterized as heterozygous by PCR, 7 were found to have a complex genotype, 9 a compound one and the remaining 1 without any mutation. The latter had a mild early-onset phenotype and had been on medication for 15 years, but discontinued colchicine after the NGS analysis. This FMF-like pts is in clinical remission 7 years off medication (Table 1). The frequency of p. Arg202Gln was higher by NGS 61.3% than by PCR 12.9% (p=0.09) and correlated with FMF phenotype.
Rare mutations were detected by NGS in 5/26 pts (19.2%), namely p.Arg761His, p.Glu148Val, p.Glu167Asp, p.Phe479Leu, p.Arg408Gln and p.Pro369Ser. NGS genetically confirmed the clinical diagnosis (heterozygosity to compound or complex genotype) in 19 pts. The above findings highlight the mutational heterogeneity in our FMF pts.
Conclusion: Although sequencing by PCR & hybridization is the standard technique in clinical practice, NGS can be judiciously applied in selected cases. Since PCR sequencing analyzes a rather limited number of genomic regions, uncommon mutations might be missed, as in 19.2% of our studied pts. NGS screens though the whole MEFV exome. Thus, it clarifies genetic profile in pts with atypical phenotypes and supports management decisions, regarding the treatment.

Funding
Roche Hellas, Novartis Hellas and Friends' Association of Children with Chronic Rheumatic Diseases supported the reagents supply.

Disclosure of Interest
None declared

Table 1 (abstract P030). Genotype update by NGS among 19 FMF pts

PCR & Hybridization	NGS
Negative (2)	M694V/R761H/R202Q
M694V/0 (8)	M694V/R202Q (3)·M694V/M680I/R202Q (2) ·M694V/E148V/R202Q·M694V/R202Q/R202Q ·M694V/M694V/ R202Q/R202Q
M680I/0 (5)	M694V/M680I/R202Q·M680I/R202Q·M680I/V726A ·(-)·M680I/M680I
M694I/0	M694V/R202Q
K695R/0	K695R/R202Q
P369S/0	P369S/ R408Q
V726A/0	V726A/E167D/F479L

P031

Fostering patient registries as platforms for future epidemiological, clinical and translational research

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Introduction: Autoinflammatory diseases (AID) are characterized by recurrent, self-limiting, systemic inflammatory reactions and are associated with a dysregulation of the innate immune system. AID are characterized by their symptoms (fever, serositis, joint, abdominal and skin involvement, etc.) raised inflammatory markers and, in hereditary diseases, by a positive mutation analysis. Since the discovery of the various auto-inflammatory diseases, a number of national and international patient registries have been set up: for instance EUROFEVER started in 2008 on an European basis, AIDnet took place in 2009 in Germany and the JIRcohort was founded in 2013.
Objectives: To develop a collaborative research project on different existing patient registries within the PRES working party on AID.
Methods: A kick-off meeting was held on 9th June 2020 with the main persons in charge of the 3 databases collaborating in this project (EUROFEVER, AIDnet and JIRcohort). Common research questions will be defined by the project managers and analyzed separately in every registry. Results of the research questions will then be shared between the different project partners and comparative analyses will be carried out centrally. Results including the patients of all 3 databases will be presented jointly.
Results: The EUROFEVER database, the AIDnet registry and the JIRcohort represent a unique collection of information on patients with HPFs with only a minimal overlap of individual patients. Conducting joint epidemiological or clinical studies on patients from different databases remains a real challenge, mainly for reasons of IT interoperability and regulatory issues. Yet success in conducting such studies will also be a real advance in our knowledge of these diseases. Several initiatives to harmonize the different databases and develop common strategies for such studies have been launched. An example of this type of initiative is the MERITA project led by the European Rare Disease Network RITA which main objectives are to promote the interoperability of the different ERN registers and to develop a new registry for sharing essential clinical data provided by different European registries. In parallel of this initiative, we propose here an additional research strategy that will be complementary to the MERITA initiative and that could also be applied to registries that are not harmonized a priori.
Conclusion: If the experience shows to be feasible in these 3 different registries managed by 3 different teams, the methodology could be extended to other existing cohorts or registries and open the way for collaborative registry studies regardless of IT operability. Furthermore some common data elements identified during this study protocol could be shared prospectively in the MERITA project and thus participate to a wider European initiative.

Disclosure of Interest
None declared

P032

MRI as a diagnostic tool in protracted febrile myalgia

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Introduction: Protracted febrile myalgia syndrome (PFMS) is a rare complication of familial Mediterranean fever (FMF). The diagnosis is based on clinical symptoms and is often challenging especially when PFMS is the first ever manifestation of FMF.
Objectives: The aim of this report was to present the magnetic resonance imaging (MRI) findings in pediatric patients with PFMS.
Methods: Four children with PFMS attending 3 different medical centers are described. Clinical data were collected from the medical files, and all MRI scans were revised by an experienced radiologist.

All patients were genetically tested by Sanger sequencing for the 9 most common MEFV mutations.
Results: There were three girls and one boy aged 6 months to 12 years. All had Mediterranean ancestry. PFMS was the first manifestation of FMF in all patients. One patient had familial history of FMF and two patients had clinical background supporting the diagnosis. Two of the patients had more than one episode of PFMS. All patients had extreme asymmetric myalgia, 3 of them had high-grade fever, and all had elevated inflammatory markers. A long comprehensive work-up was performed during hospitalization, including multiple CT and CT-angiography scans, bone marrow aspirations, and skin and muscle biopsies. MRI of the extremities as part of the workup yielded findings suggesting myositis with normal CPK levels. After diagnosis, all patients were referred for Sanger sequencing for the 9 most common MEFV mutations (M694V, M694I, M680I, K695R, R761H, A744S, P369S, V726A, E148Q). One was homozygous for M694V mutation, two were heterozygous for M694V mutation, and one was hemizygous for the M694V and V726A mutations.
Conclusion: MRI is a noninvasive no radiation method that may serve as an auxiliary diagnostic tool in the challenging diagnosis of PFMS.

Disclosure of Interest
None declared

P033

Trisomy 8 – a genetic mimic of early-onset behçet-like disease?

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Pediatric Rheumatology 2020, **18(Suppl 2):**P033

Introduction: Behçet disease (BD) is a systemic vasculitis presenting with bipolar ulcers, uveitis, skin lesions and organ inflammation. Etiology is considered multifactorial with participation of genetic susceptibility and environmental triggers. More recently, monogenic mimics of early-onset BD have been reported.
Objectives: To present a case of early-onset Behçet-like disease associated with trisomy 8 in order to further expand the spectrum of genetic mimics of early-onset BD.
Methods: Retrospective chart review from initial presentation to last follow-up. Informed parental consent was obtained for genetic analysis and for publication.
Results: The patient, a 15-year-old Caucasian adolescent, developed recurrent fevers at age 6 months. Subsequently, oral and genital ulcers, cutaneous manifestations (severe acneiform lesions, folliculitis) and asymptomatic anterior uveitis occurred. At age 7, progressive peripheral neuropathy of the right foot was noted, evolution was eventually favorable after two surgical interventions and intensive physiotherapy. She had important biologic inflammation during disease flares, but normal inflammatory markers in between flares. Trisomy 8 mosaicism was suspected on next-generation sequencing and confirmed by FISH. Treatment with colchicine, prednisone, methotrexate and golimumab was partially efficient, symptoms finally improved on azathioprine and adalimumab.
Discussion. Behçet-like disease has previously been reported in adults with myelodysplastic syndromes and acquired somatic trisomy 8. More recently, a BD-like disease has been described in a few patients with constitutional trisomy 8 with and without mosaicism (1). Characteristic symptoms included early-onset recurrent fever episodes, mucocutaneous ulcers and bleeding diatheses. These patients were found to have increased monocyte activation and upregulated IL-1, TLR- and NFkB-related genes; they responded to TNFα or IL-1 blockade. We reported lately a 17-year-old Caucasian woman with developmental delay and multiple malformations resulting from a *de novo* complex partial 8p23.1 trisomy associated with a monosomy 7p (2). She had recurrent episodes of fever since infancy, and subsequently developed bipolar aphthosis, abdominal pain, polyarthritis and non-thrombocytopenic purpura. Topical and systemic corticosteroids as well as colchicine were partially efficient; eventually anakinra was started with excellent response and complete resolution of inflammatory symptoms.
Conclusion: Trisomy 8 with or without mosaicism may mimic early-onset BD. Recognition of genetic mimics of BD may help to understand the underlying pathology and guide treatment.

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Disclosure of Interest
None declared

P034

Covid-19 infection in pediatric and adult patients with autoinflammatory diseases and immunosuppressive therapy: a case series

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Pediatric Rheumatology 2020, **18(Suppl 2):**P034

Introduction: Poor outcome in coronavirus (COVID-19) infection correlates with clinical and laboratory features of cytokine storm syndrome (CSS) [1]. The macrophage activation syndrome (MAS) is a special form of CSS [1]. Cytokine targeting therapies particularly started early in disease course may achieve cytokine neutralization. Increased IL-1β release has been reported in COVID-19 patients [2]. Several ongoing clinical trials investigate the role of anti-IL-1, anti-IL-6 and anti-INFɣ therapies in COVID-19. Risk factors for poor outcome in COVID-19 are old age, male sex and comorbidities, whereas pediatric patients with immunosuppressive therapy seem not to be at increased risk for severe disease course [3]. So far, there is scarce data on COVID-19 in patients with autoinflammatory diseases (AID).
Objectives: To assess disease course of COVID-19 in AID patients treated with immunosuppressive therapy.
Methods: Case series. Patient 1 is a 34 year-old women with rheumatoid arthritis and unclassified AID treated with methotrexate (MTX) 20 mg/weekly. She developed rhinitis, fever, headache, fatigue, cough and was tested positive for *SARS-COV-2* eleven days after symptom onset. On day 10 she reported loss of taste and an episode of gastrointestinal symptoms. On day 14 she developed respiratory insufficiency with need for oxygen. On day 21 computed tomography showed typical signs of COVID-19 pneumonia. On day 40 she still suffered from dyspnea, fatigue, loss of taste and muscle pain. **Patient 2** is a 14 year-old girl with Cyropyrin-Associated Periodic Syndrome (CAPS; variant *Q703K*) on anti-IL-1 maintenance therapy since 5 years (Canakinumab 150 mg/month). Last administration was 25 days before diseases onset. **Patient 3** is a 13 year-old boy with CAPS (variant *Q703K*) treated like patient 2. Patients 2 and 3 developed fever, cough, fatigue and rhinitis 10 days after patient 1. Loss of taste was reported from day 4 to 13. On day 6 both had gastrointestinal complaints. After 14 days they recovered and anti-IL-1 maintenance therapy was administered. On day 28 a painful rash appeared on both arms of patient 3. As all patients live in the same household, patients 2 and 3 were not tested but clinically diagnosed for COVID-19.
Results: Patient 2 and 3 displayed typical COVID-19 disease symptoms but had a mild disease course without complications while on

anti-IL-1 maintenance therapy, which was held back in the acute episode, and restarted after recovery. Patient 1 experienced a disease course more severe and ≥ 2 times longer than patients 2 and 3. Maintenance MTX treatment was paused since onset of COVID-19 symptoms.
Conclusion: As excessive IL-1 seems to be involved in COVID-19 immunopathology, IL-1 inhibition may prevent a severe disease course in COVID-19 infected AID patients. Both juvenile CAPS patients on anti-IL-1 maintenance therapy showed a milder disease course compared to the adult patient on MTX. This might be due to their younger age but also due to type of immunosuppressive therapy. This is one of the first reports about patients with AID on anti-IL-1 maintenance therapy with COVID-19. Data collection and merge of reports about these rare cases is needed to compile reliable insights on the effects of immunosuppression for AID on COVID-19 disease course.

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Disclosure of Interest

T. Welzel: None declared, S. Samba: None declared, J. Kuemmerle-Deschner Consultant for: Novartis, SOBI

P035

A multi-centre service evaluation of access to care for children diagnosed with chronic recurrent multifocal osteomyelitis in the UK

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Pediatric Rheumatology 2020, **18(Suppl 2):**P035

Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO) is an autoinflammatory bone condition causing bone pain, swelling and disruption to musculoskeletal function in children(1). Although CRMO is uncommon, significant disease burden has been described from patient and family perspectives, one such example being delay to diagnosis (2).
Objectives: To describe the clinical pathways leading to CRMO diagnosis within three tertiary paediatric rheumatology centres, thereby identifying and addressing delays to diagnosis.
Methods: A retrospective review of medical records was undertaken for patients presenting over a 5 year period who ultimately received a diagnosis of CRMO. A standardised spreadsheet was used to capture demographics, clinical presentation, investigations and management, and referral pathway details.
Results: A total of 45 patients were included for whom details of symptom course, referral and diagnosis were known (68.9% female, 95.3% Caucasian ethnicity, median age at symptom onset 10 years 3 months). The median time from symptom onset to diagnosis was 7 months; most (median 5 months) was within secondary care between first appointment and diagnosis. Patients saw a median of 2 specialties (range 1-5). 14 children (32.5%, n=43) waited > 12 months to receive a diagnosis; median time 17 months (IQR 15-22). In patients presenting with pain exclusively in the lower limbs (n=15) the median time from symptom onset to diagnosis was 11 months compared with 5 months for patients presenting with clavicle pain (n=9). Median time from symptom onset to first rheumatology consultation in the whole group was 6 months (IQR 2-14, n=42). Table 1 shows the times from symptom onset to diagnosis according to specialties patients were first referred to and ultimately diagnosed by.
Conclusion: Pattern of bone involvement which is more specific to CRMO (i.e. clavicular) appeared to be associated with quicker diagnosis. Identifying and addressing potential delays to diagnosis could help to reduce investigations and worry for patients and begin treatments sooner.

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Disclosure of Interest

None declared

Table 1 (abstract P035). Timings of symptom onset to diagnosis pathways for children diagnosed with CRMO, subdivided by specialty

	By specialty first referred to				By specialty making diagnosis			
	Specialty first referred to, n=42 (%)	Median time (months) from onset of symptoms to first secondary care appointment, n=35	Median time (months) from first secondary care appointment to diagnosis, n=33	Median total time (months) from symptom onset to diagnosis n=39	Specialty making diagnosis, n=45 (%)	Median time (months) from onset of symptoms to first secondary care appointment, n=38	Median time (months) from first secondary care appointment to diagnosis, n=35	Median total time (months) from symptom onset to diagnosis, n=43
Rheumatology	5 (11.9)	2 (n=5)	10 (n=5)	14 (n=5)	30 (66.7)	1 (n=27)	5 (n=25)	6 (n=29)
Orthopaedics	25 (59.5)	2 (n=19)	5 (n=19)	9 (n=23)	10 (22.2)	6 (n=7)	3 (n=6)	11 (n=9)
Other	12* (28.6)	1 (n=11)	3 (n=9)	5 (n=11)	5† (11.1)	1 (n=4)	5 (n=4)	5 (n=5)

* General paediatrics (9), Oncology (2) Maxillofacial surgery (1)
† Oncology (2), Infectious diseases (2), Infectious diseases/rheumatology joint service (1)

P036

Clinical features, genotype and treatment in children with deficiency of adenosine deaminase 2 in cohort of one Russian center

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Pediatric Rheumatology 2020, **18(Suppl 2):**P036

Introduction: Deficiency of adenosine deaminase 2 (DADA2) require studying in different populations because of this polyarteritis nodosa (PAN)-like disease disables patients and leads to the dramatic presentations like stroke, bowel perforation and fatal outcome.
Objectives: To describe patients with manifestations of PAN and mutations in Cat Eye Syndrome Chromosome Region 1 (CECR1) gene from National Medical Research Center for Children's Health (Russian Federation).
Methods: The retrospectively analysis of the clinical course and treatment of 7 children with CECR1 mutations and PAN features. Next generation sequencing (NGS) used to screen CECR1 gene, Sanger sequencing used to verify NGS data.
Results: Two girls died. Onset of disease at ages 2.8 and 3.1, duration of disease 4,5 and 2.7 years, respectively. Both had the recurrent febrile fever, livedo racemosa, high acute markers in the blood

serum, strokes, intestinal ulcers with perforations. Glucocorticoids, mycophenolate mofetil, cyclophosphamide, intravenous immunoglobulin, rituximab, tocilizumab were used in both cases with partial effect. In terminal stages infliximab was used in one case, adalimumab – in other case. There were homozygosis mutations in CECR1: c.1309G>A, p.Val437Met and c.139G>C, Gly47Arg, respectively.
In two siblings one girl had onset of disease at 6 months old by macrophage activation syndrome, isolated. She received tocilizumab with good effect during 1.5 years. Then she developed livedo racemose and ischemic stroke with hemorrhagic impregnation. The glucocorticoids, mycophenolate mofetil and etanercept were admitted. After that the sister of girl had onset of disease at 4,4 years old (y.o.) by livedo racemose and high C-reactive protein (CRP) in blood serum. She started treatment with glucocorticoids and etanercept. Girls have the same heterozygosis mutations in CECR1: c.1078A>G, p.Thr360Ala. After initiation etanercept girls had not clinical features of DADA2 10 months and 1 year, respectively.
In other two siblings one boy had onset of disease at 6.1 y.o. by recurrent febrile fever, livedo, colitis, ulnar nerve mononeuropathy, elevation of acute phase reactants. We followed the patient until 18 y.o., during this time he received glucocorticoids, mycophenolate mofetil, cyclophosphamide, plasmapheresis, rituximab, azathioprine with good effects. The brother of boy developed DADA2 in 7,2 y.o.. He had livedo, fever and high level of CRP. He started therapy with glucocorticoids and azathioprine with good effects, after genetic confirmation DADA2 the etanercept was initiated to prevent stroke. Boys have the same homozygosis mutations in CECR1: c.1358A>G, p.(Tyr453Cys).
7.3 years old girl developed disease by livedo, fever, arthralgia and elevation of CRP and erythrocyte sedimentation rate. She started glucocorticoids and mycophenolate mofetil with partial effect. There were detected two heterozygosis mutations in CECR1: c.1358A>G, p.(Tyr453Cys) and c.140G>C, Gly47Ala and she started etanercept. She haven`t had disease features during 4 months.
Conclusion: All patients with suspicion for PAN require the identification of CECR1 mutations to prevent serious outcomes. It is unpredictable what course of DADA2 will be developed in patients with the same mutations, like in siblings. Further identification of mutations in different populations with PAN will help in understanding disease management.

Disclosure of Interest
A. Mamutova Speaker Bureau of: Novartis, E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, T. Dvoryakovskaya Speaker Bureau of: Novartis, Pfizer, MSD and Roche, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, K. Isayeva: None declared, A. Chomahidze: None declared, A. Fetisova: None declared, O. Lomakina: None declared, K. Chibisova: None declared, M. Gautier: None declared, D. Vankova: None declared, I. Kriulin: None declared, E. Krekhova: None declared, M. Shingarova: None declared, A. Pushkov: None declared, K. Savostyanov: None declared

P037
Number of episodes can be used to monitor disease activity in patients with familial mediterranean fever
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Pediatric Rheumatology 2020, **18(Suppl 2):**P037

Introduction: Monitoring disease activity in FMF is essential to define disease effects on the general health and quality of life (QoL) of patients, to determine treatment response, optimize disease follow-up and prevent complications. The importance of monitoring disease activity and doing regularly are highlighted in the international recommendations for the management of autoinflammatory diseases. It is necessary to assess disease activity easily in research and clinical practice.
Objectives: The aim of this study is to compare Pediatric Quality Life Inventory (PedsQL), Childhood Health Assessment Questionnaire (CHAQ), the four-item Morisky Medication Adherence Scale (MMAS-4), Wong-Baker FACES pain rating scale (FACES), Children's Depression Inventory (CDI) among the patients with FMF grouped according to the number of episodes in a year to define if it is the key element to detect the disease activity in FMF.
Methods: In this cross-sectional study, patients were recruited from the pediatric rheumatology outpatient clinics of tertiary hospitals in Turkey. Patients with FMF were evaluated face to face interviews to complete outcome measures such a PedsQL, CHAQ, MMAS-4, FACES, and CDI. We also recorded demographic data, main clinical symptoms of the episodes, treatment modalities, genetic mutations, possible triggers of episodes.
Results: A total of 239 patients (male 44.4%, female 55.6%) were grouped according to the number of episodes in a year: first group consist of 74 patients (31%) without any attacks in a year (Group 1), 99 patients (41.4%) have 1-4 episodes in a year (Group 2), 66 patients (27.6%) have more than 4 episodes in a year (Group 3). Age at diagnosis, gender, consanguinity, family history and history of amyloidosis were not different among the groups ($p>0.05$). The main clinical symptoms were similar among the groups ($p>0.05$). The comparison of fatigue, stress, sadness among the groups were significantly different, respectively $p=0.008$, $p=0.002$, $p=0.002$. All of these symptoms were more common in the last group than others. Most of the patients (232 of 239 patients, 97.1%) were treated with colchicine. Groups were similar in terms of M694V, and V726A allele frequency ($p=0.843$, $p=0.46$).
For parent and child PedsQL scale scores, patients in no episode group (Group 1) had higher scores that means better HRQoL than Group 2, and Group 2 had higher scores (better HRQoL) than Group 3. CHAQ scores of patients in Group 1 were significantly lower than Group 2 ($p=0.006$). Patients in Group 2 had lower CHAQ scores than patients in Group 3 ($p=0.004$). Both parent and child MMAS scores were not different among the groups. In Group 3, patients have higher parent CDI scores than no episode (Group 1) group ($p<0.001$). Child CDI scores were significantly lower in Group 1 than Group 2 ($p=0.01$), and in Group 2 than Group 3 ($p=0.03$). Both parent and child FACES scores were significantly lower in no episode group than Group 2, and patients in Group 2 lower than Group 3.
Conclusion: In a homogeneous patient population in terms of demographic features, mutation types, clinical symptoms, and treatment, PedsQL, CHAQ, CDI, and FACES have significantly different among the groups according to number of episodes in a year. We speculate that number of episodes is the key element of disease activity in patients with FMF and can be used to assess disease activity by alone

Disclosure of Interest
None declared

P038
Kawasaki disease and auto inflammation, a retrospective study on 80 children in montpellier university hospital center
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Pediatric Rheumatology 2020, **18(Suppl 2):**P038

Introduction: The physiopathology of Kawasaki disease (KD) remains unknown even if Pediatric Multi System Inflammatory Syndrom (PMIS) consecutive to COVID 19 infection have been largely studied. Autoinflammatory pathway have been evoked as a major component of KD, unexpectedly clinical studies about overlap between KD and autoinflammatory diseases are rare.

Objectives: The aim of this study is to evaluate the occurence of an autoinflammatory disease among KD patients.
Methods: This is a monocentric retrospective study that include all chidren under 15 years old diagnosed as KD in the Montpellier University Hospital Center between may 2012 and may 2019. Clinical and biological data were collected (sex, age, type of Kawasaki disease, inflammatory biomarkers, hepatic cytolysis) as well as the results of echocardiographies and treatments received. Follow up consultations have been analyzed to assess the onset of relapsing fever.
Results: 80 patients were included between 2012 et 2019. There was 57 boys and 23 girls.The average age was 30.2 months. Fifty percent of the patients had an anormal echocardiography. Height patients presented relapsing fever. Among these 8 patients, 3 patients met the criteria of PFAPA syndrome (Periodic Fever Adenitis, Pharyngitis Aphtous), which is more than expected in the general population ($p<0.05$).
Conclusion: This study shows a significant increase of PFAPA syndrome frequency in children that have presented KD. A genetic popensity to auto inflammatory syndroms and altered immune response can be discussed. This association suggests an auto inflammatory origin to the KD.

Disclosure of Interest
None declared

P039

The utility of a next generation sequencing panel in diagnosing systemic autoinflammatory diseases in India - a single centre experience

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Pediatric Rheumatology 2020, **18(Suppl 2):**P039

Introduction: Systemic Autoinflammatory Diseases (SAIDs) are a diverse group of genetic diseases caused by dysregulation in the innate immunity and often presenting with overlapping phenotypes. Advances in genetic testing over the past 20 years have led to the discovery of more than 50 monogenic AIDs but they remain largely under-recognised, undiagnosed and consequently underreported in India largely due to poor awareness in doctors and reliance on foreign collaboration for costly genetic testing.
Objectives: 1. To make available a genetic testing facility for SAID in India and to test a shortlisted high-risk population of patients with the above panel.
2. To study the yield of this panel and to identify novel mutations, if any, in our population.
Methods: We suspected 38 children from our clinic to have SAID based on multisystem inflammatory disease (fever, rashes, arthritis, mucocutaneous manifestations, serositis and organ specific symptoms) occurring recurrently or with prototypic features, onset early in life, consanguinity or a positive family history and elevated acute phase reactants during episodes. A 53 gene panel was curated and a local laboratory performed next generation sequencing (NGS) under our instruction. In addition to multilingual consent for genetic testing and research / publication, ethics clearance for data collection and publication was obtained. Patient contributions were supplemented by funds from donors for testing.
Results: 11 of 38 patients (28.9%) received a closure in their diagnosis. Thus, in addition to the 27 patients who were previously diagnosed (largely by personal request to international centres), the total count of patients molecularly confirmed to have monogenic SAID in our centre rose to 38 (*Table 1*).
Conclusion: Our centre reports the first experience in India, to use a gene panel and test locally in a shortlisted group to arrive at a diagnosis in SAID. This study will hopefully provide impetus to other Indian studies, thereby identifying the commoner SAIDs in India, resulting in the use of abbreviated and cheaper panels. With consanguinity and endogamy prevalent in our country (reaching as high as 38% in some states), and a population of 1.2 billion, in a backdrop of colonisation by various European nations where these diseases are regularly recognised, this study opens our eyes to the tip of this looming iceberg.

Disclosure of Interest
None declared

*Novel mutations identified
**13 from our center include SPENCD (2), Hereditary C1q deficiency (7), H syndrome (4)
*** 32 from other centres in India include TRAPS (10), DITRA (1), HA20 (2), APLAID (5), AGS (4), FMF (2), FCAS (1), MWS (3), NLRP12 (1), IBD (3)

Table 1 (abstract P039). Number of patients with SAIDs in our clinic and total number reported in India

SAID	Using NGS Panel To date (38 patients tested)	Diagnosed outside of this initiative	Total in our centre today / total reported in India survey (until Aug. 2019)
Blau Syndrome	2	3	5 / 26
CINCA/NOMID	-	3	3 / 15
Majeed Syndrome	3*	2	5 / 3
DADA2	1	6	7 / 13
MVK/HIDS	2	0	2 / 17
DIRA	1	0	1 / 2
LACC-1	2	0	2 / 0
Others	0	13**	13 / 32***
Total	11 / 38 (28.91%)	27	38 / 108

P040

Characterization of a group of patients with mevalonate kinase deficiency

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Pediatric Rheumatology 2020, **18(Suppl 2):**P040

Introduction: Mevalonate kinase deficiency (MKD) is a very rare, autosomal recessive autoinflammatory disease with multiple organ involvement. MKD is caused by mutations in the gene encoding mevalonate kinase (MVK) that lead to its reduced or deficient activity. However, not all patients have typical symptoms at the time of onset. MKD treatment remains an unsolved problem, since none of the modalities previously used for MKD treatment are fully effective in the disease control.
Objectives: To analyze clinical features, laboratory, molecular genetic data and response to therapy of a group of patients with MKD.
Methods: We characterize 26 patients (15 males, 11 females, median age 4.9 years (range 0.2–17 years), including four familial cases, with MKD diagnosis confirmed by detection of the *MVK* gene biallelic mutations via Sanger sequencing or targeted NGS panels. Mevalonic acid in urine was determined by gas chromatography-mass spectrometry in 14 patients.
Results: Median age at disease onset was 1.5 months (range birth–30 months). Clinical characteristics were very diverse: all patients had periodic fever, 25/26 - peripheral lymphadenopathy, 23/26 -

abdominal pain, 20/26 – nausea/vomiting, 19/26 – diarrhea, 9/26 – hepatomegaly, 11/26 – splenomegaly, 6/26 – hepatosplenomegaly, 10/26 - respiratory failure. Rash was seen in 12/26 patients and one patient had periorbital edema and hyperemia during attacks. Myalgia, arthralgia were observed in 14/26. Oral ulcers were noted in 15/26 children. 8/26 patients had neurological involvement including two patients who suffered from epilepsy, one - from ataxia and cerebellar cortical atrophy and one from paraparesis with myopathic syndrome. All patients had increased laboratory inflammatory markers (C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Also most patients had a variety of hematologic abnormalities: neutropenia was present in 2/26 patients, thrombocytopenia – in 4/26, macrophage activation syndrome –in 1/26. In 3/14 patients tested increased level of mevalonic acid, and in 5/14 - of mevalonate lactone in urine were noted. In our cohort the p.Val377Ile mutation was the most common *MVK* gene mutation. However, we have identified 10 novel *MVK* mutations and four of them occurred twice in our cohort. 23/26 patients are currentlyy receiving anti-IL-1 therapy, with complete remission in 17/23 and partial in 3/23.

Conclusion: MKD symptoms can be variable and sometimes atypical, which requires physician's awareness. In our cohort of MKD patients anti IL-1 therapy was highly effective.

Disclosure of Interest
None declared

P041

A rare rheumatological cause of death secondary to aortic calcification: a case report of singleton-merten syndrome

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Pediatric Rheumatology 2020, **18(Suppl 2):**P041

Introduction: Singleton-Merten syndrome (SMS) is a Type 1 Interferonopathy characterised by skeletal, dental and cardiac abnormalities classically caused by a gain-of-function mutation in the interferon-induced helicase C domain-containing protein 1 (IFIH1) gene.
Objectives: We describe a case of SMS leading to death at 13 years secondary to rapidly progressive aortic calcification.
Methods: Case report
Results: A white-British girl of non-consanguineous parentage presented at 5 years of age with calcaneovalgus and hallux valgus deformities, proximal muscle weakness and stiffness of the joints without synovitis or swelling. A heliotrope rash was present with prominent nail fold capillaries and ichthyoses vulgaris but no Gottron's. Dentition was abnormal with dentine hypoplasia, unformed roots of permanent teeth and crowns of abnormal morphology. Routine echocardiogram showed asymptomatic pericarditis and screening of her eyes revealed severe glaucoma causing unilateral amblyopia. Autoantibodies were abnormal with positive anti-nuclear (hep2, Elisa 4.4), anti-double stranded DNA (88iu/ML), rheumatoid factor (97 IU/l) and anti-cardiolipin IgG (73 U/ml) antibodies.
A tentative diagnosis of a connective tissue disease overlap with juvenile Systemic Lupus Erythematosus was given with glaucoma likely secondary to previous untreated uveitis. Treatment was commenced with prednisolone, methotrexate, hydroxychloroquine and low-dose aspirin. She responded well and surgery for glaucoma was also successful. Two years on, she developed anterior uveitis and worsening skin rashes with livedo reticularis, chilblains and vasculitic lesions. She was commenced on infliximab and remained clinically well for the following three years with CRP, ESR, autoantibodies and complement factors repeatedly within normal limits.
Aged 11 years, a diagnosis of SMS was confirmed via Deciphering Developmental Disorders with trio whole exome sequencing identifying a de novo mutation of the IFIH1 gene (c.2465 G>A). Around this time, she was noted to have an ejection systolic murmur. Echocardiogram and cardiac magnetic resonance imaging confirmed aortic stenosis with mild-moderate left ventricular outflow tract narrowing.
Over the following two years, she continued on infliximab with no evidence of an ongoing inflammatory process. Regular echocardiograms were stable and she remained asymptomatic. However, during a six-month interval, the aortic stenosis worsened significantly. Imaging showed unexpected and severe calcification of the aortic annulus, aortic cusps and the aortic wall up to the level of the descending aorta. Our case was discussed at length but the extent and severity of calcification was not amenable to cardiac intervention and the decision was made for palliative care. It was agreed to continue her disease-modifying medications to avoid a flare of inflammation and for symptomatic control. Sadly, three months after the aortic calcification was first noted, our patient collapsed suddenly and died later that day.
Conclusion: SMS is a rare condition with fewer than twenty affected families reported. Twelve cases are reported to have succumbed to aortic calcification at variable ages from 6 to 60 years. Early treatment with aortic valve replacement has been reported. There is little known about the mechanism of arterial calcification in the context of SMS, and control of inflammation does not appear to influence progression.
We report this case to highlight consideration of SMS in a child with features of an inflammatory disorder, glaucoma, abnormal dentition, lower limb deformities and cardiac disease. Our case highlights that aortic calcification in SMS can progress unexpectedly rapidly and lead to early death, despite regular cardiac monitoring and good inflammatory control of disease.

Disclosure of Interest
None declared

P042

Correlation of a whole-body MRI derived radiological activity index with disease activity in chronic nonbacterial osteomyelitis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P042

Introduction: Due to the lack of validated diagnostic criteria, chronic nonbacterial osteomyelitis (CNO) remains a diagnosis of exclusion. Whole-body MRI (WB-MRI) has become one of the mainstays in supporting the diagnosis of CNO.
Objectives: Based on the recently developed ChRonic nonbacterial Osteomyelitis MRI scoring tool (CROMRIS), in order to quantify the bone involvement at multiple sites in CNO patients, we developed a Radiological Activity Index (RAI-CROMRIS).
Methods: WB-MRI images were assessed using the CROMRIS. Parameters included in our RAI-CROMRIS were: bone marrow hyperintensity, signal extension, soft tissue/periosteal hyperintensity, bony expansion, vertebral collapse. These parameters were evaluated for each bone unit yielding a score from 0 to 7. A total score was obtained adding up the scores of all bone units. We analyzed 76 treatment-naïve patients with CNO collecting clinical and radiological findings at baseline. Clinical disease activity was evaluated using a physician's global assessment (PGA). Fourty-six of 76 patients were evaluated at 6 and 12 months after baseline.
Results: A significant correlation of the RAI-CROMRIS with the PGA (r_s=0.32; p=0.0055), in particular with presence of functional impairment and increased inflammatory markers was found at baseline. During the follow-up, the RAI-CROMRIS decreased significantly (p=0.0039) from a median of 17 (IQR 12-26) at baseline to a median of 12 (IQR 6-20) at 6 months and remained stable at a median of 11 (IQR 4-20; T12 vs baseline p=0.0030 and T12 vs T6 p=0.52) at 12 months. A significant correlation between the RAI-CROMRIS and the PGA was observed at baseline and during follow up with a moderate correlation at T0 (p=0.0044; r_s=0.41) and a weak correlation at T6 (p=

0.025; r_s=0.33) and T12 (p=0.010; r_s=0.38). Patients who subsequently received bisphosphonates had higher baseline RAI-CROMRIS (median 20, IQR 13-42) compared to that of patients who received other treatments (median 12, IQR 8-18; p=0.0078). In patients who received bisphosphonates, a decrease of the RAI-CROMRIS was observed from a median of 20 at baseline (IQR 13-42) to a median of 15 at T6 (IQR 4-25) (p=0.0032).
Conclusion: The RAI-CROMRIS provides a measure of the overall radiological burden of disease in individual CNO patients. It is well correlated with clinical and laboratory measures of disease activity and it shows significant short-term changes following treatment with bisphosphonates. This tool can be used in clinical practice and clinical trials after validation.

Disclosure of Interest
None declared

P043

Observation and treatment experience in children with multisystem inflammatory syndrome, associated with covid-19 in Morozov children's city clinical hospital of the Moscow City healthcare department

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Pediatric Rheumatology 2020, **18(Suppl 2):**P043

Introduction: COVID – 19 infection in children is commonly evaluated as mild or asymptotic.
However, from the start of May 2020, there was published some reports from Europe and North America describing children and teenagers, with multisystemic inflammatory syndrome characterized as Kawasaki-like syndrome. These patients required ICU hospitalization.
Hypothesis about connection this syndrome with COVID-19 was based on mostly positive serology tests.
Objectives: Boys to girl's ratio was 2:1, median age = 5 (± 4,5). All patients met Kawasaki-like symptoms (fever more than 5 days, rash, scleritis, cheilitis, lymphadenopathy, edema of palms and feet), also 6/9 children had meningeal symptoms, 2/9 had acute renal injure. All patients had myocarditis.
Methods: We observed 9 children with: multisystem inflammatory syndrome diagnosis, which were stated in may 2020. Our evaluation covers clinical symptoms, general blood test, CRB, PCT, ferritin, Il-6, CT, ultrasound.
Results: According to laboratory tests most symptoms was similar to systemic inflammatory diseases. All patients had increase of CRP in 9 times or more than normal, PCT was positive in 7/9 cases, increased ferritin from 62,7 to 1175 μg/l. Hypoalbuminemia was common symptom in all cases (18-24.8 g/l). Leukocytosis in 5/9 children (55,5%), thrombocytopenia in 4/9 cases (64-108*10^9/l), anemia in 4/9 cases (44.4%). In 8/9 (88.8%) children detected increased troponin (36 pg/ml - 899 pg/ml).
5/9 patients were undergoing through lumbar puncture, 3 out of this 5 had aseptic meningitis.
COVID IgM – positive -1/9; COVID IgG – positive 9/9 children.
Results of diagnostic interventions: pericarditis – 5/9, 1/9 – coronary alterations (ectasia LCA and RCA), pleuritis – 7/9, ascites – 4/9.
Treatment – all patients received antibacterial therapy, IVIG, steroids – 4/9, 1 patient was on hemodialysis. 1/9 patient required pleural puncture.
Conclusion: Multisystemic inflammatory syndrome patients require complex treat with help of various specialists (rheumatologists, cardiologists, surgeon, neurologists, resuscitationist).
No described strategy of management of such patients is available. Our experience declares that it's rational to administrate antimicrobial treatment (ceftriaxone, vancomycin, linezolid, sulperazone, cefepime, amikacin, meropenem), IVIG with steroids.

Disclosure of Interest
None declared

P044

Novel mutation in psme4 involved in proteasome-associated-autoinflammatory-syndrome

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Pediatric Rheumatology 2020, **18(Suppl 2):**P044

Introduction: Proteasome-associated-autoinflammatory-syndrome (PRAAS) is an extremely rare congenital interferonopathy with high morbidity and mortality. In this disease, autoinflammation is caused by dysfunction of the ubiquitin-proteasome-system. So far, PRAAS-causing mutations have been restricted to genes encoding components of the proteasomal core complex and assembly helpers. These mutations may be both monogenetic (homozygous or compound heterozygous) as well as digenic.
Objectives: The aim of this study is to identify further components of the ubiquitin-proteasome-system involved in autoinflammation.
Methods: Experiments were conducted using whole blood and primary fibroblasts from a clinical index patient, the patient's mother and unrelated disease and healthy controls.
Results: In this work, we could detect a significantly increased expression of interferon-stimulated-genes in a clinically confirmed PRAAS patient who was devoid of genomic alterations in any of the previously published PRAAS-associated genes. Remarkably, patient's fibroblasts recapitulate diseases hallmarks including perturbed protein homeostasis, as evidenced by reduced proteasome activity and concomitant accumulation of ubiquitin-protein conjugates. Trio exome sequencing allowed us to identify in this subject a paternally inherited variant affecting the proteasome activator PSME4- as well as two maternally inherited variants within the ubiquitin-E3-Ligase HECW2 and the amino acid sensor kinase EIF2AK4 (also referred to as GCN2). *In silico* predictions classify these variants as disease-causing.
Interestingly, cells carrying these heterozygous variants failed to express the corresponding unaffected alleles at protein level, suggesting a dominant negative mode of action. Finally, and similarly to other PRAAS patients, proteasome impairment in our subject was associated with an exhausted unfolded protein response in the IRE1α-, ATF6- and PERK-pathways.
Conclusion: Thus, we propose that mutations in genes encoding proteasome activators and/ protein ubiquitination can also cause multigenic PRAAS.

Disclosure of Interest
None declared

P045

Real-life evaluation of recommendations regarding resistant FMF by pera research group-a delphi consensus survey

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Pediatric Rheumatology 2020, **18(Suppl 2):**P045

Introduction: Familial Mediterranean fever (FMF) is a serious condition with no clear diagnosis and management protocols.
Objectives: To review the current landscape of FMF diagnosis, quality measures for follow-up, decision making for management and settling a protocol for prolongation of biologic treatment intervals and take advantage of an expert panel consensus
Methods: A total of 14 pediatric rheumatologists (PR) across Turkey expertised in the management of FMF participated to the study. A detailed literature search was performed by a fellow and systematic review of the literature was executed. A shortlist of 15 key points were selected by 3 PRs. Key-points were converted to 78 statements with a 9-point Likert scale and a 3-round modified Delphi panel was assessed. A sum of 75% or above agreement was accepted as consensus.
Results: Consensus was reached on 46 statements. Panelists agreed that the screening periods of patients with FMF should not be longer than 6 months of duration, SAA test at each visit was accepted as mandatory in patients resistant to colchicine, had subclinical inflammation and had family history of amyloidosis. There was no consensus regarding to routine SAA, protein/creatinine in spot urine, sedimentation testing at each visit. 64 % of the panellists found scoring systems as applicable at each visit. There was unity among panellists regarding commencing colchicine at the time of diagnosis and starting the drug to the patients with subclinical inflammation, ordering genetic analysis when clinical findings support FMF, starting colchicine when pathogenic mutations plus nonspecific findings and family history of amyloidosis are present. Response to colchicine treatment was defined as decrease in duration and number of attacks and was accepted in consensus. Defining colchicine resistance as presence of 6 or more attacks/year or ≥3 attacks in 4-6 month period or elevation of 2 of the acute phase reactants in incomplete attacks were confirmed with consensus of the panellists. All participants confessed starting biological agents to resistant FMF patients and patients with amyloidosis. Presence of adverse reactions to colchicine was not accepted as a reason for initiating biologics in consensus. Except cost of the biologic agents; efficiency, ease of use, treatment adherence, accessibility and presence of adverse events were accepted in consensus as factors choosing biologic agents. Decrease in duration and number of attacks and ceasing of subclinical inflammation was accepted as response to biologics, but scoring systems applicable at each visit for evaluating response were not accepted in harmony. In patients whose attacks went in to remission with biologics, prolongation of the duration of application of biologics were considered and asked to the panellists, they collectively welcomed this statement. All participants voted in favour of curtailing the frequency of injections in patients who are in remission both clinically and in laboratory means during last six months of biologic treatment.
Conclusion: Even though recommendations are present for diagnosis, screening and treatment of patients with FMF, use of these issues in real life is not so clear. Herein, data concerning applicability and relevance of these points and prolongation of biologic intervals were evaluated with PRs who are dealing with large number of FMF patients

Disclosure of Interest
None declared

P046

Osteoporosis in enthesitis related arthritis

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Introduction: Osteoporosis is seen in all subtypes of juvenile idiopathic arthritis (JIA). The loss of bone mass and microarchitectural abnormalities lead to an increased risk of fractures with associated morbidity.
Objectives: Our objective is to describe the bone involvement observed in our patient population of JIA in its Enthesitis-related arthritis form (ERA) and to determine the relative effects of the activity of the disease, corticosteroids and physical activity on the development of osteoporosis in JIA.
Methods: This is a retrospective monocentric study that collected patients with ERA according to ILAR criteria, in whom a bone densitometry was performed by dual-energy x-ray absorptiometry (DEXA, in order to determine their bone status. An assessment of the factors linked to the disease and to the environment which could influence the modification of the bone architecture was also carried out.
Results: We enrolled 22 patients (sex ratio M / F 10); average age of onset of the disease 13.1 years. The clinical presentation was purely axial in 4 patients, peripheral in 12 patients and enthesitic in 4 patients. The average BASDAI score was 55.3 / 100, the average MASES score was 2.7. Seven patients were on general corticosteroid therapy and only 9 of our patients participated in regular sports activities. The results of the bone densitometry measured concluded that normal bone mineral status was found in 13.3%, osteopenia was objectified in 20% of patients and osteoporosis in 36.7%.
An agreement was assessed between the absence of sports activity and osteoporosis ($p = 0.01$) as well as osteopenia ($p = 0.03$). A high BASDAI is strongly associated with osteoporosis ($p = 0.04$). No association was observed between BASDAI and osteopenia ($p = 0.3$). No correlation was observed between the MASES score and osteoporosis ($p = 1.2$). No link was observed between taking corticosteroid therapy and bone architecture abnormalities ($p = 0.8$).
Conclusion: Osteoporosis is frequent in ERA. Like the adult onset of spondylarthritis, low bone mass is influenced by disease activity and sedentarity.

Disclosure of Interest
None declared

P047

The cytokine profile in the patients with chronic non-bacterial osteomyelitis, juvenile idiopathic arthritis, insulin-dependent diabetes melitus and healthy controls: the data of prospective cohort study

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Pediatric Rheumatology 2020, **18(Suppl 2):**P047

Introduction: Chronic non-bacterial osteomyelitis (CNO) is an autoinflammatory disorder of bone, which primarily affects children and adolescents. Dysfunction of the immune system as well as cytokine dysbalance is a key point for CNO pathogenesis.
Chronic non-bacterial osteomyelitis (CNO) is an autoinflammatory disorder of bone, which primarily affects children and adolescents. Dysfunction of the immune system as well as cytokine dysbalance is a key point for CNO pathogenesisChronic non-bacterial osteomyelitis (CNO) is an autoinflammatory disorder ofbone, which primarily affects children and adolescents. Dysfunction of the immune system aswell as cytokine dysbalance is a key point for CNO pathogenesis.
Objectives: The aim of our study was to evaluate the cytokine levels in the pediatric CNO patients and compare to other immune-mediated diseases and healthy controls.
Methods: In the prospective study 42 children with CNO were included. For comparison plasma of non-systemic juvenile idiopathic arthritis (JIA) patients (n=28), insulin-dependent diabetes mellitus (IDDM) patients (n=17) and healthy controls (HC, n=30) with similar age were collected. In each CNO patients and comparison groups the levels of 14-3-3-η protein, S100A8/A9 protein, interleukine - 4 (IL - 4), interleukine - 17 (IL - 17), interleukine - 18 (IL - 18), interleukine - 1β (IL - 1β), tumor necrosis factor-α (TNF-α) were measured by ELISA assay. We used the chi-squared test or the Fisher's exact test,

Kruskall-Wallis test, Spearman's correlation analysis and univariate and multivariate linear regression and discriminant analysis.
Results: All studied cytokines in the CNO patients were higher compare to controls and IDDM, 14—3-3 protein, IL-18, IL-4, IL-17, IL-1β and TNF-α were less than in JIA patients (table 1). In discriminant analysis ESR, 14-3-3 protein, S100A8/A9, IL-18, IL-4 and TNF-α can discriminate CNO from JIA and 14-3-3 protein, S100A8/A9, IL-18, IL-17, IL-4 and TNF-α can discriminate CNO from other diseases and HC. Table 1. Cytokine levels in immunocompromised patients and healty controls

Conclusion: our data indicate the role of cytokine imbalance in the pathogenesis of CNO. The increased level of pro-inflammatory cytokines confirms the role of monocyte-driven inflammation in CNO patients. More research is needed to validate the role of cytokines as biomarkers and potential therapeutic targets for CNO.

Trial registration identifying number: This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001)

Disclosure of Interest
None declared

Table 1 (abstract P047). See text for description

Parameters	CNO (n=42)	JIA (n=28)	IDDM (n= 17)	HC (n=30)	p	p1	p2	p3
14-3-3η, pg/ml	20.2 (18.4; 27.1)	53.1 (39.7; 60.7)	-	15.2 (10.2; 17.9)	0.00001	0.0000001	-	0.000006
Calprotectin, pg/ml	5.9 (5.2; 6.7)	3.6 (3.1; 15.0)	-	0.54 (0.3; 0.8)	0.00001	0.115	-	0.0000001
IL-6, pg/ml	126.3 (112.9; 137.5)	132.5 (117.4; 142.9)	16.3 (10.4; 20.0)	4.1 (2.1; 5.4)	0.00001	0.160	0.0000001	0.0000001
IL-18, pg/ml	270.1 (201.1; 316.1)	388.4 (373.9; 405.1)	49.7 (39.4; 70.9)	119.4 (115.6; 128.4)	0.00001	0.000003	0.0000001	0.0000001
IL-4, pg/ml	15.3 (11.5; 18.2)	18.7 (16.2; 20.2)	0.004 (0.0; 0.1)	0.0002 (0.0; 0.02)	0.00001	0.003	0.0000001	0.0000001
IL-17, pg/ml	83.2 (71.1; 97.3)	99.1 (87.4; 115.8)	1.5 (1.0; 2.4)	0.33 (0.2; 0.4)	0.00001	0.004	0.0000001	0.0000001
IL-1β, pg/ml	47.4 (42.0; 51.3)	70.8 (65.3; 73.7)	3.3 (2.5; 7.7)	0.95 (0.7; 1.3)	0.00001	0.0000001	0.0000001	0.0000001
TNF-α, pg/ml	19.4 (17.9; 21.3)	23.1 (20.2; 25.9)	2.1 (1.5; 5.1)	0.9 (0.6; 1.3)	0.00001	0.0008	0.0000001	0.0000001

P048

Osteocalcin: assessing bone mineral density in patients with juvenile idiopathic arthritis

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Introduction: A principal manifestation of juvenile idiopathic arthritis (JIA) is the skeletal system alteration. One of the disease complications is a decrease in bone mineral density (BMD) with the possible osteoporosis (OP) formation. The latter can lead to a life quality deterioration and possible disability in adulthood. In rheumatic diseases, BMD impairment contributes to osteoblast function inhibition, especially in patients taking steroids. Therefore, an essential addition to dual-energy X-ray absorptiometry (DXA) in children with JIA is the assessment of biochemical markers of osteosynthesis, which include osteocalcin (OC).
Objectives: We aimed to establish the specificity and sensitivity of OC levels in relation to the DXA data of JIA patients to make an intermediate assessment of BMD without the use of X-ray absorptiometry.
Methods: The BMD data and serum OC levels were estimated in 134 JIA patients (88 girls, 46 boys) aged 5 to 17 years. 24 patients had the systemic form of the disease, 46 of them had oligoarticular form, and 64 had polyarticular form. The mean age was 11.5 ± 0.4 years, and the mean disease duration was 5.2 ± 0.4 years. 64 children (48%) took methotrexate, 70 (52%) took immunobiological drugs (tocilizumab (24), adalimumab (44) and etanercept (2)). Specificity and sensitivity were calculated according to generally accepted formulas.
Results: The reference values of serum OC were 2-22 ng/ml, which were significantly lower than the levels of JIA patients with whom we were dealing. Thus, it was decided to determine the median [5th; 95th procentile] for the OC levels of our JIA patients, in which DXA indices were within the normal range, and establish the sensitivity and specificity of this value. Sensitivity was measured according the formula: Sensitivity = TP / (TP + FN) × 100%, where TP is the number of true positive results in the patient group, FN is the number of false negative results. Specificity was calculated according the formula: Specificity = TN / (TN + FP) × 100%, where TN is the number of true negative results in the patient group, FP is the number of false positive results. The median OC value of JIA patients, in which BMD results were correlated to chronological age, was 26.9 [19.4; 36.9] ng/ml (83 children out of total 134 patients). There were 13 patients with the DXA Z-score ≤ -2 SD and 80 patients with the DXA Z-score > 2 SD among the 93 patients with OC values within the 5th and 95th procentile (19.4-36.9 ng/ml). Based on this, the sensitivity of these OC values was 86%. There were 36 children with negative DXA results and 5 children with positive DXA results (the OC level values exceeded the 95th procentile in more than 3 of them) among 41 children, whose OC values were not in the 5th-95th procentile range (< 19.4 or > 36.9 ng/ml). The specificity of the calculated OC values was 87.8%.
Conclusion: Osteocalcin levels within the 19.4-36.9 ng/ml with a sensitivity of 86% and a specificity of 87.8% correspond to the chronological age-related bone mineral density assessed by the dual-energy X-ray absorptiometry. The obtained data can be useful for the intermediate assessment of BMD without the use of DXA in JIA patients.

Disclosure of Interest
None declared

P049

an ethical dilemma in the time of SARS-COV2: a case report of delayed investigation and management of kikuchi syndrome with secondary Haemophagocytic Lymphohistiocytosis (HLH)

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Introduction: Kikuchi syndrome, histiocytic necrotising lymphadenitis, is a rare and idiopathic disorder of the lymph node. Prompt investigation is required to rule out malignancy and to reduce complications including life-threatening secondary HLH[1].
Objectives: Case report of a 14 year old girl with Kikuchi syndrome and features of secondary HLH presenting during the 2020 SARS-COV2 pandemic
Methods: A 14 year old girl presented with a 5 week history of cervical lymphadenopathy and febrile neutropenia. She had no features of systemic disease including arthritis, serositis and vasculitis. Initial blood tests revealed a pancytopenia. Bone marrow aspirate was negative for leukaemia and HLH but on-going blood monitoring showed an increasing inflammatory process. Infection

screening including CMV, EBV, hepatitis, HIV and blood cultures were negative as was an auto-antibody screen. CT chest was unremarkable. MRI whole body showed significant right sided cervical lymphadenopathy. She was treated with tazocin, vancomycin and amphotericin but the inflammatory markers continued to rise.
An urgent lymph node biopsy was required for diagnosis, which led to concerns about her SARS-COV2 status. She had a negative SARS-COV2 PCR at her referring centre and a normal CT making the diagnosis of SARS-COV2 unlikely. It was felt by the anaesthetic and surgical teams that repeat SARS-COV2 testing was required and that it was unsafe to take her to theatre prior to the results being available. Her excisional biopsy was postponed pending results. During this time her ferritin increased to 16000. She developed an oxygen requirement and an ECHO showed a pericardial effusion. She met HLH HScore 196 and required urgent treatment with steroids. With the underlying pathology unknown this could have led to delayed treatment of a malignancy. She received intravenous immunoglobulin on 2 consecutive days. This afforded some improvement but she continued to have pyrexia, a spreading follicular rash and a ferritin of >10000. She was eventually taken to theatre for lymph node extraction on day 7 of admission and was successfully treated.
Results: The current pandemic has caused unprecedented disruption to healthcare provision worldwide.
Ethical dilemmas have included resource allocation with routine clinical care being postponed to accommodate high volumes of emergency work and the balance of providing care for patients while limiting risk to healthcare professionals. In this case emergency surgery was delayed to limit risk to medical staff which led to acute and potentially life threatening deterioration in this patient. One negative SARS-COV2 swab and a normal CT chest had to be balanced against the perceived risk of SARS-COV2 spread to multiple members of staff. This case puts the beneficence for the patient in direct conflict with the management of risk to professionals and makes us ask: how far does the ethical principle of non-maleficence apply to all those involved?
Conclusion: This case illustrates one of numerous patients whose inpatient management was delayed during the SARS-COV2 pandemic; in addition to cancellations of elective surgeries, deferred preventative measures and outpatient appointments. This patient made a full recovery; she expressed understanding for the delay in management and gratitude to her medical team. The question still remains: was this a risk worth taking?

Disclosure of Interest
None declared

P050

Management strategies for children with rheumatic diseases during the covid-19 pandemic

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Pediatric Rheumatology 2020, **18(Suppl 2):**P050

Introduction: The SARS-COV-2 infection (COVID-19), which causes severe acute respiratory syndrome, was accepted as a pandemic by the World Health Organization on March 11, 2020, resulting in 4.258.666 confirmed cases of COVID-19 (World Health Organization. Coronavirus disease 2019 Situation reports. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports, last access 14 May 2020).
Patients with rheumatic diseases are known to have increased infectious risks due to a general disorder of the immune system specific to the disease itself and it is also associated with the use of immunosuppressive drugs.
Since immunosuppression is WHO-defined risk factor for a more severe course of COVID-19, the patients with pre-existing rheumatic diseases who used immunosuppressive and biological therapies assume to have heightened vulnerability to develop COVID-19. The prevalence of COVID-19 in children with rheumatic diseases is lacking in literature. Moreover, we do not clearly know the effect of pre-existing rheumatic disease, immunosuppressive and biological therapies on COVID-19 course in children. Here, it is aimed to determine the frequency and course of COVID 19 of patients who use biological agents for childhood rheumatic diseases and to detect of risky patients who need to withdrawal of their treatment.
Objectives: To determines the frequency and course of COVID 19 of patients who use biological agents for childhood rheumatic diseases.
Methods: A telephone-based survey was administered in Turkey to 52 patients who received biological therapies for rheumatic diseases from the 11th of March to 13th of May 2020. The survey included demographics, clinical information of patients about rheumatic disease, the incidence of COVID-19, the presence of definite or possible COVID-19 in the household, the frequency of respiratory symptoms of suspected viral infections and the course of rheumatic disease.
Results: All patients were treated with biological therapies (26 etanercept, 17 canakinumab, 6 adalimumab, 2 rituximab, 1 infliximab), about 80% of patients were receiving conventional disease-modifying drugs. None of the patients using biological therapies had any possible or definitive COVID-19. Fifty have maintained stable disease activity without experiencing flare-ups.
Conclusion: Our preliminary outcomes are hopeful for potentially more susceptible patients to COVID-19. Children with rheumatic diseases receiving biological therapies should be monitored for the risk of COVID-19, but it is reasonable not to withdrawal of their treatment to avoid flare-ups of rheumatic diseases.

Disclosure of Interest
None declared

P051

Multisystem inflammatory syndrome with features of atypical kawasaki disease: a case report from iran during the covid-19 pandemic

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Pediatric Rheumatology 2020, **18(Suppl 2):**P051

Introduction: Although Kawasaki disease (KD) is the most common self-limited systemic vasculitis in pediatrics, the exact etiology of the disease and its association with other diseases and pathogens is still unknown. In order to achieve a better understanding and management of the disease, documentation and reporting of atypical cases is justified, particularly with the growing number of children with inflammatory syndrome with clinical features simulating KD during the ongoing COVID-19 pandemic.
Objectives: Based on similar reports of KD from numerous countries with temporal relation to COVID-19 infection in the community, it is essential for general pediatricians to be on alert for such atypical presentations and early referral to tertiary care should be considered as appropriate.
Methods: Here we present a case of an atypical case of KD presenting as Multisystem Inflammatory Syndrome (MIS) during the COVID-19 pandemic.
Results: The patient is a 7-year-old girl who developed fever (39°C) and erythematous multiform rash on the abdomen and along with erythema and edema on the extremities. Laboratory evaluation revealed neutrophilia and lymphopenia along with elevated C-reactive protein, erythrocyte sedimentation rate, troponin, lactate dehydrogenase, ferritin, and D-dimer. Although the patient didn't fore fill the KD criteria, based on approved guidelines and approaches regarding atypical KD and Multisystem Inflammatory Syndrome in Children (MIS_ C) during the COVID-19 pandemic, intravenous immunoglobulin along with aspirin was administered for the patient. The patient's symptoms resolved with an uneventful post-discharge course.

Conclusion: Early diagnosis and treatment of patients meeting full or partial criteria for KD are critical to preventing end-organ damage and other long-term complications, such as myocarditis and coronary involvemt, especially during times of public crisis and global health emergencies, such as the novel coronavirus pandemic.

Disclosure of Interest
None declared

P052

The impact of covid-19 pandemic on pediatric rheumatology patients under immunosuppressive therapy: a single-center experience

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Pediatric Rheumatology 2020, **18(Suppl 2):**P052

Introduction: During severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) disease 2019 (COVID-19) pandemic, several drugs already with essential roles in rheumatology practice emerged as promising treatment alternatives with encouraging results. On the other hand, dysregulation of innate immunity and virus-host interactions in the etiopathogenesis serve a major concern for patients in an immunosuppressive state or under immunosuppressive treatment.
Objectives: This study set out to determine whether COVID-19 showing a milder course in children entails a risk for patients with rheumatic diseases in terms of immunosuppressive therapy either disease-modifying anti-rheumatic drugs (DMARDs) or biologic disease-modifying anti-rheumatic drugs (bDMARDs).
Methods: Telephone-survey was administered by conducting interviews with the parents and inviting them to participate. A message containing a link to the questionnaire was sent to their phones simultaneously. The medical records of the patients were reviewed for gathering information about demographic data and clinical follow-up.
Results: Patients who were followed up with immunosuppressive treatment (n=439) were attempted to be contacted between 1 May 2020 and 15 May 2020. The diagnostic distribution of patients who were accessible and eligible for the study was as follows: juvenile idiopathic arthritis (JIA) (n = 243, 58.7%), autoinflammatory diseases (n = 109, 26.3%), autoimmune connective tissue diseases (n = 51, 12.3%) and vasculitis (n = 11, 2.7%). In the entire cohort, mean age (at the study) was 12 ± 4.7 years and 54.1% (n=224) of the patients were female. We identified that one patient with seronegative polyarticular JIA, receiving methotrexate and leflunomide has been diagnosed with COVID-19. Table 1 details the survey results.
Conclusion: In our cohort consisting of patients who received DMAR Ds and bDMARDs for various rheumatological diseases, we identified that one patient has been diagnosed with COVID-19. None of the patients, including the patient diagnosed with COVID-19, had any severe symptoms. More than half of the household contacts have not been required to attend a hospital because they were asymptomatic. Since similar complaints were encountered in the course of rheumatic diseases, the hospital attendance rate was low among patients who had complaints such as arthralgia, myalgia, and fever during the pandemic process and no history of contact. The findings of this study support the idea that COVID-19 rarely causes serious disease in children and the use of immunosuppressive therapy does not pose an additional risk in patients with rheumatic diseases.

Disclosure of Interest
None declared

Table 1 (abstract P052). Telephone Survey Results

Analyzing Survey Data	Results, n(%)
Symptoms	
Fever	20 (4.8)
Non-productive cough	8 (1.9)
Sputum production	-
Sore throat	9 (2.2)
Rhinorrhea	3 (0.7)
Fatigue	8 (1.9)
Arthralgia,	49 (11.8)
Myalgia	15 (3.6)
Anosmia/dysgeusia	3 (0.7)
Dyspnea	1 (0.2)
Headache	-
Nausea/vomiting	2 (0.5)
Diarrhea	8 (1.9)
Rash	4 (1)
Confirmed diagnosis in the family (household contact)	17 (4.1)
History of contact with confirmed or suspected cases	18 (4.3)
Attendance at a hospital emergency department for suspicion of COVID-19	9 (2.1)
History of contact (n)	6
Computed tomography for COVID-19	4 (0.9)
History of contact	3
Consistent with COVID-19	-
Pharyngeal swab test	9 (2.1)
History of contact	6
Positive for COVID-19	1
Treatment interruption during the outbreak	59 (14.3)
Concern about an increased risk	16 (27.1%)
Trouble in medicine supply	14 (23.7%)
Inability to reach the healthcare provider or health institution	29 (49.2%)

P053

A meta-analysis of sex bias in covid-19

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Introduction: A striking anecdotal feature of the Coronavirus disease 2019 (COVID-19) outbreak, caused by the novel severe acute respiratory syndrome coronavirus SARS-COV-2 is the difference in morbidity and mortality between the sexes. In contrast to the female

preponderance seen in many autoimmune diseases, there appears to be a male sex bias in COVID-19 deaths and intensive treatment unit (ITU) admissions.
Objectives: We present a meta-analysis of 206,128 globally reported cases, in order to determine whether males are statistically more susceptible to severe disease outcome from COVID-19 than females.
Methods: A search of government websites and published literature was performed for reports on COVID-19 cases that included sex as a variable in data describing case number, ITU admission or mortality. Covariates such as lifestyle and comorbidities could not be controlled for as data were available at the level of country summary, but not at the level of covariates for all individuals.
Meta-analysis was performed to estimate an overall proportion of male infected cases with 95% confidence intervals (CI) and to estimate odds ratios (ORs) with 95% CI associated with male sex for ITU admission and death, based on pooled average effect measures that were weighted according to the size and precision of each report. Fixed and random effects models were estimated and are reported. Meta-analyses were performed using R and the "meta" package.
Results: 42 reports were found from across the world, from 01.01.2020 - 30.03.2020. Reports were excluded if they did not report total infections by sex, if they were thought to overlap in reported cases or for containing less than five cases. This left a total of 29 reports from 27 different countries (two included for analysis of ITU admissions only and excluded from case and mortality analysis). For the analysis of case numbers by sex, the 27 reports described 206,128 infections. Five reports included ITU admission by sex, describing 43,075 cases with 1,758 ITU admissions. 12 reports included data on mortality by sex, describing 170,983 cases and 6,961 deaths.
The proportion of male cases with COVID-19 in these reports was only slightly over half at 0.52 (95% CI=0.52,0.53, p=2.3e-97 for fixed effects model; 95% CI=0.50,0.53, p=0.12 for random effects model) demonstrating that males and females have similar number of infections. Male sex associated with an increased risk of ITU admission (OR=2.50; 95% CI=2.25, 2.78; p=3.8e-64 and 7.3e-64 for fixed and random effects models, respectively). Male sex also associated with an increased risk of mortality (OR=1.62, 95% CI=1.54, 1.71, p=5.5e-77 for fixed effect model; OR=1.60, 95% CI=1.41, 1.82, p=7.4e-13 for random effects model). Funnel plots and sensitivity analyses indicated these results were unlikely to be influenced by reporting bias.
Conclusion: We report that although differences do not exist in the rates of infection between sexes, males are more likely to require ITU admission and more likely to die from COVID-19 than females. Important differences in the immune response to infection exist between sexes, which are likely to contribute to the male bias in infectious diseases and the female bias in autoimmunity. An appreciation of how sex is influencing COVID-19 outcomes will have important implications for clinical management and mitigation strategies for this disease and highlights the importance of sex as a variable in all biological research.

Disclosure of Interest
None declared

P054

Kawasaki disease during covid-19 epidemic

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Pediatric Rheumatology 2020, **18(Suppl 2):**P054

Introduction: At the peak of the pandemic, clinicians across Europe have identified clusters of Kawasaki-like disease. Italy was one of the most involved country by COVID-19, mainly in northern regions as Lombardia (37.8% of Italian cases). Verdoni *et al.* reported an outbreak of severe Kawasaki-like disease in Bergamo, a city of Lombardia.
Objectives: To compare incidence and features of patients affected by Kawasaki disease (KD) in the last two years in Naples.
Methods: Retrospective analysis of patients diagnosed by KD in two main pediatric centres in Naples during the first four-month period (January-April) of the years 2019 (group 1) and 2020 (group 2). Diagnosis of KD was defined according to the 2017 criteria of the American Heart Association, including both the classic and incomplete types.
Results: The number of cases is similar in the two groups: 12 patients in group 1 (10 males, 2 females) and 13 patients in group 2 (7 males, 6 females). It is evident a different ratio of males to females, respectively 5:1 and 1,1:1. Average age at onset was 20.5 months in groups 1 (range 3-68 months) and 23 months in group 2 (range 4-65 months). Typical form is most represented in both group: 10/12 (83%) in group 1, 10/13 (77%) in group 2. Mean value of the inflammatory indexes ferritin and CRP resulted higher in group 2 ($p \leq 0.05$): ferritin 317 ng/ml and CRP 134 mg/l versus ferritin 200 ng/ml and CRP 73 mg/l. MAS was not diagnosed in any of the patients. According to Italian Health Ministry guidelines, only two patients qualified investigations for SARS-COV-2, resulted negative (qualitative serology and nasopharyngeal swab). However, no signs of pneumonia were evidenced by chest X-Ray in group 2. An abnormal echocardiogram (coronary ectasia) was recorded in 4/13 patients (31%) of group 2 versus 1/12 patients (8%) of group 1. Concerning treatment, 3/12 patients (25%) presented IGIV resistance in group 1, 4/13 (31%) in group 2. In Table 1 we reported the main features of these two different cohorts. Not even case of hyperinflammatory syndrome in patients infected by SARS-COV-2 was evidenced.
Conclusion: At the end of May, Campania (region of southern Italy) recorded 2% of Italian cases of SARS-COV-2, with a cumulative incidence of 78.29 by 100000 individuals, versus 867.33 by 100000 individuals recorded in Lombardia. In our region incidence of KD seems not increased. Patients diagnosed with KD during first four months of 2020, including SARS-COV2 time, presented substantially similar features than observed in the previous year. Considering the lower incidence of SARS-COV-2 infection in southern part of Italy, our experience supports the hypothesis that the emerging disease recently described might represent post-infectious inflammatory syndrome different from classic KD.

Disclosure of Interest
None declared

Table 1 (abstract P054). See text for description

	Group 1	Group 2	p value
Number of patients	12	13	NA
Mean age at onset, months (range)	20.5 (3-68)	23 (4-65)	ns
Male	10/12	7/13	$p \leq 0.05$*
Incomplete or atypical Kawasaki disease (%)	2/12	3/13	ns
Mean CRP, mg/dl (+ SD)	73 (± 47)	134 (± 98)	$p \leq 0.05$*
Mean ferritin, ng/ml (+ SD)	200 (± 110)	318 (± 371)	$p \leq 0.05$*
Coronaritis	1/12	4/13	$p \leq 0.05$*
Immunoglobulin resistance	3/12	4/13	ns
Steroid treatment	1/12	1/13	ns

P055

A survey to understand the feelings towards and impact of covid-19 on the households of Juvenile Dermatomyositis (JDM) patients from a parent or carer perspective

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Pediatric Rheumatology 2020, **18(Suppl 2):**P055

Introduction: The COVID-19 pandemic and 'lock down' in the world is potentially a worrying time for everyone. The opinions of families

that are caring for a child/children/young person with chronic disease need to be heard and addressed appropriately.
Objectives: The aim of this study was to gain a better understanding of how they feel about the effects and impact of the COVID-19 lock down on them and their child/children/young person with JDM. We asked parents/carers of JDM patients to complete a questionnaire and add any comments.
Methods: We have approached 139 participants from the Juvenile Dermatomyositis Cohort Biomarker Study (JDCBS)database, with specific consent to approach electronically for research studies. A questionnaire with study summary was sent to participants for their parents/carers to complete by email. The questionnaire wasdesigned and managed through a secure University Software System compliant with data protection. On completion of the questionnaire data were submitted electronically. Parents/carers were informed that we were sending them the questionnaire as their child/children/ young person is part of the UK wide JDM study consent was already present to approach by email for such studies.
The data recorded from the questionnaire will be analysed in relation to demographics. Demographics of the whole cohort of JDCBS participants will be compared between those sent the questionnaire and those who were not. Descriptive analysis will be carried out on the data collected from the completed questionnaires. Median and inter-quartile-range (IQR) of the scores from the cohort will be used. Free text will be analysed using thematic analysis.
Results
Conclusion: This study will provide important additional insights to the Juvenile Dermatomyositis Cohort Biomarker Study during the current time of COVID-19 lock down in the United Kingdom. The answers from the questionnaire will enable us to assess how to support the participants and their families further now and in the future.

Disclosure of Interest
None declared

Table 1 (abstract P055). Comparative data between those sent the questionnaire and those who were not

	JDM cohort	
	Questionnaire sent (n = 136)	**Questionnaire not sent (n = 454)**
Age at diagnosis (years), median (IQR)	7.57 (4.63 – 10.53)	7.46 (4.80 – 10.91)
Current age (years), median (IQR)	18 (12.39 – 22.92)	20.52 (14.60 – 26.35)
Time since diagnosis (years), median (IQR)	9.18 (5.20 – 13.59)	12.05 (6.97 – 17.55)
Female sex, No. (%)	90 (66.18%)	323 (71.15%)
Ethnicity:		
White	106(77.94%)	348 (76.65%)
Black-Caribbean	6 (4.41%)	14 (3.08%)
Black-African	6 (4.41%)	20(4.40%)
Black other	1 (0.74%)	8 (1.76%)
Indian	3 (2.21%)	11 (2.42%)
Pakistani	4 (2.94%)	14 (3.08%)
Bangladeshi	0 (0.00%)	6 (1.32%)
Chinese	0 (0.00%)	1 (0.22%)
Other Ethnic group	10 (7.35%)	32 (7.05%)

P056

A cohort of 20 cases of paediatric inflammatory multisystem syndrome temporally associated with SARS-COV-2 managed by a UK tertiary paediatric centre.

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Pediatric Rheumatology 2020, **18(Suppl 2):**P056

Introduction: In April 2020 in the midst of the COVID-19 pandemic, a UK alert reported seriously ill children presenting with hyper-inflammation and shock with evidence of present or recent SARS-COV2 infection in a proportion of these. The Royal College of Paediatrics and Child Health then proposed a case definition for these named Paediatric Inflammatory Multi-system Syndrome Temporally Associated with SARS-COV2 (PIMS-TS). Presenting features are a spectrum of manifestations of hyper-inflammation mainly overlapping those of Kawasaki Disease and/or Toxic Shock Syndrome.
Objectives: To describe the clinical features and outcomes of cases seen at Leeds Children Hospital.
Methods: We reviewed 20 patients with suspected PIMS-TS between 01/05/20 & 05/06/20. All were managed by a PMIS-TS multidisciplinary team including rheumatology, cardiology, infectious diseases, haematology, intensive care and general paediatrics.
Results: 15 (75%) were male, mean age was 7 years (3 months - 15 years), 6 (30%) were from Black and Asian ethnic groups. All patients were tested for SARS-COV-2 infection by polymerase chain reaction (PCR) on nasopharyngeal swab, stool and endo-tracheal secretions if intubated. Serology samples were taken for all patients and testing is in progress. 2 (10%) patients tested positive for COVID-19 on PCR. All patients except one had no pre-existent conditions. The length of stay was 6.3 days. 6 patients (30%) required short paediatric intensive care admission for inotropes administration; one required intubation. Clinical features were fever (100%), skin rash (65%) -mainly maculopapular-rash resembling Kawasaki disease and less frequently Henoch-Schönlein Purpura , gastrointestinal symptoms (55%), circulatory shock or hypotension requiring fluid resuscitation (45%), conjunctivitis (40%), lips and oromucosal changes (30%), extremities changes -mainly hyperaemia and oedema- (25%), and lymphadenitis (20%). CRP was significantly raised in all cases with the highest CRP value being 0-100mg/L in 30%, 100-150mg/L in 20%, 150-200mg/L in 20%, and >200 in 30%. Other laboratory features included liver dysfunction (84%), raised d-dimer (80%>range 466 - 41758ng/ml), lymphopenia (75%, with 30% <1), hypoalbuminaemia (70%), anaemia (55%), coagulopathy (50%), thrombocytopenia (45%, range 51 - 14710^9/L) and raised ferritin (45%, range 324 - 1104ug/L).
Most had abnormal echocardiograms, showing impaired function and peri-cardial effusions with prominent left coronary artery a common early finding (55%). Troponin and pro-BNP were abnormal in 35% and 80% respectively. 16 (80%) received immunoglobulin therapy at 2g/kg (a single infusion in 75% and twice in 25%), 9 (45%) required IV methylprednisolone pulses (10 mg/kg, usually repeated for three consecutive days), and 6 (30%) patients received both. 19 received aspirin initially at high dose then low dose until follow-up. There have been no deaths and all patients have been discharged home with plan for cardiology and rheumatology follow-up. Preliminary follow-up data are reassuring.
Conclusion: Our cases of PIMS-TS showed a range of hyper-inflammation features overlapping with typical or atypical Kawasaki Disease and/or Toxic Shock in a large proportion of cases. Distinct clinical features included the high prevalence of early cardiologic involvement (mainly myocarditis and pericardial effusions) which responded well to immune-modulatory treatment. Distinct laboratory features included very raised CRP, d-dimer and cardiac enzymes. Treatment rapidly resolved the hyper inflammation in all cases. Short term outcomes were excellent and follow-up for a minimum of 6 weeks is planned for all patients as longer-term cardiac outcomes of the condition remain uncertain.

Disclosure of Interest
None declared

P057

Acral erythematous/cyanotic lesions associated with vessels architecture distortion define a new clinical entity during covid19 pandemic

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Pediatric Rheumatology 2020, **18(Suppl 2):**P057

Introduction: Skin manifestations, in particular acral lesions, commonly identified as "Covid Toes" have been observed during the Covid-19 pandemic. Inflammation of the microcirculation of the extremities has been implicated in the pathogenesis. Whether it is the result of a viral-induced immune response remains to be address
Objectives: Our prospective longitudinal study aims at (1) describing the clinical features of these skin lesions in children, (2) assessing their association with SarsCoV2 infection, (3) performing a throughout investigation of the immune-mediated events and metabolic changes occurring during the disease course
Methods: 15 children referred for erythema pernio-like lesions in April-May 2020 were enrolled at admission (T1) and reassessed 4 weeks later (T2). Evaluation of the lesions was performed combining serial pictures, physical examination, capillaroscopy, dermatoscopy and skin biopsy (in selected cases). SarsCoV2 molecular (nasal and fecal) and serological tests were carried out. Samples were collected to perform immunological (blood) and metabolomic (serum, saliva, urine and stools) studies
Results: All patients (9M:7F, median age 13.2yrs IQR:12.58-14.23) presented with erythematous/cyanotic lesions at the periungual area of the toes. Lesions were bilaterally distributed in 14 (93.3%), heels were involved in 5 (33.3%). Ulceration complicated 1 case, while desquamation developed in 3 (20%) cases during follow-up. A concurrent bilateral involvement of the fingers was observed in 1 subject. Commonly associated signs/symptoms were pain (8, 53.3%), swelling (7, 46.6%), erythema (6, 40%), pruritus (5, 33.3%) and burning sensation (3, 6.6%) of the involved areas. Concomitant sore throat (2), cough (1), diarrhea (1), dysgeusia (1) were rarely reported. Upper respiratory symptoms preceded (~20days) the onset in 3 (20%) subjects. One patient had a past history of acrocyanosis and 5 (33.3%), including 2 siblings, had a family history of autoimmunity.
Three patients had uncertain contact with Covid19 cases. Nasal swab was negative for SarsCoV2 in all patients. Rapid test showed negative IgM/IgG in 7 tested cases. Quantitative serology and molecular analysis for SarsCoV2 in the stools are ongoing. Labs were within normal ranges in all patients at T1, except for a mild elevation of the complement C3 fraction (ave.1.24±0.20, unl=0.95 g/l), notably found in all patients. Dermatoscopy revealed active inflammation in 8 (53.3%) cases and a skin biopsy (obtained in 4) revealed lymphocyte infiltration. Capillaroscopy showed dilated capillaries in 7 (46.6%) and winding organization of vessels in 2 (13.3%) patients. Clinical improvement was observed in all 4 children who received the T2 clinical assessment. Immunological and metabolomic analysis are ongoing
Conclusion: A novel clinical entity characterized by bilateral erythematous/cyanotic lesions of the periungual area of the toes is emerging in children. Microscopic signs of lymphocyte infiltration, evidence of vessels architecture distortion, associated with an increase of the complement C3 fraction suggest an inflammatory process of the micro-vascular compartment in the derma. While our preliminary data do not support an association with SarsCoV2, we cannot exclude that a delayed immune activation in response to a viral infection might play a role in the genesis of these lesions. Our ongoing immunological and metabolomic studies will contribute to clarify the events leading this clinical emerging picture

Disclosure of Interest
None declared

P058

Psychosocial impact of SARS COV-2 outbreak on patients with pediatric onset systemic lupus erythematosus and their caregivers

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Pediatric Rheumatology 2020, **18(Suppl 2):**P058

Introduction: An aggravation of psychological and psychiatric illnesses is expected in patients with pediatric onset SLE (pSLE)and their caregivers during the SARS-COV-2 outbreak.
Objectives: To assess peritraumatic distress, sleep disturbances, abnormalities of affect and psychosocial impact of SARS COV-2 outbreak on patients with pSLE and their caregivers.
Methods: Patients with pSLE (diagnosed at an age of < 16 years)under follow-up in Pediatric Rheumatology clinic of Advanced Pediatrics Center, PGIMER, Chandigarh and their caregivers were recruited in the study. We conducted telephonic interviews and sent the questionnaires through email or WhatsApp® services to the eligible patients and their caregivers.Participants who had difficulty in understanding the questions were excluded. The study was approved by the Institute's ethics committee. The demographic and clinical data were extracted from the clinic files. We used four different questionnaires:
1. Peritraumatic Distress Inventory (PDI)
2. Insomnia Severity Index (ISI)
3. Positive and Negative Affect Schedule short form (PANAS-SF)
4. SLE-COVID-19 stress questionnaire: 23 questions for qualitative assessment of different components of psychosocial well-being during the COVID-19 pandemic. Stress was evaluated under 4 domains: COVID-19 related stress, SLE related stress, hydroxychloroquine (HCQ) related stress, family and social relations related stress.
The data were recorded through telephonic interviews and Google forms® and transferred onto a MS Excel® database and analyzed using the SPSS software
Results: Telephonic contacts were made with 80 patients with pSLE, 2 patients were excluded, 61(78.2%) patients and 55(70.5%) caregivers answered the questionnaire. Two patients experienced a disease relapse during the period of lockdown, telephonic consultations were sought by 10 (12.8%) patients for disease related queries and 3 (3.8%) required hospitalization during the lockdown period. Assessment of PDI revealed that 20 (32.8%) patients and 18 (32.7%) caregivers experienced significant peritraumatic distress. Maximum distress was experienced in the factor domain of life threat (mean score: 9.04±3.3 in patients and 9.2±2.256 in caregivers). Sleep disturbances were noted in almost all patients with SLE and their caregivers as per the ISI. Significant insomnia was noted in 50 (82%) patients and 39 (70.9%) caregivers. Caregivers of patients with minor organ involvement faced significantly more insomnia related problems than caregivers of patients with major organ involvement ($p = 0.013$). High positive affect scores were seen in 65.5% patients and 78.2% caregivers, low positive affect scores were noted in 34.5% patients and 21.8% caregivers.
Higher risk of COVID-19 was perceived by 23% patients, 98.3% participants practiced social distancing, 86.6% patients showed good compliance to therapy, 38% faced difficulties in procurement of medications/HCQ, 78.7% patients and 80% caregivers were aware of HCQ use for treatment of COVID-19, 52.5% patients and 43.6% caregivers knew about side effects of HCQ, 23% patients felt that their regular use of HCQ will protect them from COVID-19, 12% patients thought about giving HCQ to other family members. Female patients with pSLE reported significantly higher HCQ related stress than males (0.313, $p=0.014$). Male caregivers reported significantly higher COVID-19 related stress ($p= 0.001$). Patients with major organ involvement showed higher HCQ related stress ($p= 0.033$).

Conclusion: Patients with pSLE and their caregivers are at risk of psychosocial abnormalities during the COVID-19 pandemic. These patients and their caregivers may benefit from early psychological interventions.

Disclosure of Interest
None declared

P059

What happened in the pediatric rheumatology clinic during covid19 pandemia

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Pediatric Rheumatology 2020, **18(Suppl 2):**P059

Introduction: Since the first reports of cases from Wuhan, COVID-19 was recognized as a pandemic by the WorldHealth Organization (WHO) on March 11th, 2020. Although children tend to experience only mild symptoms, younger previously healthy adults have also succumbed to Covid-19.In Turkey as well as in other countries, the disease was less in children..Patients with any rheumatic disease (eg. juvenile idiopathic arthritis, lupus) are considered at-risk for serious infections due to their immunocompromised state resulting from their underlying immune conditions and use of targeted immune-modulating therapies such as biologics.
Objectives: We aim to share our experience in pediatric patients during pandemia.
Methods: We admitted the patients observed during the pandemic time, from March 2020 to May in the study.The COVID 19 suspected patients was accepted as follow: -The patients admitted to hospital with complaints of fever and acute respiratory infection symptoms (cough and/or respiratory distress) that were not explained for any other reason and who needed hospitalization. -The patients who have at least one of the symptoms of fever, cough or respiratory distress, and have also a history of contact with a patient with COVID-19 infection.The patients diagnosed the cytokine storm syndrome, hyperinflammation were defined as follow: 1) A child presenting with persistent fever and systemic inflammation, with or without evidence of single or multi-organ involvement with additional features. This may include children fulfilling full or partial criteria for Kawasaki disease; 2) Exclusion of any other microbial cause and of flare of a chronic underline inflammatory disease.
Results: We evaluated 1024 patients who applied to our outpatients clinic between 11 March and 15 may were included in the study. Except those patients, 847 appointments were postponed, and the schedule of treatments in 50 patients was adjusted via telemedicine.COVID-19 outbreak caused exacerbation of 25 patients due to lack of medication or delayed drug change.145 (14%) of the all patients admitted to the outpatient clinic were hospitalized, 28 (19.3%) of them were covid suspects.34 patients were hospitalized with suspicion of COVID related situation. While 21 (62%) patients were diagnosed before the pandemic, 13 (38%) patients were diagnosed during the pandemic period.The demographic findings of these 21 pre-diagnosed patients were as follows: 11 females, 52.3%, median age 8.5 years,; median disease duration 2.5 years (range 1–4). Among them, 4.8 % of all patients were on hydroxychloroquine (HCQ), 14.2% on prednisone (≤7.5mg/day), 33% on methotrexate, and 28.5 on any biologic drugs (etanercept, tosilizumab and canakinumab). Eight patients (38%) with familial Mediterranean fever were on colchicine.The sixteen patients (57% of the total population) had swab and or thorax CTconfirmed COVID-19**.** While 25(89.3%) patients had clinical-COVID-19 findings, 3 were asymptomatic. 7 patients (25%) established contact with a COVID-19 patient.The cytokine storm syndrome, hyperinflammation were observed in 13 patients, 1.3 % of all admitted patients. The general characteristic of them were as follows: 4 female, median age 5,5 years who were younger than others (p<0,01). All cases treated with medium-low dose steroid , 5 was treated IVIG, 5 was cyclosporine and Anakinra or Tocilizumab.
Conclusion: The COVID-19 epidemic is now a pandemic and mayaffect millions of people worldwide. The patients with chronic diseases, in particularimmunosuppressed subjects, should be aware of the possible risks linked to the drugs used to treat rheumatologic disorders.Use of social isolation and hygienic measure arefundamental in order to decrease viral spread.

Disclosure of Interest
None declared

P060

The impact of covid 19 on a spanish pediatric rheumatology unit: patient-reported outcomes (pro) utility

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Pediatric Rheumatology 2020, **18(Suppl 2):**P060

Introduction: COVID-19 outcomes remain poorly understood in children with rheumatic diseases.
Objectives: To describe the impact of COVID-19 in a cohort of pediatric patients with rheumatic diseases attended in a Spanish tertiary hospital; assessing the possible effects on the clinical course, functional ability using Juvenile Arthritis Functionality Scale (JAFS) and health-related quality of life (HRQoL), through patient-reported outcomes (PRO).
Methods: A cross-sectional study was conducted. We performed an e-health record review and an e-survey. We collected:Juvenil Arthritis Multidimensional Assessment Report (JAMAR)1, questions related to activity from other autoimmune or autoinflammatory diseases (AIDs), JAFS, HRQoL tests and COVID-19 aspects. We also included questions about medical visits and the ease of contacting with the rheumatologist during the lockdown.
Results: 146 patients received the survey, of which 94 answered, 50 of them did not answer back in time, and 2 refused to participate. Mean age was 14 years. Of the 94 patients who answered the survey, the diagnoses were: 45 (47.9%) non-systemic JIA; 10 (10.6%) childhood-onset Systemic Eritematous Lupus (cSLE); 10 (10.6%) AIDs, including HIDS and OCMR; 8 (8.5%) systemic JIA (sJIA); 4 (4.3%) Behçet disease; 4 (4.3%) vasculitis; 2 (2.5%) Juvenile Dermatomyositis; and 1 (1%) Juvenile Scleroderma.
45.7% of them received biological disease modifying anti-rheumatic drugs (bDMARDs): Adalimumab (ADA) 16%, Tocilizumab (TCZ) 9.6%, Etanercept 7.4% and Belimumab 3.2%, among others. 36.26% of patients were treated with methotrexate and 10,5% with hidroxychloroquine.
Related to SARS-COV2 infection, 12 patients (12.8%) reported being under COVID-19 suspicion. 5 patients underwent PCR, of which 2 of them were positive. Both patients also suffered from pneumonia. One of the children, treated with Canakinumab due to sJIA, was admitted to the Intensive Care Unit and the other one, diagnosed with cSLE, did not required hospitalization. No deaths were registered.

Regarding bDMARDs, 3/12 children (25%) of infection confirmed or suspected group (ICSG) were on treatment (ADA, TCZ and Canakinumab) compared with 39/82 (47.56%) of healthy group. 3 bDMARDs were interrupted by medical judgment, none reported by patient's choice.
Concerning COVID-19 related symptoms, headache was the most frequent (26, 27.7%), followed by cough (19, 20.2%) and fever (14, 14.8%). Only 2 (2.1%) patients reported dysgeusia or anosmia. 49 (52.1%) children were asymptomatic.
16/94 patients (17%) had at least one COVID19- confirmed contact, and 14.9% of the group had at least one COVID19-confirmed closed relative.
The mean physical function test result was 0.79 (12-0), being ICSG results slightly higher (1.08 vs 0.76). In relation to HRQoL assessment, mean score for total group was 3.15 (0-18). The ICSG showed, as well, subtly worse results (4.17) compared to non-infected group (3.04). Mean rating of patient's pain intensity and level of disease activity on a visual analogue scale was 0.97 and 1.33, respectively. 8 patients (8,5%) reported physical impairment and psychological balance due to COVID-19 pandemic, 15 (16%) only physical impairment and 8 (8,5%) only psychological balance.
Conclusion: PRO could be a good option for patient assessment during a lockdown period when the outpatient visit was limited. Some important aspects such as disease activity, functional ability, HRQoL and risk of COVID- 19 could be evaluated.Worse results at physical function and HRQoL tests were detected on ICSG.
Around 50% of children were symptomatic during the pandemic period, so COVID-19 may be underdiagnosed in pediatric patients with rheumatic diseases. However, only 2 of them had a confirmed diagnosis. Therefore, further investigations may be necessary.

Disclosure of Interest
None declared

P061

Kawasaki disease and covid-19 analysis and review

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Pediatric Rheumatology 2020, **18(Suppl 2):**P061

Introduction: The coronavirus disease 2019 (COVID-19) has been an emerging, rapidly evolving situation in China since 2019 then became world pandemic. The first case of severe childhood novel coronavirus pneumonia in China was reported in March 2020, nearly five months after the onset of this disease in Wuhan city, China.
Objectives: The severity differs between adults and children, with a lower death rate and lower severity as age decreases to less than 20 years old. Increased cased of Kawasaki disease (KD) was reported from New York city and some area of Italy and U.K. with almost 6-10 times increased when compared with previous years.
Methods: We conducted this article to compare the clinical characters and laboratory data between KD and COVID-19 in children. A total of 24 COVID-19 children were collected from the literature review and 234 KD cases were from our hospital via retrospective chart review.
Results: We found that patients with KD had higher white blood cell (WBC), platelet, neutrophil percentage, C-reactive protein, procalcitonin, AST and body temperature while COVID-19 had higher age, hemoglobin and lymphocyte percentage. After multiple logistic regression analysis, age, WBC, platelet, procalcitonin and AST provide identical markers for distinguish COVID-19 from KD.
Conclusion: In this pandemic period of COVID-19, clinician should pay attention to COVID-19 children when higher WBC, Platelet, procalcitonin and AST to provide precision treatment with intravenous immunoglobulin for Kawasaki-like disease .

Disclosure of Interest
None declared

P062

The cov-asaki survey from the pediatric tuscany network during covid-19 era

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Pediatric Rheumatology 2020, **18(Suppl 2):**P062

Introduction: At the end of April 2020, national and international Pediatrics scientific societies diffused an alert about a rise in the number of pediatric severe, inflammatory syndrome, coronavirus 2 (SARS-COV-2) related, resembling Kawasaki disease (KD).
Objectives: The Pediatric Rheumatology Tuscany Network worked out the COV-ASAKI survey to track children who received a KD diagnosis in during COVID-19 pandemic in a region hosting 593.606 people aged less than 18 years.
Methods: We retrospectively collected demographics, clinical findings, treatment and outcome of KD children between February 1st to April 30th,2020 comparing the cases in the 2020 index trimester with the same trimesters of the previous 5 years and with the total number in the last 5 years.
Results: Eight children were diagnosed as KD, with an incidence rate of 2.6 per month. Only 1/8 children could be classified as an incomplete KD. Seven were Caucasian and 1 Asiatic, without any underlying disease. Six out eight recovered after one course of intravenous immunoglobulins (IVIG), no specific intensive support was required. One patient needed two IVIG courses and a young girl developed an incipient macrophage activation syndrome (MAS) responsive to a single steroid pulse. The SARS-COV-2 on nasopharyngeal swab, available in 6/8 children, was always negative. Four KD children were sampled for antibodies after recovery and resulted negative. No coronary involvement was reported. From February 1st and April 30th, 1992 nasopharyngeal swabs have been performed to the Tuscan children admitted to the hospitals: 85/1992 (4.3%) resulted positive for SARS COV-2. Fifty serological tests have been performed with 7 children positive results. Considering the previous 5 years, 165 children were diagnosed with KD (incidence 2.7 per month). Fifty-nine were incomplete forms; 3 developed MAS and 1 experienced Kawasaki disease shock syndrome (KDSS). Thirty-eight showed coronary involvement during the acute phase, 11 received steroid pulses and additional 3 biologic therapy. No statistically significant difference regarding the incidence/month was found (RR 1.09, 95% CI 0.52-2.04, p=0.76), neither limiting the analysis to the 45 KD children diagnosed during the same corresponding 3-months of the last 5 years: 3 vs 2.6 (RR 1, 95% CI 0.46-1.98, p=0.96). Chi square analysis with Fisher's exact test correction failed to detect significant differences among the principal outcomes of KD children observed during the COVID-19 time and in the last 5 years: incomplete KD 59 *vs* 1, c^2=1.82; KDSS 1 *vs* 0, c^2=0.04; MAS: 3 *vs* 1, c^2= 3.85; coronary involvement 38 *vs* 0, c^2=2.36. The same results have been detected adjusting the analysis for the 45 cases during the corresponding trimesters of the last 5 years (p=n.s, Fisher's exact test).
Conclusion: In Tuscany, during the COVID-19 pandemic, almost all KD patients, showed a mild disease course and completely recovered without complications. Our data underline the important role of our pediatric network during COVID-19 pandemic. The long-lasting collaboration and the well-structured communication provided a prompt intervention in new KD cases and allowed a comparison between 2020 KD cluster and the previous ones, referring to the Tuscany KD register. A comparison between our data and the results seen worldwide will be helpful to define the multifaceted nature of the pediatric COVID-19 disease and its potential relationship with the KD.

Disclosure of Interest
None declared

P063

Emergence of kawasaki disease related to SARS-COV-2 infection in children, a time-series analysis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P063

Introduction: Kawasaki disease (KD) is an acute febrile systemic childhood vasculitis which has been known to be triggered by respiratory viral infections.

Objectives: Here, we examined whether the ongoing COVID-19 epidemic is associated with an increase of Kawasaki disease.

Methods: We conducted a quasi-experimental interrupted time series analysis over the last 15 years in a tertiary center in a French epicenter of COVID-19.The main outcome was the number of KD cases over time, estimated by quasi-Poisson regression. In the same center, we described the evolution (2005-2020) of hospital admissions from the emergency department and the evolution of the respiratory pathogens identified by nasopharyngeal multiplex PCR (2017-2020). These data were compared with the evolution of daily admissions due to confirmed COVID-19 in the same region, recorded by Public Health France.

Results:

We included 230 patients with KD. On April 2020, we identified a rapid emergence of KD related to SARS-COV-2 (+497% increase, 95% CI [+72; +1082], p=0.0011), starting two weeks after the peak of the COVID-19 epidemic. SARS-COV-2 was the only virus circulating at high levels during this period, and was found in 80% (8/10, SARS-COV-2 positive PCR or serology) of KD patients since April 15th. Among these patients, five had a complete KD and 5 patients had fever with only 3 other KD criteria. The age of KD patients ranged from 18 months to 15.8 years. Six children (60%) had cardiac abnormalities, including one major coronary aneurysm (Z score: 12) and five myocarditis. Six patients (60%) required intensive care and five had inotrop treatment (50%). None required mechanical ventilation, and no fatal outcome was observed. A second peak of KD hospitalizations was detected by the model in December 2009 (+365% increase, 95% CI [+31; +719], p=0.0053), concomitant with the influenza A (H1N1) pandemic.

Conclusion: Health care providers should be prepared to manage an increased surge of patients with severe KD, particularly in countries where the peak of COVID-19 has just been reached.

Disclosure of Interest
None declared

P064

Acral lesions in a pediatric cohort during covid-19 epidemic

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Pediatric Rheumatology 2020, **18(Suppl 2):**P064

Introduction: From the end of March, during COVID-19 epidemic, pictures of chilblain-like lesions with similar characteristics were diffused by social networking among pediatricians and dermatologists in Italy.

Objectives: Describe features of a pediatric cohort affected by acral lesions during COVID-19 epidemic.

Methods: Patients ≤ 14 years old with acral lesions were recruited from Paediatric Department of Santobono-Pausilipon Hospital during the month of April 2020. In addition, information from outpatients was obtained by Italian Federations of General Pediatricians Doctors (F.I.M.P.) through a questionnaire sent to family paediatricians of Campania to collect clinical details of patients with similar lesions managed by territorial primary pediatric care during the same period.

Results: Clinical information was obtained for 25 patients (14 males, 11 females), 18 by FIMP questionnaire and 7 evaluated in Santobono-Pausilipon Hospital. Age range from 2 to 17 years (median 11 years). No one referred contact with COVID-19 individuals, previous history of perniosis or drug intake. Lesions involved acral regions: foot (toes and heels) was mostly involved (92%) with symmetrical involvement in 80% of patients, hands in 2 patients (8%). Lesions presented as erythrocyanotic discoloration of the fingers or toe, erythemato-violaceous papules or macules of foot and hand. Associated symptoms were: erythema in 11 patients (44%), swelling in 10 patients (40%), pain in 6 patients (24%), itching in 6 patients (24%). Among hospitalized patients, all of them performed laboratory assessment: no alteration was found in blood count, inflammatory indexes, hepatic and kidney function, coagulation parameters including D-dimer, LAC, antiphospholipid antibodies, S protein, C protein, homocysteine, autoimmunity. Level of vitamin D resulted insufficient (median value 19,2 ng/ml). No infection was found. Qualitative serological test for COVID was performed resulted negative for IgM in all patients, IgG positive in one patient. 5 patients performed nasal and pharyngeal swab for SARS-COV-2 resulted negative. 2 patients underwent biopsy with similar result: lymphocytic vasculitis with edema and thickening of vessel wall associated to mural and perivascular infiltrate of lymphocytes. Concerning treatment, all patients applied topical emollient. Topic steroid was used in 12 cases outpatient, 1 case inpatient. Heparin cream was mainly used in patients with worsening of lesions after the first week. Improvement of lesions started mostly after one week, in certain cases lesions blistered and ulcerated. Resolution occurred in variable time, up to 4 four weeks from the onset, sometimes with desquamation.

Conclusion: Italy was one of the most involved country by COVID-19 pandemic, extraordinary restricted measures were performed all over the national territory. Up to the May 4, at the end of the first phase, 211.938 cases were assessed, 1.9% of patients in the age 0-18 years. There has been an outbreak of chilblain-like lesions observed mainly in young patients during COVID-19 epidemic, unreported in the previous years. The direct connection with COVID-19 is not demonstrated yet, however a role has been assumed. In most patients of our cohort there was not evidenced a defined correlation with clinical or laboratory findings of COVID-19. Improvement of lesions started mostly after one week spontaneously or with topical treatment. The new life habit due to the lockdown (physical inactivity, barefoot) could play a role mimicking a similar pathway of cold exposition. Further studies are necessary to better understand mechanism underlying COVID-19 in children.

Disclosure of Interest
None declared

P065

Patterns and rate of non-referral to adult care of patients with Juvenile Idiopathic Arthritis (JIA) at a tertiary paediatric rheumatology centre.

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Pediatric Rheumatology 2020, **18(Suppl 2):**P065

Introduction: In cohort studies and transition research there has been little focus on the rate of non-referral of patients with Juvenile Idiopathic Arthritis (JIA) for ongoing adult care and the reasons why this occurs.
Objectives: To determine the characteristics of JIA patients at a tertiary paediatric rheumatology centre not referred for adult care and the frequency of and reasons for non-referral.
Methods: JIA patients in the Royal Children's Hospital (RCH) rheumatology database who turned 18 y.o. between 2012-18 were identified. The medical record of each patient was examined and those who had not been referred for adult care were entered into the study. Data regarding diagnosis, treating clinician and date of first and last RCH visit was collected. Note was made of any documented plan where the last RCH visit was intentionally the final visit for formal rheumatologic care and of subsequent events where it was unintentional.
Results: 177 patients were identified. 63 (~35%) were not referred for adult care. Of these, 24 (38.1%) had been in long term remission and were discharged back to the GP. The commonest JIA subtypes in this group were persistent oligoarticular (45.8%) and systemic JIA (25%). The remaining 39 (61.9%) patients were not referred as they had been lost to clinic follow-up at a mean age of 15.1yr. Of this group, 21 (53.8%) had been in long-term remission. 16 (41%) were lost to follow-up despite having recently active disease or being on clinic-prescribed medication, most frequently in the context of multiple missed and cancelled clinic appointments.
Conclusion: At our centre a significant minority of patients with JIA are not referred for adult care. In many cases this is due to patients being in long-term remission and occurs as either a deliberate decision by the treating rheumatologist or their failure to attend clinic appointments and eventual loss to follow-up. A substantial number of patients are lost to follow-up despite having active disease and/or being on clinic-prescribed medications. The outcome of these patients is unknown.

Disclosure of Interest
None declared

P066

Patterns and rate of confirmed transition to adult care of patients with Juvenile Idiopathic Arthritis (JIA) at a tertiary paediatric rheumatology centre

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Pediatric Rheumatology 2020, **18(Suppl 2):**P066

Introduction: Juvenile Idiopathic Arthritis (JIA) commonly persists with clinically active disease into adult life. The transfer of these patients into adult healthcare services can be a challenging process, with previous studies showing successful transfer being as low as 50% in spite of a coordinated transfer effort.
Objectives: To determine the number, characteristics and referral pattern of JIA patients being transitioned from a public tertiary paediatric rheumatology centre to adult care and the rate of confirmed transition.
Methods: JIA patients in the Royal Children's Hospital (RCH) rheumatology database who turned 18 y.o. between 2012-18 were identified. The medical record of each patient was examined and those referred for adult care entered into the study. Data regarding diagnosis, treating clinician, date of first and last RCH visits, date of referral for ongoing adult care and confirmation of transition, defined as proof of establishment of follow-up with the referred service, was collected.
Results: 178 patients were identified. 64% were referred for adult care. Mean follow-up prior to transition was 7.4 years. The commonest subtypes referred were seronegative polyarticular (30.7%) and oligoarticular JIA (19.3%). 65.8% were referred to public hospital rheumatology services with the remainder referred to private rheumatologists. Confirmation of transition occurred in 62.3% with correspondence received from adult services in 49.1%. There was no difference in rate of return correspondence from public versus private providers (47.9 vs. 53.8%, p=0.69). 37.7% had an unknown outcome after referral to adult care as a result of no correspondence from the adult service and no follow-up at the RCH. The use of 'backstop' appointments – final review at RCH several months after the estimated date of adult review – was more likely in those with confirmed transition (66% vs. 30%, p=0.0002).
Conclusion: Lack of confirmation of transition for JIA patients moving to adult care is common and has the potential for suboptimal outcomes in substantial numbers of patients during this critical period. Strategies to improve communication with the referring centre following initial assessments with adult services and vigilance regarding potential loss to follow-up during this time by paediatric centres would minimise this risk.

Disclosure of Interest
None declared

P067

State of iodine supply of children with Juvenile Idiopathic Arthritis of north - east region of Ukraine

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Pediatric Rheumatology 2020, **18(Suppl 2):**P067

Introduction: The problem of combined organ damage (organ-specific autoimmune syndromes) is relevant in systemic processes, which include juvenile idiopathic arthritis (JIA). Such lesions in rheumatoid arthritis in adults include autoimmune diseases of the thyroid gland, primarily chronic autoimmune thyroiditis. On the other hand, the basis for the development of thyroid pathology is endemic iodine deficiency. In accordance with the results of studies conducted in 2002 in 22 regions of Ukraine (with the participation of the Ministry of Health, NAMS of Ukraine, Goskomstat, specialized scientific research centers and UN Children's Fund (UNICEF), iodine deficiency detected in all studied territories. Ubiquitous iodine supplementation can lead to its excessive consumption, which is a problem in individuals who already have thyroid disorders, such as nodules, hyperthyroidism and autoimmune thyroid disease.
Objectives: To evaluate the current state of iodine supply in children with JIA living in the North-Eastern region of Ukraine.
Methods: Target group included 52 schoolchildren (29 girls and 23 boys) with JIA (according to ILAR classification, Edmonton, 2001) aged from 7 to 16 years (11.8±2.71). Control group included 11 children (5 girls and 6 boys), residents of the same region, of comparable gender and age (13,6±3,12). Methods: dietary iodine intake evaluation by urinary iodine concentration (Sandell-Kolthoff reaction), followed by calculation of the median. The average concentration of iodine in urine (median of urinary iodine concentration) can be used to assess iodine supply of the population. A cohort of schoolchildren is the most reflect average consumption iodine in a given territory in the general population. According to the WHO recommendation, iodine intake is considered sufficient with a median of 100–299 mcg/l in school-age children.
Results: Median urinary iodine excretion in children with JIA was at the lower normal range and amounted to Me=101.7μg/l; [QR 56.5; 169.9]. Moreover, the median iodine in urine was significantly lower

than in the group of healthy peers (Me=101.7 μg/l vs Me=183.7 μg/l, p=0,003).The survey revealed that only 50,1±6,9% of children had adequate iodine supply (Me=144.8 μg/l; [QR 119.1; 215.1]). Mild iodine deficiency was diagnosed in 28,8±6,2% patients (Me=33.5 μg/l; [QR 20.4; 36.2]). Moderate iodine deficiency (Me=87.7μg/l; [QR 70.7; 97.1]) has been identified in 17.3±5.2% children with JIA. Severe iodine deficiency was diagnosed in 3.8±2,6% patients (Me=14.1 μg/l; [QR 12.43; 15.7]). JIA girls had worse results (in girls: Me= 97.7 μg/l; [QR 77.8; 130.2] vs in boys: Me=109.6 μg/l, [QR 48.4; 154.1] p= 0,051). Indicators of iodine excretion did not depend on the variant, activity and duration of the JIA.
Conclusion: The risk of developing pathological changes in the thyroid gland in children with JIA is caused not only by systemic immune disorders, but also by a deficiency of iodine intake. The obtained results can serve as the base for screening testing of thyroid function in JIA and for resolving the issue of prescribing iodine-containing drugs. This should be taken into account to improve the overall prognosis of the disease and the quality of life in adulthood.

Disclosure of Interest
None declared

P068
The 15-year evolution of JIA biologic therapy patterns in the Czech Republic

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Pediatric Rheumatology 2020, **18(Suppl 2):**P068

Introduction: Collection of structured clinical information in the form of disease and/or pharmacovigilance registries have become a standard for many rare diseases including juvenile idiopathic arthritis (JIA). Although the total JIA paediatric population is not known in the Czech Republic participation to the Rheumatic Diseases Biologics Registry (ATTRA) has been required in order to secure drug reimbursement by insurance companies. Patient data including demography, disease activity and damage scores, comorbidities and concomitant therapies have been prospectively collected in the ATTRA registry since 2002 for the spectrum of rheumatic diseases under the auspices of the Czech Rheumatological Society. Paediatric patients have been entered since biologic therapies became available for children with JIA in late 2004.
Objectives: To present country-specific policies and practice in JIA biologic therapy and analyse major trends in their use over the past 15 years.
Methods: Description of the biologic therapy organisation within the Czech healthcare system. Analysis of the main demographic and disease characteristics from the JIA part of the ATTRA registry from 2005 up to January 2020.
Results: JIA biologic therapy is concentrated in paediatric rheumatology units satisfying the predefined criteria agreed by the Czech Rheumatological Society. These include personnel qualifications as well as unit equipment and availability of specialised paediatric services. When used in approved indications majority of common biologics including etanercept, adalimumab, golimumab and tocilizumab are fully reimbursed via the special budget-limited contracts among approved healthcare providers and insurance companies. Reimbursement of IL-1 blockers, abatacept and rituximab requires formal application which is time consuming, but usually successful. Over the past 2 years number of units prescribing biologics has expanded from 3 towards currently 7 approved centres in the country of over 10 million population. Nevertheless, the 3 "oldest" units care for 94% (701/743) of registered patients who were further analysed. The number of registered (=ever biologic-treated) patients has been steadily increasing from the total of 50 individuals in 2005 by the 5-year annual mean of 77 patients (calculated from years 2015-20). When data from 2005 were compared with 2015-20, interval from the diagnosis to the introduction of the first biologic as well as the JADAS-71 (range 0-101) at therapy onset have been steadily decreasing from the median (5-95th centile) of 4.8 (4-12.7) years and 21.2 (8.9-59.5) respectively to 1.1 (0.2-8.8) years and 14.3 (1.4-34.7), respectively. From the total of 1186 patients currently followed by the 3 largest units 30% (356) of patients are receiving following biologics: TNF inhibitors (85%), tocilizumab (10%), IL-1 inhibitors (5%). Data on patient demography, JIA subtype distribution and disease complications (mainly uveitis), treatment efficacy, relapse and switch to different agent rates as well as adverse events are further presented in detail.
Conclusion: Biologic therapy has been well established in the Czech Republic and is currently being received by one third of JIA paediatric patients. Its accessibility is somewhat limited by reimbursement rules and by the budget, but TNF and IL-6 inhibitors are readily available without delay when used in approved indications. Decreasing interval from disease onset to the start of therapy as well as generally milder disease (as reflected by JADAS) required for treatment initiation illustrate their expanding use over the past years in line with available treatment recommendations and similar to other JIA series.

Disclosure of Interest
None declared

P069
Change in damage index values in children with systemic lupus erythematosus duration of two and more years

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Pediatric Rheumatology 2020, **18(Suppl 2):**P069

Introduction: High disease activity, the presence of prognostically unfavorable syndromes of systemic lupus erythematosus in children much more often requires the appointment of a more aggressive than in adults complex of immunosuppressive therapy (hormones, cytostatics, immunobiological drugs). The development of endothelial dysfunction, immaturity of the regulatory systems (central nervous and endocrine) further create the conditions for the formation of irreversible damage in many organs with the development of their insufficiency. The nature of these injuries in childhood and the period of their formation remain unclear.
Objectives: The purpose of the study was to determine the frequency and nature of irreversible changes (damage index) in children with systemic lupus erythematosus (SLE), depending on the duration of the disease, the nature of the course, and activity of the process.
Methods: 53 patients with SLE at the age of 7-18 years old and suffering from more than one year were examined in dynamics twice at intervals of 12 months. The average duration of disease was 37,92± 7,90 years at the time of the first examination. Changes in the cardiovascular system were determined (using an ECG in 12 main leads, an echo test, a 6-minute walk test), kidneys (according to glomerular filtration rate, serum creatinine concentration, proteinuria level and the range of changes in the specific gravity of urine during days), pulmonary system (according to X-ray examination and spirometry). The presence of pathology of the organ of vision, the nervous system (assessment of neurological status, conductivity, sensitivity of the cranial and peripheral nerves, EEG, MRI of the brain, the use of the Montgomery and Åsberg Depression Rating Scale), changes in the musculoskeletal system (by X-ray, ultrasound, MRI of the joints , bone

densitometry) were studied. The blood lipid spectrum of patients (total cholesterol, triglycerides, HDL, LDL, VLDL-cholesterol, atherogenic coefficient) was investigated.
Results: In half of children and adolescents with SLE (52.83%), potentially irreversible organ injuries were revealed. During the initial examination lesions of the nervous system dominate (20.75%), lung injuries were next (13.21% of patients), which were represented mainly by pleural fibrosis. Visual organ damage (11.32%) in the form of cataracts was registered with a slightly lower frequency. On repeated examination the frequency of irreversible changes has increased (68,92%), wherein eyes lesions (18,87%), stunted growth (18,87 %), lungs changes (16,98 %) are added, that is a feature characteristic of juvenile debut SLE. Growth retardation (9,43%)was characteristic of the age of SLE onset up to 8 years. Menstrual disorders were observed in 13.04%, mainly at the onset of SLE at 8-12 years. Presence of atherogenic dyslipoproteinemia (22.64%), insulin resistance (13.21%), osteopenia (22.64%) can be considered as precursors of damage (atherosclerosis, diabetes mellitus, osteoporosis) in the further course of the disease. The accumulation of irreversible organ damage occurs with an increase in the duration of the disease ($r = 0,355$; $p < 0,001$) and is associated with persistent activity of the lupus process ($r = 0,515$; $p < 0,001$) and long-term cytostatic therapy ($r = 0,3$; $p < 0,01$).
Conclusion: The results of study indicate the need for prospective monitoring of the state of organs and systems for the formation of persistent damage in order to timely correction of therapy.

Disclosure of Interest
None declared

P070

A systematic review exploring the bidirectional relationship between puberty and autoimmune rheumatic diseases

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Pediatric Rheumatology 2020, **18(Suppl 2):**P070

Introduction: Adolescence and puberty are associated with significant changes which are initiated and mediated by sex hormones. There is evidence that sex hormones also influence the development and regulation of the immune system, and with it auto-immune rheumatic diseases (ARDs).
A clear sex bias exists in the incidence of ARDs, with females being at significantly higher risk. However, there is a limited understanding of the physiological mechanisms for sex-specific immune modulation.
Previous research has observed a relationship between puberty and ARD onset, suggesting that sex hormone changes at puberty play an immunomodulatory role in triggering ARD onset and development. In addition to triggering autoimmunity, sex hormones can influence various outcomes of ARDs, and testosterone is thought to exert a protective effect.
No previous systematic reviews have addressed the impact of puberty on disease outcome measures in ARDs, or the impact of ARDs on puberty-related outcomes. Understanding the interplay between the neuroendocrine and immune systems can provide valuable insights into the immune-pathogenesis of the peri-pubertal onset of ARDs, and help to improve the clinical approach to treatment of these patients in the long term.
Objectives: To elucidate the bidirectional relationship between puberty and autoimmune rheumatic diseases (ARDs).
Methods: Studies published in English until October 2019 were identified using a systematic search on bibliographic databases and manual checking of reference lists. Information was extracted on study design, sample size, demographics, puberty outcome measures, and main findings. The methodological quality of the studies included was analysed using the Newcastle-Ottawa Scale (NOS) for non-randomised trials.
Results: 14 non-randomised studies reporting on the impact of puberty on ARD outcomes (n=7), ARD impact on puberty-related outcomes (n=6), or both (n=1) have been identified. One study focused on patients with juvenile idiopathic arthritis (JIA)-associated uveitis, all others investigated patients with juvenile systemic lupus erythematosus (JSLE) or healthy controls who developed adult-onset SLE. Quality assessment of studies showed a small to moderate risk of bias overall (NOS 4-9/9). Due to large heterogeneity of the studies it was not possible to perform a meta-analysis. Multiple studies reported on delayed puberty in patients with JIA/JSLE, menstrual and hormonal abnormalities, and lower height and weight than controls. Earlier (pre-pubertal) onset of JSLE was correlated with more severe disease and more need for systemic treatment.
Conclusion: It is clear that a bidirectional relationship exists between puberty and ARDs. More and better research is required to elucidate this relationship. Therefore, we propose a comprehensive set of clinical assessments of patients with ARDs, to be recorded at hospital visits.
Increased awareness of the relationship between puberty and ARDs, and subsequent monitoring of the impact of disease and treatment on the normal development of young people with ARDs, can benefit clinicians, patients and their families. Moreover, it will facilitate future research into new strategies of minimising the negative impact of ARD on pubertal development as well as managing ARD flares from a broader perspective, which should take into account puberty-related outcome measures, ultimately shedding light on this complex but important relationship.

Disclosure of Interest
None declared

P071

Long-term outcome of juvenile idiopathic arthritis in adult patients under biological therapy

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Pediatric Rheumatology 2020, **18(Suppl 2):**P071

Introduction: As available treatment options for juvenile idiopathic arthritis (JIA) have expanded over the last decades, there is a need for studies to characterize its long-term outcome, especially in patients treated with biological therapy.
Objectives: To study clinical and patient related outcomes of adults with JIA on biological treatment after transition to adult care.
Methods: In this cross-sectional study, adult JIA patients under treatment with biologicals and followed in the University Hospital of Leuven were included. Patient-administered questionnaires were used to examine social and professional participation, overall well-being(VAS), physical disability(HAQ), health-related quality of life(SF-36), fatigue(MFI-20), perception of illness(IPQ-R), coping(UCL) and self-efficacy(ASES). We registered disease and treatment characteristics, disease activity(DAS28-CRP), joint damage(JADI-A), systemic sequelae and side effects of biologicals from the patient's medical record.
Results: Twenty-five patients with a mean age of 32.6 years were included. All JIA subgroups were represented, but the polyarticular JIA was the most common. At their last hospital visit, 7/25 patients used low-dose steroids, 12/25 were treated with cDMARDs and 24/25 were on biological therapy. After a mean follow-up time of 23.6 years, 4/25 participants had active disease defined as DAS28≥ 2.6. The mean JADI-A and HAQ score were 6.5 and 0.8 resp. 3/25 patients developed serious infections, 4/25 developed MAS during their disease course. None developed malignancies. Arterial hypertension was present in 8/25, pulmonary hypertension occurred in 2/25. Two patients had osteoporosis, while 6 had osteopenia. Growth failure was

identified in 4/25. 5/25 developed discrepancy in leg length. 2/25 underwent surgery for excessive varus or valgus deformity of the limbs. Patients scored their health-related quality of life with a mean of 71.6/100±18.3 on the VAS. The SF-36 physical and mental component score (PCS and MCS) were calculated, resulting in a mean (± SD) of 40.9±11.7 for PCS and 52.0±12.2 for MCS. A mean (± SD) of 13.2±4.4 was found for the MFI-20 subscale "general fatigue". The mean (± SD) for the ASES subscale "pain" was 3.3±0.8, and for "other symptoms" 3.8±0.7. Almost 3/4 of participants practiced sports. 18/25 participants were employed, 15/25 were in a relationship and 6/25 had a child.

Conclusion: In this cross-sectional study, we examined clinical and psychosocial outcomes of JIA patients under treatment with biological therapy after transition to adult care. Although the population was biased to a more severe subtype due to our inclusion criteria (use of biological therapy), disease activity at the last hospital visit was lower in our cohort compared to previous studies. The proportion of patients using steroids and cDMARDs remained stable during follow-up but the steroid dose declined over time. The presence of side effects of biological therapy was in line with data from previous studies. Despite lower disease activity and joint damage scores, our patients experienced more physical disability and pain compared to the general population and recent studies in adult JIA patients. Their fatigue, illness perception and coping levels were however comparable to those of patients with other rheumatic conditions. Compared to the general population, our cohort had a similar health-related quality of life, employment rate and social participation. Participation in sports was surprisingly high. Overall, we may conclude that the access to biological therapies for JIA patients seems to improve disease control, resulting in an overall good physical functioning as well as psychological well-being.

Disclosure of Interest
None declared

P072

Multidisciplinary and systematic care model of a transitional rheumatic clinic in Mexico

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Pediatric Rheumatology 2020, **18(Suppl 2):**P072

Introduction: The caregiver is the most active in caring for a child with a rheumatic disease, once the patient grow, the responsibility of care need to be passed to the adolescent. Transition programs in rheumatology have shown improving quality of life and disease activity.The best transitional care model in rheumatology is still uncertain.

Objectives: The aim of this study was to describe the process of design a program that provide an uninterrupted, multidisciplinary and coordinated attention to adolescents during transition from pediatric to adult services in Mexico

Methods: Between January and June 2017 we created the care model protocol according to three steps: **1. Creation a Multidisciplinary team.** A group of specialists were invited to participate. **2. Evaluation of transition skills of patients and caregivers**.The Spanish version of the Got Transition questionnaire was applied to youth and parents/caregivers, includes: "Transition Importance and Confidence", "My Health" and "Using the Health Care System". Analyzed using SPSSv.24, concordance were compared using Spearman's test. **3. Establish a model of care**.We appraise variables which includes chronological age, maturity, medical status, adherence, independence, transitional issues, adolescent readiness, and availability of an adult physician.

Results: Step 1.Creation a Multidisciplinary team. The team was made up of three pediatric rheumatologists, two adult rheumatologists, two physical medicine and rehabilitation specialists, one child psychiatrist, two nutritionists, one clinical psychologist, one nurse and one social worker.**Step 2. Evaluation of transition skills of patients and caregivers.** 38 questionnaires were applied to 19 patients and their caregivers. Most of the youth were female (79%), with median age of 18 years. Juvenile Idiopathic Arthritis and Systemic Lupus Erythematosus were the most frequent.We observed that parents/caregivers reported less confidence about their child´s ability to change to an adults' doctor. We also observed a low correlation (rho coefficient < 0.7) between the reported skills (in "My Health" and "Using the Health Care System" items) by youth and the parent/caregiver perception. **Step 3. Establish the model of care.** We established a three steps model: pre-transition, transition clinic and pos-transition, divided in eight phases. Each phase includes different administrative activities and abilities which must be met in order to continue with the next phase. (Figure 1)

Conclusion: The transition clinic that we presented represents the first step to establish a program to get selfcare capabilities in patients from a low-resource setting. Approaching in a multi-assessment manner, allowing personalized interventions.The transition model proposed is a possible intervention in developing countries.

Disclosure of Interest
None declared

P073

Lipid spectrum in children with Juvenile Idiopathic Arthritis in a prospective study

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Pediatric Rheumatology 2020, **18(Suppl 2):**P073

Introduction: It is known that in adult patients with rheumatoid arthritis (RA) the risk of cardiovascular disease associated with atherosclerosis increases by almost 50% compared to the general population. Atherosclerotic process usually begins long before its clinical manifestation. Similar studies are also conducted in the pediatric population of patients with JIA. However, how persistent these changes are in childhood is not fully understood.

Objectives: The aim of the study was to determine the state of the blood lipid spectrum in dynamics under the conditions of treatment of the disease.

Methods: 65 children (8-18 years) with JIA (oligoarthritis 61.5% and polyarthritis 38.5%) were examined twice in the dynamics with an interval of 1 year. Among patients females predominated (66.2% (43 girls) vs males 33.8% (22 boys)). The average duration of the disease was (74.1 ± 6.3) months. All patients received methotrexate (MTX), including in combination with TNF-α blocker -adalimumab 8 people (12.3%).The physical development of children was within the age population norms. Children with signs of chronic rheumatoid cachexia or overweight and obesity were not included in the development. Control group included 19 children, residents of the same region, of comparable gender and age.

General clinical assessment, disease activity and drugs were rated. Total cholesterol (TCh), triglycerides (TG), high density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL),very low-density lipoprotein cholesterol (VLDL)apolipoprotein B, ApoA-I and lipoprotein-α, atherogenic coefficient were evaluated. Results were analyzed using IBM SPSS Statistics for Windows with $p<0.05$ considered spastically significant.

Results: Analysis of the lipid profile in children with JIA showed that patients had significantly higher rates of TCh (5.0 ±0,1 vs 3.8 ±0.2

mmol/l in control group; p <0.05), TG(1.0 ±0,1 vs 0.7±0.1 mmol/l; p <0.05), LDLP cholesterol (3.0 ±0,1 vs 2.3±0.1 mmol/l) and cholesterol VLDL (0.5 ±0,0 vs 0.1±0.1 mmol/l, p <0.05), that led an increase in the level of atherogenic coefficient (2.4 ±0.2 vs 1.9±0.2 mmol/l, p < 0.05) and the atherogenic dyslipoproteinemia's formation.
The study of the lipid spectrum of the blood in a year showed a reduction of the level of TCh in compare with first results (4.6±0,11 vs 5.0±0,11 mmol/l; p <0.05), TG(0.8 ±0,1 vs 1.0±0.1 mmol/l), LDLP cholesterol (2.7 ±0,1 vs 3.0±0.1 mmol/l) and uptrend of cholesterol VLDL (0.4±0.1vs 0.5±0.0 mmol/l), downward trend of the level of atherogenic coefficient (2.4 ±0.2 vs 2.0±0.2 mmol/l, p <0.05) that indicates positive changes of lipid's spectrum. The dynamics of lipid profile indices did not differ depending on the applied complex of therapy except from the atherogenic coefficient, which was significantly reduced during treatment with methotrexate and adalimumab (2.9 ±0.3 vs 1.6±0.1 mmol/l, p <0.05) and did not change with monotherapy by methotrexate (2.1 ±0.2 vs 2.0±0.1 mmol/l).
Conclusion: In children with JIA on the background of active inflammatory process revealed a traditional model of formation of atherogenic lipid spectrum of blood. Appointment complexes of basic therapy with methotrexate in combination with immune biological drugs leads tonot only reduce inflammation but and normalization blood lipid spectrum.

Disclosure of Interest
None declared

P074

Pregnancy outcome and impact on disease activity in young women affected by Juvenil Idiopathic Arthritis (JIA): a monocentric experience in a tertiary centre in Milan.

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Pediatric Rheumatology 2020, **18(Suppl 2):**P074

Introduction: Juvenile Idiopathic Arthritis (JIA) is a chronic inflammatory disease affecting children and adolescents, but many refractory forms continue into adulthood. In the era of biologic therapy we experienced an increasing willing for childbearing in many patients due to outcome improvement. Currently data regarding pregnancies in JIA patients are scarce.
Objectives: The aim of this study was to describe a monocentric case series of pregnant women affected by JIA and therefore to evaluate pregnancy outcome, the presence of major complication in newborns and the impact of gestation on disease activity.
Methods: All pregnant women affected by JIA referring to the Transition Clinic, Division of Rheumatology, G. Pini Institute of Milan, in a period of twenty years were enrolled in this study. Data regarding pregnancy outcome, drug exposure and disease activity were recorded. Gestational age, birth weight, APGAR score and newborn conditions were also collected.
Results: We collected data from 28 women affected by JIA and 35 pregnancies. All patients presented long standing refractory JIA. All patients were treated with DMARDs close to conception, of whom 85,7 % with bDMARDs.Exposure to biologic treatments included mostly anti-TNF agents (17 etanercept, 3 adalimumab, 5 golimumab and 2 certolizumab), but also other agents (3 rituximab,1 sarilumab). bMARD were used in monotherapy (28/30) or in association with csDMARDs (1 leflunomide, 1 methotrexate), hydroxycloroquine (3), or both (1 cyclosporine and hydroxycloroquine). All patients discontinued therapy at gravindex positive test or during first trimester. Pregnancies outcomes and data regarding drugs exposure are reported in table 1. One case of cleft palate was observed. We did not observe any major early or late complications in infants. Eight patients underwent intra-articular glucocorticoid injections during pregnancy, while 23 patients resumed therapy shortly after childbirth. One patient needed to start a biologic treatment after delivery.
Conclusion: Despite a large amount of studies demonstrating the safety of anti-TNF during pregnancy, data in young women affected by JIA who become pregnant are still limited. In our monocentric experience, no greater number of unexpected complications were observed during pregnancy and also in children, compared to other autoimmune disease. Discontinuation of therapy increased the risk of flares confirming that EULAR recommendations for the use of biologics during pregnancy may be applied also in JIA patients.[1,2]
1-Bazzani C et al. Prospectively-followed pregnancies in patients with inflammatory arthritis taking biological drugs: an Italian multicentre study. Clin Exp Rheumatol. 2015 Sep-Oct;33(5):688-93.
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Disclosure of Interest
None declared

Table 1 (abstract P074). Summary of results

Total sample (n)	28
Pregnancies (n)	35
Age at conception, mean (S.D.), years	30,5 (4,8)
Duration of disease at conception, mean (S.D.), years	23,26 (6,4)
Time of discontinuation of therapy, mean (S.D.), week	7,48 (5,7)
Time of exposure to bDMARDs, mean (S.D.), days	51,58 (41)
Pregnancy outcome	3 voluntary interruption, 4 early miscarriage
Mean time at delivery (week)	37,47
Maternal complications	1 gestosis, 1 placental detachement
Neonatal complications	1 cleft palate, 2 premature births, 1 phenylketonuria

P075

A scoping review to support the development of pGALSplus: a multi-professional tool and resource

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Pediatric Rheumatology 2020, **18(Suppl 2):**P075

Introduction: Musculoskeletal (MSK) problems in children and young people (CYP) are common. The majority will present to healthcare professionals in the community but it can be challenging to identify those with serious disease requiring onward referral. pGALS (paediatric Gait, Arms, Legs and Spine) was developed as a simple, quick MSK clinical assessment to discern abnormal joints. Anecdotally, pGALS can detect joint and functional problems in CYP with other serious conditions but alone is unlikely to be specific enough.
Objectives: Our aim was to scope the literature about MSK assessments applicable to CYP used in clinical practice, focusing on evidence of validity in the context of diagnosis and assessment of Juvenile Idiopathic Arthritis (JIA), Mucopolysaccharidoses (MPS),

Muscular Dystrophy (MD) and Developmental Coordination Disorder (DCD) to develop an extended pGALS (to be called pGALSplus).
Methods: Scoping review using the Newcastle University Library search tool and Google Scholar, and consulting NICE guidance and pathways. Search terms included dyspraxia, paediatric MSK assessment, screening tools, balance, rheumatology, assessment tools for MD, MPS, JIA. Studies cited within relevant articles uncovered through searches were also checked. The search was conducted between 1st October and 1st December 2018, publication date limited to post 1998, and all languages included unless translation was unavailable.
Results: 32 journal articles were deemed appropriate, describing specific assessment or screening tools in the context of diagnosis of our target conditions. Within DCD, motor co-ordination test batteries are part of specialist assessment, but are regarded as too lengthy for the purpose of screening; a questionnaire may be useful as a first-step diagnostic tool, along with an assessment of static balance (found to be significantly worse in children with DCD). In paediatric rheumatology, pGALS is the only validated screening tool to discern normal from abnormal joints. Other tools to assess health and well-being, disability and function are validated in the context of established disease only. For neuromuscular conditions the North Star Ambulatory Assessment is valid, reliable and practical as a functional assessment, and includes activities that are necessary to remain functionally ambulant. With regards to MPS, searches did not reveal specific MSK tests, but evidence suggests that skeletal malformations and joint problems were the most frequently presenting signs. pGALS performs well to identify abnormal joints with restriction within an MPS group.
Conclusion: This review supports the development of 'pGALSplus' to facilitate identification and assessment of CYP with potentially serious MSK disease. pGALSplus will be targeted at community-based clinicians and likely include physical examination, questionnaire(s) and appropriate adjuncts. Our group is currently developing pGALSplus, aimed at multi-professionals to describe feasibility and acceptability with educational and training resources.

Disclosure of Interest
None declared

P076

Explaining Juvenile Idiopathic Arthritis (JIA) and its treatment to paediatric patients using pictorial education materials and easy-to-read texts

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Pediatric Rheumatology 2020, **18(Suppl 2):**P076

Introduction: In order to reach adherence to therapy, understanding of the disease and the treatment options are of utmost importance. Standardised validated pictorial education materials and texts in an easy-to- read language are an important tool to improve patients' knowledge of JIA.
Objectives: To develop specially designed graphic depictions complemented by standardised, easy-to-read textual information materials supporting a comprehensible informative medical dialogue with paediatric patients starting from school-age. The information material was tested in order to validate its comprehensibility.
Methods: The graphic depictions were designed by a graphic artist after detailed introduction to the topic by pediatric rheumatologists. Informative texts were written by pediatric rheumatologists and consecutively transformed to easy-to-read language to improve comprehensibility.
The materials are designed as a modular system allowing physicians to select individually the information needed for each specific patient.
The materials were tested for comprehensibility in healthy children and adolescents (controls) and in children and adolescents affected by JIA (patients). A standardised presentation to the probands was given by a student of psychology. Gain of knowledge about the illustrated items was quantified using a short questionnaire before and after the training session.
Results: 38 patients and 45 unaffected healthy individuals were tested in a standardised setting. In both groups gain of knowledge was significant (patients: $M = 2.58$, $SD = 2.13$, $t(37) = 7.48$, $p<0.001$, controls: $M = 3.53$, $SD = 2.14$, $t(44) = 11.08$, $p <0.001$).
Conclusion: Explanation of rheumatic diseases and therapeutic strategies is a time- consuming part of our daily practise. To avoid incomprehensible explanations in medical jargon, graphics with accompanied easy-to-read texts were created. Standardised presentation of the newly created materials resulted in a highly significant improvement of disease knowledge in patients and controls.
Our created graphics allow a fast instruction to the disease and its management that can also be performed by trained medical staff.

Disclosure of Interest
None declared

P077

Transitional care in rheumatology: current practice in Switzerland

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Pediatric Rheumatology 2020, **18(Suppl 2):**P077

Introduction: About half of the children with rheumatic diseases need ongoing medical care during adolescence and adulthood. A good transition into adult rheumatology is essential. A structured transition process has therefore been recommended by the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology European Society (PReS). However, these recommendations are not yet widely implemented.
Objectives: To assess the current practice of transitional care (TC) in Switzerland in relation to EULAR/PRES standards and to describe gaps and challenges in following the recommendations.
Methods: All ten pediatric Swiss rheumatology clinics offering transition service to adult care agreed to participate. In each clinic the responsible pediatric (n= 10) and adult (n= 10) rheumatologist were separately interviewed using a structured manual addressing EULAR/PRES transitional care standards.
Results: The median number of patients in follow-up in pediatric centers ranged from 50 to 363 (median 140). Fifteen of twenty rheumatologists reported to have a written procedure for TC. Three pediatric and two adult rheumatologists used a checklist. The start of TC varied between the ages of eleven and twenty. Adherence to medication and appointments followed by disease activity and age were rated as important for initiating TC. Topics discussed most often by rheumatologists during consultations were vocational issues (n= 17), effects of alcohol, smoking on disease/treatment (n= 16) medication (n= 16) and the impact of disease/treatment on daily life, sexuality, fertility and pregnancy (n= 15). All pediatric teams performed consultations with the patients alone whereas only two performed consultations with the parents alone. Median clinical experience of

all rheumatologists in TC was ten (range 3 to 40) years. Only two centers had a transition coordinator. Slightly more pediatric (70%) than adult (60%) rheumatologists rated their TC process as good or very good. Only half of the adult rheumatologists, but all pediatric colleagues evaluated support provided for self-management skills of the young patients as good or very good. None of the physicians carried out formal evaluations of their TC, including patient satisfaction. The main barriers identified for further development of local TC included lack of funding and staff.

Conclusion: The current practice of TC in Swiss rheumatology centers is heterogeneous. About half of the rheumatologists were satisfied with their current practice, although no structured evaluation was conducted. To ensure that patients' needs are sufficiently addressed during transition further evaluation within the network of pediatric and adult rheumatologists is needed.

Disclosure of Interest
None declared

P078

Pediatric rheumatology research in Sweden; available prerequisites, ongoing projects, and interest for future registry studies

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Pediatric Rheumatology 2020, **18(Suppl 2):**P078

Introduction: The Swedish Pediatric Rheumatology Registry is a national quality register containing diverse clinical data of children with rheumatologic diseases. Despite this, incoming requests for its use in registry-based research are few.
Objectives: To survey ongoing pediatric rheumatology research in Sweden and to evaluate prerequisites and common interest for future registry studies.
Methods: An electronic questionnaire was sent by e-mail to practicing physicians in all 32 pediatric rheumatology units in Sweden.
Results: Thirty-three physicians from all pediatric rheumatology units in Sweden replied. Thirteen units (41%) reported 25 ongoing research projects in pediatric rheumatology, 20 (80%) of these were reported by physicans from university hospital units. The study designs included basic, pre-clinical and clinical studies performed locally or in national or international collaboration. Eight (25%) of the pediatric rheumatology units had local access to a biobank for sample storage. Most projects were JIA related, other approached Kawasaki disease, autoinflammatory diseases, Juvenile scleroderma, SLE and EDS. Only 5 (20%) of the studies used data from The Swedish Pediatric Rheumatology Registry. In order to improve the interest for registry-based research in Sweden, measures to improve registration habits, better information about research possibilities and guided research support were proposed. Suggested topics for future registry studies were validation of registry data, population based descriptive studies and national or international comparisons of patient reported outcomes, clinical care and treatment effects. The need of a better understanding on how to individualize treatment regimens was acknowledged. Likewise, a better feedback to enable evaluation of local activity and coherence to national recommendations was requested. Twenty-five physicians (76%) were interested to participate in a national research meeting in order to collaborate in planning for future registry studies.
Conclusion: The current activity of pediatric rheumatology research in Sweden was considerable, relatively widespread throughout the country and a subject for diverse study topics. Although a minority of ongoing studies included data from The Swedish Pediatric Rheumatology Registry, the interest in future national collaboration in registry-based studies was high.

Disclosure of Interest
None declared

P079

Preliminary evaluation of our newly launched Sub-Specialty Pediatrics E Case Series (SPECS) to increase pediatricians' watchfulness regarding untouched diseases in children in an Indian state of Gujarat

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Pediatric Rheumatology 2020, **18(Suppl 2):**P079

Introduction:
There is very limited information and awareness about pediatric rheumatic and immunodeficiency diseases amongst primary physicians in Gujarat and to make this matter even worse, we are not having a single exclusive pediatric rheumatology and immunology center for a population of around 60 million.[1-3]
Objectives:
To measure an effectiveness of Subspecialty Pediatrics e-Case Series (SPeCS) in spreading awareness and alertness amongst pediatricians about rheumatic and immunodeficiency diseases in children.
Methods:
On 28th may 2020, I and my endocrinologist colleague decided to deliver weekly one e-class consisting of three real life case discussions from a single or two pediatric subspecialties .Duration of e-class was kept limited to 45 minutes. We propagated this idea for the next two days through various social media platforms to reach to a maximum numbers of pediatricians. Pre e-class evaluation forms were sent to the registered participants. First preliminary e-class was completed on 31st may 2020 which was a fusion of one endocrinology and three rheumatology cases. Post e-class feedback forms were sent to the registered participants. Second e-class was completed on 5th June 2020 which was again a fusion of endocrinology and rheumatology cases.
Results:
Though the numbers of participants were less during first e-class but the feedbacks from the attendees were outstanding. Subsequently in a second e-class there was a wonderful response and social media feedbacks from all the participants. On 7th June 2020, SPeCS was officially launched with some innovative modifications under the aegis of Rajkot academy of pediatricians (AOP) in view of outstanding feedbacks given by the attendees. The next e-class would be planned under a new name SPeCS-AOP Rajkot in a couple of weeks with more fascinating talks and cases from practicing pediatricians under a guidance of senior expert pediatricians and subspecialists from our region.
Conclusion:
SPeCS is proven to be successful in terms of spreading awareness and alertness amongst pediatricians about untouched diseases which are used to be missed easily in day to day practice. A new model would be definitely more beneficial for presenters, attendees, residents and ultimately our little patients.

Trial registration identifying number:
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PratapKumarPatra, ManishKumar
Department of Pediatrics, All Institute of Medical Sciences, Patna, Bihar, India

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Pediatric rheumatology: An under-recognized subspecialty in India
Year : 2017 | Volume : 4 | Issue : 2 | Page : 47-53
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Disclosure of Interest
None declared

Table 1 (abstract P080). See text for description

Area	Main request	N°
Patient's clinical information-diary	Fever attacks and symptoms registration	12
	Repository of health information	5
Community	Online chat, blog and forum patient to patient	14
	Direct connection with the physician	11
Personal agenda	Calendar for therapy, visits, exam scheduling	13
	Alerts (appointments, deadlines, reminders)	4
Clinical and practical information	Disease information (in medical and simple language)	20
	Legal information-patients' rights	7

P080

Development of an app for the management of autoinflammatory diseases using an innovative patients-clinicians codesign approach

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Pediatric Rheumatology 2020, **18(Suppl 2):**P080

Introduction: Autoinflammatory diseases are rare conditions characterized by recurrent episodes of inflammation with fever associated to elevation of acute phase reactants and symptoms affecting mainly the mucocutaneous, musculoskeletal or gastrointestinal system. These diseases affect negatively the quality of life of patients and their families
Objectives: Aim of this project is to develop a tool able to ameliorate patients' management of the disease and to enhance patient-physician communication
Methods: In order to develop a tool based on real-life needs, we involved patients and caregivers since the initial phase of the project. A first workshop designed to capture their needs and desires was organized. Innovative co-design activities were performed through "Lego Serious Play™" (LSP) methodology. During a first phase of "divergence" 13 patients (from teen-agers to adults) affected by different AIDs (FMF, TRAP, CAPS, MKD) and 2 physicians where involved in the LSP activities. Participants were asked to describe, through LEGO and metaphors: 1) The disease, 2) Themselves in comparison with the disease, 3) Solutions and supports which could help them in managing the disease. After each step the participants presented their LEGO model and everyone was engaged in the discussion. The ideas collected during the three phases allowed to have, at the end of the workshop, a list of functionalities identified as necessary for the app to be developed, the so-called "Killer-Features". Due to the actual Sars-COV-2 sanitary emergency the second phase of the project, aimed at presenting the participants the results of the first meeting and procede with the App finalization was performed through following web-based meeting and surveys in which the patients and caregivers actively participated
Results: In the first phase patients and caregivers participated actively expressing various needs, that we subsequently summarized in 4 main areas (table 1). In the second phase (still ongoing) they were further involved and their opinion taken into consideration for the User Experience and User Interface definition for the development of the Mobile App including the required functionalities (after a further activity of prioritization).
Conclusion: our project shows that active involvement of patients and caregivers in the design of a mobile-App can be achieved through innovative approaches. The objective is to obtain an App tailor-made on the real patients' needs and a consequent high satisfaction and long-term adoption of the tool.

Acknowledgement
Project promoted and funded by Novartis
Special thanks to the patients and parents of patients who participated in the project with enthusiasm, contributing to the definition of the App

Disclosure of Interest
None declared

P081

Analysing symptomatic female patients with Lesch-Nyhan Syndrome

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Pediatric Rheumatology 2020, **18(Suppl 2):**P081

Introduction: Lesch-Nyhan Syndrome (LNS) is an X-linked recessive disorder caused by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyl transferase (HGPRT). This occurs due to mutations on the HPRT1 gene found on the X-chromosome. HGPRT deficiency causes a body wide build-up of uric acid leading to hyperuricaemia and hyperuricosuria. Symptoms of LNS include severe gout, kidney problems and neurological problems. One of the most striking features of LNS is self-mutilation (e.g. lip and finger biting). Since LNS is an X-linked recessive it is almost exclusively symptomatic only in males. Females which are heterozygous for LNS are usually asymptomatic, but they can experience increased levels of uric acid excretion and therefore may develop symptoms of hyperuricaemia (e.g. gout in later years). Few reported cases of LNS in females have been reported.
Objectives: The primary purpose of this paper was to summarise the phenotypic characteristics of symptomatic, female Lesch-Nyhan patients. A secondary objective was to identify the genetic causes of LNS in these patients.
Methods: To identify articles and case reports involving symptomatic female LNS patients, a search was carried out across 3 scientific databases. These were: Pubmed, Web of Science and the Library of Congress.
Results: 18 papers were identified where a female sufferer of LNS was present. A consistent theme emerged that if a female patient suffered from LNS they suffered a classical, complete LNS. All the patients described had decreased HPRT levels causing gout, neurological problems, and intellectual disabilities. The severity of LNS was generally consistent but we noticed one singular case where the symptoms were more severe. This patient presented with acute renal failure at 2 months. As expected, there was a strong genetic component in families of symptomatic female LNS sufferers. 13 papers mentioned more than one family member being affected by LNS. Most papers however showed that female sufferers of LNS had asymptomatic mothers or siblings. These unaffected family members all expressed the causative mutant alleles for LNS at similar frequencies to the affected family members in peripheral blood cells. All female LNS patients had a mutation on the gene where HGPRT is expressed as well as x-inactivation of the other normal HGPRT expressing allele. Finally, A minor link between being a twin and suffering from LNS also emerged.
Conclusion: In conclusion, our results show that female patients who develop LNS are fully symptomatic in a manner similar to their male peers. Furthermore, this review shows that for LNS to develop in a

female two concurrent genetic events are required: a mutation at the specific disease gene and an inactivation of the corresponding normal allele. Finally, since there appeared to be a small link between twins and x-linked diseases then it could potentially be said that (as with many other reported cases of x-linked diseases), that the process responsible for monozygotic twinning may play a part to the emergence of LNS in females (potentially by triggering skewed X-inactivation).

Disclosure of Interest
None declared

P082

SLCO1B1 RS4149056 variant as the predictor of methotrexate – related gastrointestinal toxicity in children with Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P082

Introduction: Methotrexate (MTX) administered at the dose 10-15mg/m^2 is currently recommended as the first-line therapy in most of juvenile idiopathic arthritis (JIA) subtypes. Gastrointestinal side effects are the most prevalent clinical demonstration of MTX toxicity, frequently leading to the discontinuation of otherwise effective treatment. Genetic variability within *SLCO1B1* gene has been associated with MTX efficacy and toxicity in paediatric patients with acute lymphoblastic leukaemia.
Objectives: The aim of our study was to determine the association between single nucleotide polymorphisms (SNPs) in *SLCO1B1* gene (rs4149056, rs2306283) on 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 after starting MTX. SNP genotyping was performed using genomic DNA isolated from peripheral blood samples.
Results: *SLCO1B1* rs4149056 CT/CC variant was significantly associated with 4.5 times higher odds ratio of MTX gastrointestinal side effects occurrence (OR=4.55, 95%CI 1.37-15.13; p=0.0135) in comparison to wild-type allele.
Conclusion: *SLCO1B1* rs4149056 may become the determinant of MTX gastrointestinal toxicity in children with JIA.

Disclosure of Interest
None declared

P083

The relationship of ebv infection with paediatric autoimmune diseases

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Pediatric Rheumatology 2020, **18(Suppl 2):**P083

Introduction: The Epstein–Barr virus (EBV) is a virus which can cause severe infections in patients with immunodeficiency due to its high incidence in the population, the possibility of latency and reactivation. For many years a connection with the triggering of autoimmunity has been postulated as well. The aetiology of autoimmune disease is multifactorial: including genetic, hormonal, immunological, environmental, and infectious factors. There are studies confirming the existence of an association of EBV infection with some autoimmune diseases but other studies fail to confirm the existence of any such relations. The presented study concerns children. Primary EBV infection in the majority of the population occurs in this group. In children, the time between primary EBV infection and the onset of autoimmune disease is the shortest.
Objectives: The purpose of this work is to examine the following two questions: 1. Is the history of EBV infection (measured as the presence of anti-EBV antibodies in the IgG class, in a titer considered positive) related to the frequency of selected autoimmune diseases in children (ICD10: E10.9, M08, N04.9, L52, M30.3, D69.3, D69.0, M35.0, M35.9, M35.8) 2. Is there a difference in the immune response among children with and without autoimmune disease?
Methods: Retrospective analysis of EBV VCA IgM, EBV VCA IgG ELISA serum test results of 939 patients hospitalized in a children's clinical hospital in Lublin in the years 2012-2017.
Results: As a result of the statistical analysis of the collected data, there was no relationship between the history of EBV infection and the onset of selected autoimmune disease. There is no statistical difference between EBV VCA IgG and IgM antibody levels in healthy children and in children with a diagnosis of autoimmune disease. No statistical differences were revealed between the groups when dividing them into younger and older children. Statistically significant lower levels of IgG antibodies were found in male subjects with autoimmune diseases compared to female subjects with autoimmune diseases ($Z (N = 227) = -2.08$; $p < 0.05$).
Conclusion: Our study did not confirm the relationship between EBV infection and the onset of autoimmune diseases in childhood. Studies focusing on infectious agents (especially in the paediatric population) are subject to many difficulties, including abnormalities in the production of post-infectious antibodies in young children, or the rare occurrence of autoimmune diseases in children. The issue of the EBV infection and the phenomenon of autoimmunity requires further study.

Disclosure of Interest
None declared

P084

Clinical and molecular characteristic of 13 patients with CACP syndrome

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Pediatric Rheumatology 2020, **18(Suppl 2):**P084

Introduction: CACP syndrome (Camptodactyly, Arthropathy, Coxa vara, Pericarditis) is a rare autosomal recessive disease characterized by congenital or early onset camptodactyly, non-inflammatory arthropathy, pericarditis and progressive deformity of the proximal femur
Objectives: to describe clinical and genetic features of Russian patients with CACP syndrome
Methods: we evaluated clinical and radiological features and performed Sanger sequencing of PRG4 gene in 13 patients with CACP syndrome from 10 unrelated families.
Results: the disease most commonly starts with camptodactyly manifesting as the first symptom in 99% of cases (12 out of 13 patients) at the age of 1-2 years. In all the patients large joints were affected with symmetrical non-inflammatory arthropathy, joint swelling, restricted mobility and flexion contractures. Knee, elbow, and wrist joints were affected in 100% of cases, less often hip (61%), ankle joints and feet (69%) were involved. According to radiographic

examination, deformity of the proximal femur occurred in 70% of cases; in 26% of patients intraosseous cysts of the ischial bone connecting to the hip join had been noted. Osteoporosis and pain were reported in 53.8% and 7.6% of cases, respectively.
All patients were initially treated as juvenile idiopathic arthritis. An average time from the disease onset to the diagnosis of CACP syndrome was 7.6 years.
CACP mutations were detected in 11 patients (85%); of those 6 patients had homozygous and another 5 – compound heterozygous deleterious PRG4 variants (Table 1). The most commonly found recurrent pathogenic alleles were c.1910_1911del (p.P637fs) and c.3462_3465del (p.T1155Lfs)
Conclusion: the results complement the existing data on spectrum of clinical presentation and molecular defects associated with CACP syndrome

Trial registration identifying number: This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001)

Disclosure of Interest
None declared

Table 1 (abstract P084). Patients with PRG4 mutations

Patient ID	PRG4 mutation	Clinical manifestations
716	c.5_6insAT (p.A2fs); c.1910_1911del (p.P637fs)	Pericarditis,varus deformity of the femoral head
959,960	c.1910_1911del (p.P637fs); c.1910_1911del (p.P637fs)	intraosseous cysts of the ischial bone
965,966	c.2754_2758delGACAA (p.K918fs*10); c.3481delA (p.T1161Hfs*2)	Varus deformity of the femoral head
995,996	c.3684C>A (p.Y1228*); c.3684C>A (p.Y1228*)	Pericarditis
1010	c.1934_1935del (p.P645fs) c.3462_3465del (T1155Lfs)	Pericarditis,varus deformity of the femoral head
1078	c.2164C>A (p.P722T); c.2248G>A (p.A750T)	varus deformity of the femoral head
1393	c.3462_3465del (p.T1155Lfs); c.3462_3465del (p.T1155Lfs)	Pericarditis
1529	c.3462_3465del (p.T1155Lfs); c.3462_3465del (p.T1155Lfs)	varus deformity of the femoral head

P085

Assessment of the relationship between Epstein-Barr virus infection and the onset of Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P085

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic childhood disease of still unknown etiology. It is widely recognized that apart from the genetic factors, also environmental factors play a significant role in the disease pathogenesis. One of the potential factors which may influence the development of the disease is the Epstein-Barr virus (EBV) infection.
Objectives: The objective of the study was to define the relationship between the EBV infection and the onset of JIA.
Methods: The study estimated EBV infection markers: the number of EBV DNA copies in the peripheral blood mononuclear cells (PBMC) and the serum concentration of specific immunoglobulin (Ig) A, IgG and IgM against EBV antigens: viral capsid antigen (VCA), EBV early antigen (EA), and nuclear antigen 1 (EBNA-1) in 44 patients with JIA during the disease diagnosis, before initiating treatment, 23 children with different types of arthritis also during the disease diagnosis, before starting treatment, and in the control group of 44 children. Statistical methods were employed to estimate both the dependencies between the EBV infection and the development of JIA and other types of arthritis.
Results: In JIA group, a positive concentration of IgM anti-EA antibodies (Ab) (>1.2 U/ml) was confirmed in 11.4% of patients and a positive level of IgG and IgA anti-VCA Ab (>1.1 U/mL) was found in 43.1% and 2.3%, respectively. The presence of EBV DNA copies has been revealed in 25% of JIA patients, in 25.1% of patients with other types of arthritis, and in 36.4% of healthy children. The highest number of EBV DNA copies in 1 μg DNA in the JIA group amounted to 23.06, in the group with other arthritis types - 268.2, whereas in the control group – 23.3. The analysis of correlation between the EBV infection markers (both the antibodies against EBV antigens and viral load) and JIA activity, has not revealed any statistically significant dependency.
Conclusion: The relationship between EBV infection and the development of JIA has not been confirmed. The obtained results do not indicate a need for routine estimation of EBV infection markers among patients with JIA.

Disclosure of Interest
None declared

P086

Comparison of clinical and ultrasonographic evaluations in Juvenile Idiopathic Arthritis

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic childhood rheumatic disease affecting 1 of 1000 children worldwide (0,07 - 4.01/1000). In paediatric rheumatology, ultrasound plays an important role in narrowing the differential diagnosis and can be useful for treatment monitoring. It is superior to clinical examination in diagnosing disease activity and in detecting subclinical disease.
Objectives: The aim of this study was to determine the frequency, localization and radiological characteristics of ultrasonographic findings in patients with juvenile idiopathic arthritis and to find and characterize the relationship with clinical data.
Methods: In a prospective study were analyzed 55 Children's Clinical University Hospital patients from Department of Rheumatology with proven or suspected juvenile idiopathic arthritis, between February 2019 and March 2020. Clinical data were collected – vitamin D level, CHAQ (Childhood Health Assessment Quietionnaire), physicinan, parent and/or patient visual analogue scale (VAS) assesment, JIA type and disease duration. Each patient underwent ultrasonography of 68 joints. Ultrasonography findings were evaluated in connection with the patient's current clinical condition, physician's assessment and the course of the disease.
Results: From 55 patients 41 (74.5%) were girls, 14 (25.5%) were boys. The youngest was 2 years old, the oldest was 17 years old. Mean age 11.82, median 13 (SD ± 4.66) years. RF- polyarthritis was 24 (43.6%), RF + polyarthritis 1 (1.8%), oligoarthritis 14 (25.5%), arthritis with enthesitis 10 (18.2%), psoriatic 2 (3.6%) and undifferentiated type 4 (7.3%). The mean age of onset was 9.7 years (SD ± 5.11). Compared to JIA type, there was a statistically significant relationship between JIA type and age at onset of the disease - early onset of oligoarthritis (Fisher's test, p <0.001). Analyzing the association of JIA type with gender, a statistically significant (Fisher's test, p <0.001) relationship was found between the higher incidence of RF-polyarthritis and female gender - 53.7% (boys 14.3%) and the incidence of enthesitis-related arthritis and male gender - 64.3% (2.4% for girls). Each patient underwent ultrasonography of 68 joints, for a total of 3,740, of whom 342 (9.1%) had symptoms in the patient, 277 (7.4%) were assessed by a physician, and 108 (2.9%) were

diagnosed with ultrasonography (38.9% of those referred by a rheumatologist). Ultrasonographic changes were recorded in 42 (76.4%) study patients. It was found that changes were most often found in knee joints - 43 (39.8%), feet - 24 (22.2%) and wrists - 15 (13.9%), no changes were found in shoulder joints. The relationship between the finding of a VAS physician, the US, and the reason for the physician's referral was assessed in knee joints. Changes were found in all patients with swelling, patients with marked pain are more likely to experience synovitis and / or tendon changes in the US, no change was found in stress pain in the US. If the physician's VAS (visual analogue scale) > 3, there is a tendency for changes in the US. US changes were found in all patients with wrist pain and / or mobility impairment in combination with physician's VAS > 3. In ankle physician's VAS> 3, in combination with pain and / or swelling, increases the incidence of US changes.
Conclusion: The most affected joints by ultrasound were knee, wrist and feet, where also found correlations with a physician's assessment, which could improve the assessment of the need for US. The study looked at how to deal with unclassified US changes – effusion up to 2 mm thick, concluding that these changes are not significant and can't be interpreted - this aspect should be considered so that communication between the ultrasonographer and the rheumatologist where understandable and clear.

Disclosure of Interest
None declared

P087
Usefulness of whole-body magnetic resonance imaging in pediatric rheumatology

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Pediatric Rheumatology 2020, **18(Suppl 2):**P087

Introduction: Whole Body Magnetic Resonance Imaging (WBMRI) is a multiregional imaging technique able to study the entire body, suitable to investigate the extent of multisystem diseases without exposure to radiation, and offers a large coverage of the skeleton with a high sensitivity to bone alterations.
Objectives: The **aim** of our study is to evaluate the role of WBMRI in the work-up of children with non specific musculoskeletal features, and non indicative laboratory and instrumental data, suspected to have a rheumatologic disease.
Methods: We retrospectively analyzed medical records, including laboratory tests and radiological data, of 34 children who have been evaluated in our Pediatric Rheumatology Department from 2014 to 2019, due to non-specific musculoskeletal manifestations, and for which a WBMRI was prescribed.
Results: We included 34 children, 19 females and 15 males, median age 10 years (range 2-17 years), with the following clinical features: diffuse arthralgia (12 children), persistent fever (2 children), persistent fever and diffuse arthralgia (20 children). Serologic inflammatory markers resulted increased in 29 patients out of 34. Twenty-five children underwent a radiological examination (X-Ray and/or ultrasound) before WBMRI, all with a negative/uninformative result. WBMRI was performed 3-6 weeks (median, 3.5 weeks) after the initial presentation of symptoms.
In 21 children out of 34 (61.7%) WBMRI revealed abnormalities that supported the final diagnosis: 12 chronic recurrent multifocal osteomyelitis (CRMO), 2 polyarticular JIA, 2 infectious osteomyelitis, and primary bone lymphoma, scurvy, hypophosphatasia, Jaffe-Campanacci syndrome, eosinophilic granuloma (one each).
WBMI resulted silent or uninformative in the rest of the patients, in whom the final diagnosis was pain amplification syndrome (2 cases), malaria (1 case). Five children spontaneously recovered without a specific diagnosis was made, while in 4 cases fever persisted and were labeled as FUO.
Conclusion: The experience in our paediatric rheumatology clinic suggests that WBMRI is a helpful tool in situations characterized by non specific constitutional and musculoskeletal manifestations, in which the conventional work-up findings are negative or uninformative. WBMRI has proven to be useful both in the definition of some specific diagnosis, and in their differential diagnosis. In our experience, CRMO resulted the disease that mostly benefits from its use, allowing the early detection of lesions and defining their exact number and distribution.

Disclosure of Interest
None declared

P088
A need to train paediatric rheumatologists in musculoskeletal ultrasound scanning. How do we move forward?

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Pediatric Rheumatology 2020, **18(Suppl 2):**P088

Introduction: Only a few paediatric rheumatologists in the UK use musculoskeletal ultrasound scan (MSK-USS) in their daily practice.
Objectives: To explore the demand for a musculoskeletal ultrasound (MSK-USS) training module for paediatric rheumatology consultants and trainees.
Methods: A questionnaire was sent to paediatric rheumatologist consultants in the UK and paediatric rheumatology trainees. The questionnaire explored; current use of MSK-USS, opinion about benefits of MSK-USS done by clinicians, and interest and needs for training.
Results: 40 out of 45 paediatric rheumatologists replied (response rate of 89%) and 7 out of 14 specialist trainees responded (response rate of 50%).
All of the respondents used MSK-USS performed by radiologists. MSK-USS and MRI scans were requested equally frequent, median 4-7/month. 80% (n=32) consultants and all paediatric rheumatology trainees felt that MSK-USS performed by a clinician in clinic would benefit their patients. Majority stated that for urgent cases, it could take up to 2 weeks in their centre for a departmental USS to be done and reported. Only 32.5% (n=13) could arrange MSK- USS on the same day for urgent scans. 70% (n=28) of the clinicians and trainees have access to an ultrasound scanner. Majority of clinicians expressed their enthusiasm (median of 80%) for an interactive paediatric rheumatology musculoskeletal ultrasound online module combined with a platform in which images and clips can be uploaded and discussed. 100% (n=7) of trainees were keen to learn MSK-USS as part of their training and majority felt that they could dedicate regular time for it alongside their other clinical duties.
Conclusion: In summary, MSK-USS is a tool commonly used in paediatric rheumatology. MSK-USS performed by the clinician is seen as beneficial for the patient by the majority, but a small group reports reservations which need to be addressed. There seems to be a demand in the UK for a training module in MSK-USS in paediatric rheumatology.

Disclosure of Interest
None declared

P089
Insight into clinical cross talk between rheumatic and immunodeficiency diseases in children

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Pediatric Rheumatology 2020, **18(Suppl 2):**P089

Introduction:
There are many primary immunodeficiency diseases which present with either musculoskeletal or autoimmune features. It is vital to

detect subtle clinical clues in such cases for a complete management.

Objectives:

To unveil features which indicate primary immunodeficiency in paediatric rheumatic conditions.

Methods:

I included eight paediatric patients with suspected primary immunodeficiency diseases (PIDs) according to 2019 update of the IUIS Phenotypical Classification[1] who were seen at Dev Children's Hospital between January 2019 and December 2019. My collected data included demographics, clinical presentation and laboratory results.

Results: Average age of children (6 boys and 2 girls) in our group was 5.3 years.

Table 1 showed characteristics of eight paediatric patients with suspected PIDs in rheumatic conditions in children

Conclusion:

All above cases reemphasize the need for an extremely detailed history, family history, pattern recognition and high index of suspicion in paediatric rheumatology.. In our cohort, the features like arthritis pattern different than JIA, early age of onset for autoimmune features, endocrine manifestations, significant family history, recurrent inflammatory episodes and recurrent and/or severe and/or unusual infections at unusual site were some of the important clues which inspired me to suspect PIDs in these patients.

Trial registration identifying number:

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Disclosure of Interest

None declared

Table 1 (abstract P089). Number of '+' indicate number of patients in respective group)

PID groups	Immunodysregulation-syndromes	Phenocopies of PID	Immunodysregulation HLH	Cryopyrinopathy	Auto inflammatory syndromes
(N=number of patients)	(1)	(1)	(2)	(3)	(1)
Joint involvement	+			+++	+ (CRMO)
Cutaneous Lupus		+			
MAS/ HLH			++		
Enteropathy	+				
Type 1 diabetes	+				
Hypoparathyroidism	+	+			
Rash			++	+++	+
Serositis			++	+	
CMC		+			
Recurrent skin, ear & sinus	+		+		
Syndromic face	+				
Severe dental caries	+	+			
Recurrent mouth ulcers			+		+
Recurrent and/or predictable episodes				++	+
Significant family history	+	+	++	++	+
Suspected PID/s	IPEX[1,2] LRBA[1,3] CTLA4[1,3] STAT1 GOF[1,4]	CMC[1] APECED[1]	pHLH[1,5]	MWS[1]	Majeed sydrome[1]
Systemic inflammation			++	+++	
Ig levels	Wnl	wnl	wnl	nd	wnl
Flow Cytometry	High CD45 Very high CD25	nd	nd	nd	nd
Genetic screen	Pending	Pending	Pending (one patient died)	Negative in two patients	Negative
Complement levels	nd	wnl	wnl	nd	nd
EBV PCR	nd	nd	Negative	nd	nd

(Abbreviations: MAS = Macrophage Activation Syndrome,CRMO=Chronic Recurrent Multifocal Osteomyelitis, IPEX= Immunodysregulation PolyEndocrinopathy X-linked, LRBA= Lipopolysaccharide Responsive Beige-like Anchor protein, CTLA4= Cytotoxic T-cells Associated protein,CMC=Chronic Mucocutaneous Candidiasis, HLH= Hemophagocytosis Lymphohistiocytosis,, APECED= Autoimmune–polyendocrinopathy-candidiasis-ectodermal dystrophy,wnl=within normal limits, nd= not done, EBV= ebstein barr virus, MWS= Muckle Wells Syndrome)
There are some financial and laboratory limitations to evaluate such patients completely at our place

P090

Early diagnosis of the Autoimmune Lymphoproliferative Syndrome (ALPS)/ALPS-like syndrome in patients with undefined autoinflammatory or autoimmune disorders: a multivariate analysis approach in a pediatric rheumatology tertiary center

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Pediatric Rheumatology 2020, **18(Suppl 2):**P090

Introduction: ALPS is a rare disorder due to a defective apoptotic mechanism leading to abnormal lymphoproliferation and autoimmunity. It is characterized by lymphoadenopathy and hepatosplenomegaly with autoimmune haemolytic anemia, neutropenia or thrombocytopenia. The disease is difficult to identify in the early phase when it may be misdiagnosed. Elevated TCR alpha-beta CD4-CD8- lymphocytes (double negative T lymphocytes DNT) together with hypergammaglobulinemia, high levels of IL10, Il18, vitamin B12 and soluble Fas ligand have been suggested as the main ALPS hallmarks (1). Therefore, a specific flow cytometry panel (number of DNT cells, the ratio of CD25+CD3+ to HLA–DR+CD3+ cells, increased B220+ T-cells, and decreased CD27+ memory B cells) has been proposed to serve as a diagnostic screen for ALPS (2).

Objectives: to test the usefulness of Oliveira's diagnostic criteria and of a specific panel of lymphocyte subsets (LS) for the identification of ALPS in children referred for a suspected autoinflammatory or autoimmune disorder
Methods: The clinical data of patients referred to the pediatric Rheumatology Unit of the Istituto Giannina Gaslini Hospital for a suspicion of autoimmune or autoinflammatory condition from October 2015 to April 2018, were retrospectively analyzed. Data on clinical manifestations, laboratory workup, genetic analysis and treatments were collected. Flow cytometry including CD4-CD8-TCR αβ+ T lymphocytes (DNT), CD25+CD3+, HLA−DR+CD3+ cells, B220+ T-cells, and CD27+ memory B cells, was included among the screening panel. Data were analyzed with an univariate logistic regression analysis, followed by a multivariate analysis
Results: 475 patients were retrospectively analized. 211 patients not fulfilling the inclusion criteria were excluded. All remaining patients were classified as follows: i)Autoimmune diseases and vasculitis 26 pts ii) JIA 35 pts iii) Monogenic systemic autoinflammatory disease 27 pts; iv)PFAPA 100 pts; v) Systemic Undefined Recurrent Fever 45 pts; vi) Undetermined-SAID:15 pts; vii)ALPS 16 pts. The flow cytometry panel showed elevated DNT in all ALPS patients, even if a slight positivity was found also in other patients. The ratio CD3CD25+/CD3HLADR+ and TCRαβ+B220+ lymphocytes, were significatively altered in ALPS, but when compared to other diseases only TCRαβ+B220+ lymphocytes showed statistical significance ($p< 0.0005$). The multivariate analysis revealed 5 clinical/laboratory parameters positively and significantly associated to ALPS: splenomegaly, female gender, arthralgia, elevated DNT and TCRαβ+B220+lymphocytes
Conclusion: The use of specific LS in patients with undefined autoinflammatory or autoimmune disorders may identify a subgroup of patients with ALPS. Oliveira's criteria where useful in the identification of patients, but the cut-off identified for DNT is not probably strong enough to identify real ALPS patients when used in a pediatric population affected with different immune-mediated conditions.

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CMC and LOM equally contributed to this work

Disclosure of Interest

None declared

P091

coexistence of autoimmune diseases in different subtypes of Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P091

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. With the exception of the systemic JIA it is considered an autoimmune disease.
Objectives: To evaluate whether there are differences in the prevalence of coexisting autoimmune diseases in children according to the different subtypes of juvenile idiopathic arthritis.
Methods: A retrospective, single small center study was performed. All patients diagnosed with JIA who were examined at our pediatric clinic in the last 10 years were enrolled. JIA was classified according to the International League Against Rheumatism (ILAR) criteria. Data was collected from patients' medical records.
Results: A total of 111 patients were included. The results are presented in Table 1.
The mean age was 8.1 years. 71 patients (64%) were female. 3 patients (2.7%) were diagnosed with undifferentiated arthritis. In our cohort none of the patients had rheumatoid factor positive polyarthritis. 1 patient with systemic JIA developed macrophage activation syndrome (MAS). 28 patients (26.1%) presented with a family history of autoimmune disease.
The most common coexistent autoimmune disease was uveitis, which was most commonly present in patients with oligoarthritis and enthesitis related arthritis. Associated autoimmune diseases were most frequent in patients with oligoarthritis whereas patients with systemic and undifferentiated arthritis had none of them. This confirms the hypothesis that systemic JIA is an autoinflammatory and not an autoimmune disease.
Conclusion: Our study demonstrated that autoimmune diseases are frequently coexistent in children with JIA, especially in patients with oligoarthritis. Therefore, all patients with JIA and especially those with oligoarthritis should be regularly screened for associated autoimmune diseases.

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Disclosure of Interest

None declared

Table 1 (abstract P091). See text for description

Autoimmune disease	Oligoarthritis N=55 (49.5%)	Polyarthritis N=15 (13.5%)	Enthesitis related arthritis N= 22 (19.8%)	Psoriatic arthritis N=11 (10%)	Systemic arthritis N=5 (4.5%)
Uveitis	8 (14.5%)	1 (6.7%)	3 (13.6%)	1 (9%)	0
Autoimmune thyroid disease	2 (3.6%)	0	0	0	0
Celiac disease	2 (3.6%)	1 (6.7%)	0	0	0
Henoch- Schonlein vasculitis	1 (1.8%)	0	0	0	0
Idiopathic thrombocytopenic purpura	1 (1.8%)	0	0	0	0
Psoriasis	0	0	0	3 (27.3%)	0
Inflammatory bowel disease	1 (1.8%)	0	0	0	0

P092

Coverage and facilitators of influenza vaccine uptake among JIA patients in Greece

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Pediatric Rheumatology 2020, **18(Suppl 2):**P092

Introduction: Children with rheumatic diseases are considered as a population at risk of severe influenza disease and are therefore targeted for vaccination.Nonetheless, influenza vaccine coverage among JIA patients is still unclear.
Objectives: We investigated knowledge,attitudes& practices about influenza vaccine uptake among caregivers of children with JIA in Greece,aiming to depict the current situation and identify barriers and determinants to improve influenza vaccination rate.
Methods: This was a dual-centre cross-sectional study that took place across Pediatric Rheumatology Units in Athens,Greece.A detailed questionnaire about knowledge,practices and attitudes regarding influenza vaccination was disseminated among JIA caregivers.Chi-

Square was used to explore factors associated with vaccine uptake& the significance level was set at p≤ 0.05.
Results: A total of 65 caregivers(72% females) with a mean age of 42.1years(SD=7.6) participated.Country of origin was Greece(75%),followed by Albania(19%). The majority of the participants were employed(67.7%),married(87.7%) and held a secondary education degree(42%).Principal diagnosis was polyarticular JIA(29%),followed by oligoarticular JIA(26%),while 14% of caregivers were unaware of the child's diagnosis.JIA patients' mean age was 9.8 years(SD=3.8) with a mean disease duration of 4.7years(SD=3.3). Most of them were on systemic treatment(88%). Of note,74% were fully vaccinated according to national vaccination schedule and 80% had received influenza vaccine in the past (median:4 times),while only a patient had previously experienced vaccine-related adverse event.
A total of 46 children(71%) were vaccinated against influenza during the current season(2019-20) and in 96% the disease status was stable.Most participants were informed by their pediatric rheumatologist(65%) and/or their pediatrician(51%).The highest vaccine uptake was recorded among Greek participants(83%),while only 33% of Albanian caregivers vaccinated their children(p< 0.05).Caregivers of secondary or tertiary education were more likely to vaccinate their children(81.5% & 80.8% respectively) compared to those with elementary education(25%)(p<0.05).All children with psoriatic JIA were vaccinated,while children whose caregivers did not know the diagnosis reported the lowest vaccine uptake(11.1%)(p< 0.05).Disease duration was not related to vaccination rate.Among vaccinators,93.5% were under systemic treatment,81% were fully vaccinated according to national vaccination schedule and 96% of them had been vaccinated during the previous years(p<0.05). Caregivers who were informed of influenza vaccine recommendation by medical staff were more likely to vaccinate their children against influenza in the current season(78.5%,p<0.05).
Among non-vaccinators,78.9% did not have the chance to discuss their concerns with a specialist.Being uninformed of the need to immunize against influenza(52.6%) was the major reason for non-vaccination,while few caregivers reported fear of disease flare and not being aware of requiring flu immunization on an annual basis(10.5% respectively).Caregivers suggested that informing in advance(71%) and organizing national campaigns(63%) may improve vaccine uptake in the future,while most of them(71%) disapproved reminder calls/sms.
Conclusion: Influenza vaccine uptake in JIA patients in Greece is moderately high.Those previously vaccinated and those fully vaccinated according to national vaccination schedule were more likely to be vaccinated during the current season.Higher education, thorough informative discussion and notifying families in advance may address fears and lead to universal vaccine coverage in children with JIA and other rheumatic diseases.

Disclosure of Interest
None declared

P093

Effectiveness and safety evaluation of etanercept in children with Juvenile Psoriatic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P093

Introduction: Juvenile Psoriatic Arthritis (JPsA) is presented in 4 - 9% of children with juvenile arthritis (1,2). Biologic therapy, particularly etanercept, is proved to be effective and safe in the treatment of Psoriatic Arthritis in adults (3). However, little evidence exists in pediatric patients.
Objectives: to study the effectiveness and safety of etanercept in patients with JPsA.
Methods: open-label, single-center, prospective, observational (2012-2019) cohort clinical study included 18 patients (2-13.0 y/o) who met Vancouver and I/E criteria and received etanercept SC (0.8 mg/kg QW, max 50 mg per week) in combination with methotrexate (10-15 mg/m^2 QW).
Effectiveness evaluation was performed at months 6, 12, and 18 after treatment initiation with results reported on an intention-to-treat group. To assess articular manifestations of JPsA, we applied ACRpedi criteria, and BSA and PASI scores to estimate the surface area of involved skin and severity of psoriasis.
Results: We observed 18 patients with JPsA aged from 2 to 13 years, who were initiated by etanercept.
The clinical and demographic characteristics are presented in Table 1.
In patients with JPsA who received a combination of etanercept with methotrexate, at month 6 ACRpedi NoResp/30/50/70 was 5.56/94.4/55.56/5.56%. ACRpedi 90 and ACRpedi 100 at month 6 were not achieved.
At month 12 - ACRpedi 30/50/70 was 94.4/88.9/61.1%. ACRpedi 90 and ACRpedi 100 were 11.1% and 5.56%, respectively. Drug-induced remission at month 18 was 11.1%.
At month 18 - ACRpedi 30/50/70 was 77.8/77.8/72.2%. ACRpedi 90 and ACRpedi 100 were 33.3% and 11.1%, respectively. Drug-induced remission at month 18 was 33,3%. The BSA at months 6, 12, and 18 was 4.9 (1.0-7.0)%, 1.5 (0.75-3.15)%, 0.7 (0.5-1.0)%, respectively.The PASI 75, PASI 90 and PASI 100 at months 6 were 38.5/13.4/7.7%, at month 12 – 76.9/53.8/15.4%, and at month 18 – 69.2/61.5/23.1%, respectively. Drug-induced remission of psoriasis at month 18 was 23.1%. No serious adverse events occurred during the study.
Conclusion: our clinical study showed the effectiveness and safety of etanercept in JPsA patients with active articular manifestations and psoriatic lesions.

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Disclosure of Interest
K. Aleksanyan: None declared, E. Zholobova Speaker Bureau of: Pfizer, AbbVie, Novartis, Roche., S. Chebysheva: None declared

Table 1 (abstract P093). The clinical and demographic characteristics of patients with JPsA before etanercept therapy (n=18)

Clinical and demographic indicators	M ± σ / Me (Q1-Q3)
Girl/Boy Ratio	12:6 (2:1)
Average age, years	7,58 ± 3,7
Duration of the disease, years	3,0 (1,4-6,6)
No. active joints	8,0 (5-16,5)
No. joints with LOM	9 (5,75-18,25)
PGA of disease activity, mm	70 ± 15
Parent's global assessment of the child's pain, VAS	71,5 (65-90)
CHAQ	1,34 (1,1-1,68)
Psoriasis BSA, %	7,0 (4-13)
PASI score	5,7 (3-8,2)
ESR, mm/h	28,0 (20,75-40)

LOM - limitation of motion, PGA - physician's global assessment; VAS - visual analog scale, CHAQ - Childhood Health Assessment Questionnaire; BSA - body surface area; PASI - Psoriasis Area Severity Index, ESR - erythrocyte sedimentation rate; CRP - C-reactive protein

P094

Growth pattern in patients with Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P094

Introduction: Growth patterns may be impaired in patients with juvenile idiopathic arthritis (JIA).
Objectives: To evaluate the growth parameters of patients with JIA depending on various treatment regimens in identifying the causal factors of growth disorder.
Methods: 142 JIA patients (91 girls and 51 boys) aged 3 to 17 years were examined. All patients were divided into 2 groups depending on the therapy type. I group consisted of 70 children treated with methotrexate (MTX) (7 of them had systemic form, 29 – oligoarticular and 34 – polyarticular). II group included children treated with biological DMARDs (bDMARDs) (n=72, 17 patients with systemic form, 26 – oligoarticular, 29 – polyarticular). 23 patients were treated with tocilizumab, 47 patients with adalimumab and 2 patients with etanercept. Mean age in I group was 10.4 ± 0.5 years, in II group – 11.4 ± 0.4 years; mean disease duration in I group – 4.2 ± 0.4 years, in II group – 5.1 ± 0.4 years respectively. 34 patients from II group achieved clinical pharmacologic remission in contrast to only 9 patients from I group. To assess the impact of disease activity on patient's growth, we used a total activity index (TAI) – cJADAS-27 (4 components of the Juvenile Arthritis Disease Activity Score for 27 joints) for the last 12 months. We evaluated the growth velocity (GV) expressed in % for the previous year regarding the appropriate age- and gender values and body mass index (BMI). Some patients underwent hand X-ray to assess bone age. Insulin-like growth factor-1 (IGF-1) in blood serum were measured in children with growth delay. Quantitative indicators distribution is given as a median [5th; 95th procentile], the calculations were carried out using the Mann-Whitney U test, and the correlation was studied by multiple regression analysis.
Results: Our results demonstrated that there was no growth delay in patients with an oligoarticular form of JIA. 12 patients (8.5 %) of both groups were diagnosed with growth delay (height < -1 SD), in 6 patients with systemic form and 6 patients with a polyarticular form of JIA. GV in I group -10 [-91; 133] in case of polyarticular form, 10 [-41; 32] in case of oligoarticular form. GV in II group – 20 [-23; 240] and 12 [-10; 62] respectively. The relative growth velocity for the previous year was significantly higher in patients with both oligoarticular ($U = 225.5$, $p = 0.009$) and polyarticular ($U = 222.5$, $p = 0.0001$) forms of disease when used bDMARDs. In a group of patients on bDMARDs, the relative growth velocity is 2% higher in patients with oligoarticular form and 30% higher in patients with polyarticular form, compared with the use of MTX alone. 19 patients (13.4%) had an underweight, 8 patients (5.6%) were overweight, and 7 patients (4.9%) had obesity. Most overweight or obese children did not have a history of long-term use of corticosteroids (CS). 4 patients with height delay < 2-3 SD and 1 patient with height delay > 3 SD were ahead of the bone age by 4 years. In 17 children (10 of whom had height delay), IGF-1 in blood serum was age-appropriate. The TAI has a significant inverse correlation between the growth index expressed in SD ($\beta = -0.4$, $p = 0.005$) and GV ($\beta = -0.62$, $p = 0.000009$). Thus, the higher is the total disease activity index, the greater is the growth velocity delay. There was no detected correlation between these indicators and the disease duration, the age of onset, the total dose of CS and cJADAS-27 at the moment of the study.
Conclusion: The disease activity affects growth pattern. The relative growth velocity for the previous year was significantly higher in patients when used bDMARDs.

Disclosure of Interest
None declared

P095

Dynamics of vitamin D status in children with JIA

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Pediatric Rheumatology 2020, **18(Suppl 2):**P095

Introduction: There is well known the role of vitamin D as an immune and inflammatory mediator in autoimmune diseases, including chronic arthritis, its low serum concentration is associated with an increase of the synthesis of anti-inflammatory mediators and, accordingly, the activity of autoimmune diseases.
Objectives: The purpose of this study was to determine the status of vitamin D in children with juvenile idiopathic arthritis (JIA) depending on the age of the patients, the clinical variant of the disease and therapy in the dynamics of observation during the basic therapy and additional intake of vitamin D.
Methods: The main group included 39 patients with JIA corresponded to the ILAR criteria. Female patients predominated (74.36%, $p < 0.05$). The average age of patients was 10.8±4.6 years. The results were analyzed depending on patient's age (up to 6 years, from 6 to 10 years, from 10 to 14 years and older than 14 years), variant of the disease (oligoarthritis, polyarthritis, undifferentiated arthritis) and basic therapy (the presence of methotrexate or his absence). The study was conducted twice: the first - in the absence of additional intake of vitamin D, the second - after 6 months of supplementation of 2000 IU of vitamin D. The control group consisted of 20 peers who did not take vitamin D. Serum 25-hydroxyvitamin D [25 (OH) D] levels were measured using chemiluminescent method (Cobas 6000, Roche Diagnostics, Switzerland).
Results: The average serum vitamin D level was 22.26±2.53 ng/ml, that was significantly lower than in children in the control group (28.67±2.38 ng/ml; $p<0.05$). No gender dependence was found. A correlation was established between the age of patients and the level of vitamin D. Children under 6 years of age had a significantly higher vitamin D status compared than older children ($p<0.05$). The dependence of the concentration of vitamin D in serum on the variant of the disease in children during the initial study was not found.
An analysis of the vitamin D content in a re-examination showed that male patients had a positive trend compared with female patients; in young children compared with older patients than 14 years; an oligoarthritis compared with other variants; in the presence of basic therapy with methotrexate compared to therapy without it (table).
Conclusion: In patients with JIA there was an insufficient level of vitamin D which increased after an additional intake of 2000 preparations of vitamin D for 6 months. Girls, children over 14 years old, patients with non-deferred arthritis and polyarthritis as well as patients who did not receive basic methotrexate therapy, had insufficient level recovery of vitamin D, that requires a review of the regimen of additional vitamin D intake and basic therapy in these categories of patients.

Disclosure of Interest
None declared

Table 1 (abstract P095). Dynamics of vitamin D levels in children with JIA, M±m, ng/ml

Sings	Vitamin D level		Significance of differences
	in the absence of additional intake of vitamin D	after taking of vitamin D	
girls, n=29	22,46±3,13	26,30±4,27	p>0,05
boys, n=10	21,69±4,83	28,89±8,80	**p<0,05**
before 6y,n=15	24,51±2,01	31,13±2,87	**p<0,05**
6-10 y., n=10	22,46±2,47	26,25±3,52	p>0,05
10-14 y., n=9	20,27±2,61	25,39±3,71	p>0,05
older 14y.,n=5	18,68±3,50	19,45±4,98	p>0,05
oligo, n=17	24,27±1,89	34,47±2,30	**p<0,05**
poly, n=12	21,11±2,25	20,59±2,74	p>0,05
undifferentiated arthritis, n=10	20,22±2,46	22,23±3,01	p>0,05
MTX +	21,53±7,16	30,32±9,99	**p<0,05**
MTX -	22,42±2,86	26,37±3,42	p>0,05

P096

Correlation between serum calprotectin (S100A8/A9) levels and disease activity status in patients with Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P096

Introduction: S100A8/A9 (calprotectin) has been widely studied as candidate biomarker for predicting disease activity and treatment response in rheumatic diseases. Its high levels may also predict disease flares in systemic juvenile idiopathic arthritis (JIA). In clinical practice, ultrasound (US) could be a useful tool to define the disease activity status. To our knowledge there are no published articles to examine simultaneously the correlation between S100A8/A9 levels, clinical and US assessment in JIA.
Objectives: To explore the association between S100A8/A9, clinical and US assessment in JIA patients.
Methods: Patients with JIA were blinded assessed by clinical examination and ultrasound and serum levels of S100A8/A9 were measured by chemiluminescence solid phase assay. Ultrasonographic B-mode and Power Doppler assessment of 44 joints for each patients were performed. Clinical disease activity was evaluated using Wallace criteria.
Results: Thirty (18 F) consecutive patients with diagnosed non-systemic JIA were prospectively included in our study (Table 1). S100A8/A9 levels were also measured in age matched healthy controls. Median age at disease onset was 10.6 yrs (mean 10.8, range 2–16) and mean disease duration was 5.4 yrs (range 0.1–15.9). Clinically active disease according to the Wallace criteria was present in 14 patients and 16 patients were active according to US evaluation. US and physical examination agreed in 80% of cases. The concordance between US and physical examination to define synovitis in all joints was moderate (kappa=0.602). The median calprotectin levels was 31.2 (8.1-203.8) ng/ml in healthy control, 29.75 (5.4-198.1) ng/ml in clinically active disease and 24.8 (14.1-204.3) ng/ml in clinically inactive disease group. We found no differences in the S100A8/A9 levels in clinically active and inactive disease group (p=0.73). There were also no difference in calprotectin levels between US active disease [29.75 ng/ml (5.4-204.3)] and US inactive disease [24.8 (12.1-197.1)] (p=0.83). S100A8/A9 levels correlated moderately with CRP (Spearman r=0.4380; p=0.01) but no correlations were found with ESR (Spearman r 0.193; p=0.325). Only 6 pts (4 out of 6 with polyarticular course) showed calprotectin levels higher than normal.
Conclusion: S100A8/A9 levels were moderately correlated with CRP while no correlation were found with JIA categories. High serum calprotectin levels could be related with a polyarticular disease either in clinical activity or in subclinical remission. Our preliminary study need to be extended with large number of patients and designed prospectively.

Disclosure of Interest
None declared

Table 1 (abstract P096). Demographic and laboratory findings of patients with JIA

	Wallace Active (14)	Wallace Inactive (16)	Total (30)
Female Sex	10 (71.4%)	8 (50.0%)	18 (60%)
Mean Age yrs (range)	10.40 (2.41-17.46)	11.23 (5.18-17.22)	10.8 (2-18)
Mean Age of disease onset, yrs (range)	7.44 (1.20-16.00)	3.68 (1.60-8.20)	4.2 (1.19-16.00)
Mean Disease duration yrs (range)	2.9 (0.12-8.84)	7.54 (1.96-15.90)	5.4 (0.1-15.9)
Extra-articular involvement (uveitis)	2 (14.28)	4 (25.0%)	6 (20%)
ANA positivity, n (%)	10 (71.42%)	12 (75.0%)	22 (73.3%)
WBC median, (range)	7.15 (4.0-10.7)	6.15 (3.3-10.70)	6.7 (4-10.7)
ESR mm/h, median, (range)	18.5 (3-67)	9.5 (2-20)	12 (2-67)
CRP mg/dl, median, (range)	0.275 (0.1-4.6)	0.16 (0.1-0.98)	0.20 (0.1-4.6)

P097

Methotrexate effect on monocytes in Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P097

Introduction: Monocytic cells with production of proinflammatory chemokines are attributed a significant role in local and systemic inflammation of juvenile idiopathic arthritis (JIA) (1).
Objectives: The aim of this study was to analyze monocyte (MON) response to methotrexate (MTX) and other treatment methods for the juvenile idiopathic arthritis (JIA) patients.
Methods: We performed a retrospective single-center study. All children diagnosed with JIA were included into the study, excluding systemic JIA. Complete blood count (CBC) before (at the time of diagnosis) and during the treatment (in disease exacerbation and remission) was analyzed. All patients were divided into MTX monotherapy group (T1), MTX and biological disease modifying antirheumatic drug (bDMARD) group (T2), and other (bDMARDs only, low doses prednisolone, NSAIDS, sulfasalazine) (T3). Data were analyzed using SPSS 20. P value <0.05 was considered significant.
Results: 30 patients were included into the study, 60% of whom were female. Mean age of first diagnosis was 9.06±4.08 years. We found 77 documented exacerbations for all these patients from the first diagnosis till the retrospective analysis start. A meadian of 2.57 exacerbations per patient (min 0, max 15). 23 of them were during

MTX monotherapy, T2 – 31, and T3 – 23, In all groups, higher counts of leucocytes, neutrophils and platelets (PLT) at the time of diagnosis compared to remission were observed but it was not significant. The difference in monocyte counts in T1 vs other groups at first diagnosis and exacerbation did not differ showing that during exacerbation cells are stimulated in the same way like at the start of the disease. However, the MON during clinical remission were significantly lower in T1 compared to other groups (0.46±0.15 vs 0.64±0.2, p=0.0154). Besides, monocytes were significantly lower in MTX monotherapy group in remission vs exacerbation (0.46±0.15 vs 0.73±0.31, p=0.0104). Moreover, we combined all groups and investigated possible prediction of disease exacerbation or remission regarding monocyte count in CBC. MON below 0.3 predicted JIA remission with likelihood ratio (LR) of 2.76 (AUC 0.64, p=0.014).
Conclusion: Findings of the study could be useful to predict the course of the disease according to the changes in the MON seen in the complete blood count. Further studies are required to determinate changes of the blood cells in different stages of JIA, as this would help to define full remission in the patients of this chronic disease in cellular level.

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Disclosure of Interest
None declared

P098

Prediction of disease remission and exacerbation in Juvenile Idiopathic Arthritis from complete blood count parameters

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Pediatric Rheumatology 2020, **18(Suppl 2):**P098

Introduction: In recent years more attention has been paid for the complex parameters seen in the complete blood count (CBC) that could help to evaluate the course of chronic diseases (1). Defining the exact stage (remission or exacerbation) of the juvenile idiopathic arthritis (JIA) could influence the long term immunosuppressive treatment strategy in these patients.
Objectives: The aim of this study was to analyze changes of complete blood count (CBC) parameters during different stages of the disease in the juvenile idiopathic arthritis (JIA) patients.
Methods: We performed a retrospective single-center study. All children diagnosed with JIA in the last 7 years were included into the study, excluding systemic JIA. CBC before (at the time of diagnosis) and during the treatment (in disease exacerbation and remission) was analyzed. We compared a CBC results in different stages of the disease and evaluated the predictive ability of different parameters, such as leucocyte (LEU), lymphocyte (LYM), neutrophil (NEU) and platelet (PLT) counts, mean platelet volume (MPV), platelet distribution width (PDW), platelet larger cell ratio (P-LCR), platelet neutrophil lymphocyte ratio (PNLR) and neutrophil lymphocyte ratio (NLR). Data were analyzed using SPSS 20. P value <0.05 was considered significant.
Results: 30 patients were included into the study, 60% of whom were female. Mean age at first diagnosis was 9.06±4.08 years (min-13 months, max-17 years). We found 77 documented exacerbations for all these patients from the first diagnosis till the retrospective analysis start. An average of 2.57 exacerbations per patient (min-0, max-15) and 6.4 per year for all patients were found. Higher count of PLT in JIA exacerbation compared to remission was observed (348.12± 92.6 vs 310.5±68.9), but it was not significant (p=0.0976). Also, there were no differences in LEU, LYM, NEU, MPV, PDW or P-LCR levels between remission and exacerbation. However, we found significantly higher PNLR (604±412.8 vs 482±339.8, p=0.027) and NLR (1.74±1.99 vs 1.6±1.2, p=0.049) during exacerbation. Besides this, we looked at possible prediction of disease exacerbation or remission. PNLR below 143.9 predicted JIA remission with likelihood ratio (LR) of 5.55 (AUC 0.63, p=0.027) and NLR below 0.46 predicted remission with LR 5.55 (AUC 0.61, p=0.049). Also, we found that P-LCR more than 27.2 predicted JIA exacerbation with LR 2.42 (AUC 0.66, p= 0.039). When comparing first CBC (treatment naïve, on time of JIA diagnosis) with clinical remission CBC, we found that NEU below 3.15 predicted JIA remission with LR of 5.85 (AUC 0.67, p=0.016).
Conclusion: Findings of the study could be useful to predict the course of the disease according to the changes seen in the complete blood count parameters such as NEU, PNLR, NLR and P-LCR. Further prospective studies are required to estimate changes of the blood cells and their ratios in different stages of JIA and possible influence of different treatment strategies. This would help to define full remission in the patients of this chronic disease in cellular level.

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Disclosure of Interest
None declared

P099

Validation of the Psoriasis Epidemiology Screening Tool (PEST) and the new Early Arthritis for Psoriatic patients (EARP) in pediatric population- pilot study

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Pediatric Rheumatology 2020, **18(Suppl 2):**P099

Introduction: Juvenile Psoriatic Arthritis (JPsA) is an inflammatory arthritis associated with irreversible joint damage among pediatric population and is associated with psoriasis in most cases.
There are few validated screening tools for diagnosis of arthritis for adults patients with psoriasis those screening tools were never evaluated in children.
Objectives: The aim of this study was to evaluate two screening tools among pediatric patients with psoriasis.
Methods: Thirty nine patients with the diagnosis of psoriasis were administered two screening questionnaire: the new Early ARthritis for Psoriatic patients (EARP) questionnaire and the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire.
All patients were evaluated by rheumatologist for the diagnosis of JPsA and the diagnostic accuracy of the two questionnaires for the diagnosis of JPsA was compared.
Results: four patients were diagnosed with JPsA (10.2%). Four patients of 39 patients had a PEST questionnaire score of ≥ 3 all were with the diagnosis of JPsA. Thus, the sensitivity and specificity of the PEST in diagnosing JPsA were 100% and 100%,respectively, the median PEST score of the patients without the diagnosis of JPsA was 0 (0-2).

For the EARP questionnaire, 7 patients of 39 had a screening questionnaire score of ≥ 3 suggestive of JPsA, 4 were true positive and 3 were false positive. Thus, the sensitivity and specificity of EARP in diagnosing JPsA were 100% and 92%, respectively.
Conclusion: Both PEST and EARP questionnaire were easy to use and with high sensitivity for pediatric population with psoriasis, PEST questionnaire had higher specificity than EARP.

Disclosure of Interest
None declared

P100

When rheumatology and genetics meet: a case of Juvenile Idiopathic Arthritis in a patient carrying 18q deletion

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Pediatric Rheumatology 2020, **18(Suppl 2):**P100

Introduction: Deletions of the long arm of the chromosome 18 (18q-) occur in 1/40.000 live-born infants. Common clinical features are facial dysmorphism, short stature, foot deformities, congenital aural atresia, variable intellectual disability, microcephaly, cerebral white matter abnormalities. Kidney malformations, bone dysplasia, growth hormone deficiency, congenital heart disease, IgA deficiency are less commonly reported. Autoimmune diseases such as juvenile idiopathic arthritis (JIA), thyroiditis, type 1 diabetes mellitus (DM1)have been described.
Objectives: We report a case of a 10-years-girl suffering from JIA associated to dysmorphic features who was diagnosed to carry a distal 18q deletion.
Methods: A 10 years old girl came to our department because of pain in her left knee and ankles for the past 5 weeks. Her parents were consanguineous, her 2 sisters were healthy. She was born at term with normal weight and length. After birth inter-ventricular septum defect and pulmonic stenosis were diagnosed, and the latter was corrected through cardiac catheterisation at 12 months. At 2 years ataxic gait was noted.The musculoskeletal examination showed arthritis of the both ankles, left knee .At neurological examination horizontal nistagmus, dysmetria of finger nose test, hyporeflexia, unstable gait were present. Romberg test was negative. Her height and her weight were normal.The genetic evaluation revealed facial dysmorphism, hypertelorism, thickened ears with prominent antitragus, squared tip of the nose, smooth and long nasolabial filter, prominent chin, thin lips, dental crowding and narrow palate. Proximal implant of the first finger of both hands with hypoplastic last phalanx, and both fifth fingers clinodactyly were noted; at the feet medially deviated large first toes with short I metatarsus and short Vth finger with nail hypoplasia were detected. The geneticist requested an Array CGH and a brain MRI.
Results: Blood test revealed increase in CRP (5,52 mg/dL)and ERS (68 mm/h). ANA was positive with a titer of 1:640. Patient presented IgA deficiency (< 5mg/dL) and increase in thyroglobulin antibody (305UI/mL), with normal levels of thyroid hormones. The left knee and ankles ultrasound showed moderate joint effusion. Thyroid gland ultrasound showed a dishomogeneous echoic pattern in line with a thyroiditis. An eye examination was normal.Brain MRI showed dysmelination of white matter, segmental stenosis of the third distal part of the aqueduct of Sylvius with enlarged lateral ventricles. The Array CGH revealed a *de novo* heterozygous 18q22—>qter deletion, a syndrome which explain all features of our child. The patient underwent to steroids intraarticular injection in the left knee, then methotrexate and folic acid were prescribed. After a clinical response, one year later she presented arthritis of both ankles, so etanercept was started. A control brain MRI showed progression of ventriculomegaly and subependimal trasudation, thus she underwent endoscopic ventriculocisternotomy. At last rheumatologic evaluation the patient was in good general condition, and did not present signs of active arthritis, biologic treatment was confirmed.
Conclusion: Our report provides an example of how autoimmune diseases can associated to genetic diseases. The association of 18q deletion to several autoimmune diseases offers chances to identify one or more genes implicated in regulation of immunity and predisposition to autoimmunity. This is the first report of acqueductsl stenosis linked to the distal 18q deletion syndrome.

Disclosure of Interest
None declared

P101

Response to abatacept in JIA categories: results from the PRCSG/PRINTO JIA abatacept phase iv registry

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Pediatric Rheumatology 2020, **18(Suppl 2):**P101

Introduction: Abatacept (ABA), a selective T-cell co-stimulation modulator, has been demonstrated to be safe and effective in two Phase III studies.[1,2] The ongoing Phase IV Pediatric Rheumatology Collaborative Study Group and Paediatric Rheumatology International Trial Organization (PRINTO-PRCSG) registry aims to provide monitoring data from a real-world setting regarding longitudinal effectiveness of ABA in JIA.
Objectives: To assess effectiveness of ABA in JIA categories in patients (pts) who enrolled ≤1 month after starting treatment.
Methods: Using a standardised protocol and data collection process, clinical sites enroll pts with JIA currently receiving/starting IV/SC ABA and follow for up to 10 years. Pts are assessed at baseline (BL) and at 3, 6, 9, 12 and 24 months. JIA-ACR70 response rate was determined using a validated definition based on 5/6 JIA core set measures (CRP/ESR not included).[3] The clinical 10-joint Juvenile Arthritis Disease Activity Score (cJADAS10) used validated cut-offs for inactive disease (ID).[4] As-observed analysis is presented.
Results: As of 31 March 2018, 115 pts were included. Of these, 93 (80.9%) were female; BL mean (median) age at enrollment was 12.8 (13.1) yrs, age at JIA onset 4.9 (3.4) yrs and disease duration 2.4 (2.2) yrs. The JIA categories identified were: polyarticular RF–, 52 (45.2%); oligoarticular, 36 (31.3%); polyarticular RF+, 11 (9.6%); enthesitis-

related arthritis (ERA), 9 (7.8%); psoriatic and undifferentiated, 3 (2.6%) each; systemic, 1 (<1%). The proportions of pts achieving JIA-ACR70 response and cJADAS10 ID are shown in Table 1 (pt with systemic JIA excluded).

Conclusion: Abatacept treatment resulted in rapid, clinically important and sustained JIA-ACR70 response in all JIA categories with polyarticular or oligoarticular disease course and few achieved cJADAS10 ID. Limitations of the study include a low number of pts with ERA, psoriatic, undifferentiated and systemic JIA.

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Trial registration identifying number: NCT01357668

Disclosure of Interest

D. Lovell Consultant for: consultant: AstraZeneca, Boehringer Ingelheim, F Hoffman-La Roche, GlaxoSmithKline, Novartis, UCB; principal/co-principal investigator: Bristol-Myers Squibb Company, F Hoffman-La Roche, Janssen, Pfizer, UCB; board member: Forest Research, N. Ruperto Consultant for: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, Employee of: The IRCCS Istituto Giannina Gaslini (IGG), where NR works as a full-time public employee, has received contributions from Bristol-Myers Squibb Company, Eli Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties. The registry is funded by Bristol-Myers Squibb Company, Speaker Bureau of: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, Pharma, Sanofi, Servier, Sinergie, Sobi, Takeda, N. Tzaribachev: None declared, E. Morgan: None declared, G. Simonini Consultant for: AbbVie, Novartis, Speaker Bureau of: AbbVie, Novartis, T. Griffin: None declared, E. Alexeeva Consultant for: grant/research support and consulting fees: AbbVie, Novartis, Pfizer, Roche, Speaker Bureau of: AbbVie, Novartis, Pfizer, Roche, J. Bohnsack: None declared, A. Zeft Shareholder of: Merck, Opko Health, Teva, G. Horneff Consultant for: AbbVie, Novartis, Pfizer, Sanofi, Speaker Bureau of: AbbVie, Novartis, Pfizer, Sanofi, R. Vehe: None declared, V. Stanevica: None declared, S. Tarvin: None declared, M. Trachana Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, Novartis Hellas, Speaker Bureau of: Novartis Hellas, F Hoffman-La Roche, Pfizer, A. Huber: None declared, I. Orban: None declared, J. Dare Consultant for: grant/research support: AbbVie, Bristol-Myers Squibb Company, F Hoffman-La Roche, Pfizer, UCB, Employee of: Centene Corporation, I. Foeldvari Consultant for: Amgen, Bristol-Myers Squibb Company, Eli Lilly, Novartis, Pfizer, Sanofi, P. Quartier Consultant for: consultant: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum; board member: Sanofi, Speaker Bureau of: AbbVie, Bristol-Myers Squibb Company, Chugai-Roche, Eli Lilly, Novartis, Novimmune, Swedish Orphan Biovitrum, A. Dominique Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, T. Kou Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, R. Wong Shareholder of: Bristol-Myers Squibb Company, Employee of: Bristol-Myers Squibb Company, A. Martini Consultant for: Aurinia, Bristol-Myers Squibb Company, Eli Lilly, EMD Serono, Janssen, Pfizer, H. Brunner Consultant for: Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, GlaxoSmithKline, F Hoffman-La Roche, Novartis, Pfizer, Takeda, UCB, Wyeth (funds paid to employer), Speaker Bureau of: F Hoffman-La Roche, GlaxoSmithKline, Novartis

Table 1 (abstract P101). Proportion of patients achieving JIA-ACR responses and cJADAS ID

	Baseline	3 months	6 months	9 months	12 months	24 months
Overall population	115	83	82	49	41	23
JIA-ACR70 response	0 (0)	17 (15.5)	22 (20.6)	15 (14.9)	23 (23.0)	14 (15.2)
cJADAS10 ID	0 (0)	8 (11.4)	9 (14.3)	9 (22.0)	13 (28.9)	7 (35.0)
Polyarticular RF-	52	40	36	26	28	14
JIA-ACR70 response	0 (0)	8 (16.3)	9 (18.8)	6 (13.0)	9 (19.6)	6 (13.6)
cJADAS10 ID	0 (0)	3 (8.6)	2 (6.7)	3 (15.8)	2 (10.5)	1 (10.0)
Oligoarticular JIA	36	29	30	21	19	13
JIA-ACR70 response	0 (0)	6 (16.7)	7 (19.4)	6 (18.2)	7 (21.9)	5 (16.7)
cJADAS10 ID	0 (0)	2 (8.7)	4 (19.1)	4 (30.8)	6 (35.3)	3 (50.0)
Polyarticular RF+	11	6	7	6	5	2
JIA-ACR70 response	0 (0)	1 (10.0)	1 (11.1)	1 (11.1)	2 (22.2)	0 (0)
cJADAS10 ID	0 (0)	1 (33.3)	1 (20.0)	0 (0)	2 (50.0)	0 (0)
Enthesitis-related arthritis	9	5	7	4	4	1
JIA-ACR70 response	0 (0)	2 (25.0)	5 (62.5)	1 (14.3)	3 (42.9)	1 (20.0)
cJADAS10 ID	0 (0)	1 (20.0)	1 (16.7)	1 (25.0)	2 (66.7)	1 (100.0)
Psoriatic JIA	3	2	2	2	2	2
JIA-ACR70 response	0 (0)	0 (0)	0 (0)	1 (33.3)	0 (0)	1 (33.3)
cJADAS10 ID	0 (0)	1 (100.0)	1 (100.0)	1 (50.0)	1 (50.0)	2 (100.0)

Data are n (%)
cJADAS10=clinical 10-joint Juvenile Arthritis Disease Activity Score; ID= inactive disease; RF=rheumatoid factor

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Articular and extra-articular damage in ukrainian patients with juvenile idiopathic arthritis treated according strategy "treat 2 target"

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Pediatric Rheumatology 2020, **18(Suppl 2):**P102

Introduction: Targeted treatment of patients with Juvenile idiopathic arthritis (JIA) is recommended. The frequency of damage in children and adolescents with JIA has hardly been investigated in Ukraine.

Objectives: To assess the prevalence and accrual of damage in patients with JIA treated according modern strategy "Treat to Target" (T2T).
Methods: Study included 76 children aged 5 to 17 years with JIA treated using strategy "T2T" minimum during 6 months. The Juvenile Arthritis Damage Index Articular (JADI-A) score and the Juvenile Arthritis Damage Index Extraarticular score (JADI-E) were used for determination of irreversible changes in patient.
Results: 30.26 % of children performed JADI-A above 1 point ranged from 1 to 5 points. JADI-E was below 1 point only in 3.95 % of patients. 25.00 % of children had JADI-E equaled 1 point, 40.79 % - 2 points and 30.26 % - 3 or more points. Growth retardation, significant disproportion of leg length, severe muscular atrophy and uveitis were the most commonly reported among the JADI-E criteria. The mean values of JADI-A and JADI-E showed the absence of their dependence on sex, inflammatory activity, RF-positivity and ANA-positivity. Depending on the duration of the JIA, there was no significant difference in the mean JADI-A score. Mean JADI-E score showed a clear tendency to its gaining with increasing of the disease duration ($p < 0.05$). It was found that the mean score JADI-E was independent on the type of baseline therapy and was not significantly different in patients receiving only methotrexate compared to those, who treated with methotrexate in combination with IBT. Mean JADI-A score was significantly higher in patients treated with methotrexate alone than in children treated with combination therapy ($p < 0.05$).
Conclusion: The accumulation of irreversible persistent changes in patients with JIA does not depend on sex, disease activity, positivity in RF and ANA. With the increase in the duration of the disease, progressive accumulation of joint lesions does not occur. Therapy with methotrexate in combination with IBT significantly improves the average JADI-A score. Extra-articular changes accumulation has a clear dependence on the duration of the disease, regardless of the type of baseline therapy.

Disclosure of Interest
None declared

P103

Rf-positive Juvenile Idiopathic Arthritis: a study of 69 cases in single center

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Pediatric Rheumatology 2020, **18(Suppl 2):**P103

Introduction: Approximately 5-10% of children with juvenile idiopathic arthritis have rheumatoid factor-positive (RF+) arthritis (RF+ JIA), which requires earlier administration of more aggressive therapy due to rapid progression.
Objectives: To analyze epidemiological, clinical characteristics and treatment of patients (pts) with RF+ JIA in the single center.
Methods: Retrospective study of all consequently pts of single-center last 10 years in pediatric department by results of fulfilled examination to diagnose RF+ JIA.
Results: The diagnose RF+ JIA was verified in 69 pts (11,6% were boys) – 6.5% from all pts with JIA. The median age of JIA at onset was 12.2 y.o. (7.0; 14.0). The median of disease duration at the time of JIA verification was 6 mo (4; 12). The median of the number of active joints at the time of JIA verification was 16.5 [10.75; 23.25], 11.2% of pts had oligoarthritis at onset. RF+ were detected in 94.2% of pts, ACCP+ - in 78.2% of pts. 72.5% of pts had combination RF+ and ACCP+, 5.8% of pts had only ACCP+. The median of ESR was 29 [19.75;44.5] mm/h, CRP was 15.0 [6.9;34.4] mg/l at onset. Extra-articular manifestations observed in 26% of pts: 7.2% - fever at onset, 24.6% - lymphadenopathy, 4.3% - rheumatoid lung disease, 2.9% - rheumatoid nodules, 1.4% - pericarditis. Secondary Sjögren's syndrome was diagnosed in 15.5% of pts, autoimmune thyroiditis – in 8.5%. 19.7% of pts had family history of autoimmune disorders. The therapy included NSAIDs (97.1%), steroids (49.2%), DMARDs (methotrexate (MTX) alone – 78.3%, 2 DMARDs – 14.5%, 3 DMARDs consecutive – 7.2%), biologics (B) – 94.2% of pts. B was started during the 1st year of disease in 78.2% of pts due to the rapid progression of the erosive process. 63.8% of pts received only 1 B, 18.8% - 2 B, 7.2% - 3 B. As the 1st B used: infliximab (INF) – 5.6%, tocilizumab (TCZ) – 4.3%, etanercept (ETA) – 17.4%, adalimumab (ADA) – 10.1%, abatacept (ABA) – 44.9%, rituximab (RTM) – 7.2%, golimumab (GLM) – 2.9%, sarilumab – 1.8%. As the 2nd B used: 9.5% - TCZ, 14.3% - ETA, 23.8% - ADA, 19% - ABA, 28.6% - RTM, 4.8% - GLM. As the 3d B used: 25% - TCZ, 25% - PTM, 37.5% - ADA, 12.5% - ETA. 4.3% of pts received successively 4 B (ABA-ETA-ADA-TCZ, ABA-ETA-ADA-RTM, TCZ-ABA-ADA-RTM). The reasons for substitution therapy were serious adverse effects, subsequent loss of effect. The frequency of ACCP+ was not statistically different in groups with the effective use of only 1 B and, if necessary, replacement. In the presence of systemic manifestations, preference was given to TCZ or RTM, with secondary Sjogren's syndrome - RTM or ABA.
Conclusion: RF+ JIA is rare subtype of JIA, which characterized by high activity at onset. Most pts required the early appointment of aggressive therapy in connection with the rapid progression of the erosive process. The presence of systemic manifestations/secondary Sjogren's syndrome influence on choice of therapy. An analysis of the prescribed therapy did not reveal the effect of ACCP+ on preferred choice B or frequency of replacement B.

Disclosure of Interest
None declared

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The main challenges in the transition of patients with Juvenile Idiopathic Arthritis to adult service in Ukraine

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Pediatric Rheumatology 2020, **18(Suppl 2):**P104

Introduction: The organization of the transition of a patient with a chronic disease from the pediatric to the adult service is a global problem. Different countries have adopted different approaches to this process, while most of the difficulties encountered are similar. Maintaining continuity between services during the transition of a patient with juvenile idiopathic arthritis (JIA), treated with biologics, is fundamentally important.
Objectives: To evaluate the procedure for transferring patients to adult service in Ukraine: its characteristics, difficulties and expectations of specialists.
Methods: A survey of 49 pediatric specialist services was conducted
Results: It was determined that the transition to adult service occurs simultaneously after the patient reaches 18 years. 45(91.8%) of respondents consider it mandatory to preserve the initial diagnosis of JIA upon transition process; 4(8.2%) believe that it is possible to transform the diagnosis of JIA into one used in adult service. To assess arthritis activity, 30(61.2%) specialists at the transition stage consider it appropriate to use JADAS27 with the subsequent transition to the corresponding integral activity indices used in adult practice; 15(30.6%) consider it possible to use JADAS27 throughout the entire period of patient monitoring; 4(8.2)% suggested the simultaneous implementation of the integral index DAS28 at the stage of patient transition to adult service. 29(59.1%) pediatric rheumatologists begin preparing patients with JIA for the transition immediately when biological therapy is initiated, regardless of the patient's age; 20(40.8%) respondents prepare the patient 1-2 years before reaching 18 years of age. Differences are identified in therapeutic tactics. 39(79.5%) specialists prefer not to change the

treatment of the disease on the eve of the transition. At the same time, 25(51.0%) respondents believe that the decision to reduce/cancel biologics is advisable after the patient with JIA has been in a state of stable remission for 2 years, 2(4.1%) prefer to continue biologics until 5 years of remission. 12(24.5%) responders consider it possible to stop biologics >5 years before reaching the age of 18; 27(55.1%) think that it possible to stop them 1 year before the transfer, at the same time 10(20.4%) specialists prefer to follow therapeutic strategy without any changes. In case of combined DMADRs therapy, 37(75.5%) pediatric rheumatologists initially taper methotrexate or other synthetic DMARDS, which also differs from approaches at the adult service. Regarding the patient's readiness for transition, 26(53.1%) of responders chose the need for a comprehensive procedure taking into account the opinions of specialists from both services, parents, a psychologist and the results of a patient survey; 18(36.7%) specialists believed that a pediatric rheumatologist can independently determine the patient's readiness for transition, while 4(8.1%) believed that the results of one survey are enough. The main problem of the transfer to the adult service of 19(38.8%) pediatric rheumatologists noted the lack of a collaboration between pediatric and adult rheumatological services and 19(38.8%) noted the complication of access to the rheumatologist in the adult service.

Conclusion: In Ukraine, there is no unified approach to the procedure for transition of patients with from pediatric to adult rheumatology service. Among the main difficulties pediatric rheumatologists determined: the lack of a standardized approach for diagnosis formulation, assessing the disease activity, therapeutic tactics of a patient, including biological therapy. The issue of creating structures to coordinate the patient's transition for maintaining their access to treatment, rehabilitation programs and psychological support in Ukraine is extremely relevant.

Disclosure of Interest
None declared

P105

Comorbid infections in children with Juvenile Idiopathic Arthritis

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Introduction: Infectious complications are one of the leading causes of adverse outcomes in rheumatic diseases. The early administration of immunosuppressive and biotechnological drugs has significantly changed the course and outcome of diseases, but at the same time, it causes the risk of activation of latently ongoing comorbid infections. In this regard, it is urgent to prevent both the onset and exacerbation of chronic infections, primarily bronchopulmonary and urinary systems, which complicate the course of the underlying disease and require additional treatment costs.

Objectives: The goal of the study is to determine the frequency and role of comorbid infections in children with juvenile idiopathic arthritis (JIA).

Methods: Material and methods. A total of 147 children with JIA were examined in the rheumatology department of the 4th City Children's Clinical Hospital in Minsk. Enthesitis-associated arthritis was diagnosed in 8 children (5.4%). Systemic onset JIA was detected in 20 children (13.6%). Polyarticular JIA was detected in 48 children (32.7%). Oligoarticular JIA was observed in 71 children (48.3%). The determination of antigen in the biological environments of the body (blood, saliva, urine) was carried out by PCR. A bacteriological study of nasal and pharynx was carried out for the presence of pathogenic flora.

Results: Infection was named as the cause of the disease by 1/3 of the patients: the acute respiratory infection suffered the previous day was noted in 27 (38.1%) children with oligoarticular JIA, in 15 (31.3 %) children with polyarticular JIA, in 8 (40%) children with systemic onset JIA, in 3 (37.5%) children with enthesitis-associated arthritis. The presence of a nasopharyngeal infection (sinusitis, pharyngitis or tonsillitis) was noted in 18 (25.3%) children with oligoarticular JIA, in 10 (20.8%) children with polyarticular JIA, in 6 (30%) children with systemic onset JIA. About 1/3 of the patients answered positively to the question about the relationship of the exacerbation of the disease with an acute respiratory viral infection (35.2% of children with oligoarthricular JIA, 37.5% of children with polyarticular JIA, 35% of children with systemic onset JIA and 25% of children with enthesitis-related arthritis).

Due to the persistence of a high degree of disease activity, 18 patients with JIA were prescribed adalimumab in combination with methotrexate, and 22 patients received tocilizumab. Among children with JIA treated with methotrexate and adalimumab, a respiratory tract infection developed in 22.2%, including severe infection in 5.5% of patients. Among children treated with tocilizumab, a respiratory tract infection developed in 27.3% of patients. Herpetic rashes on the lips, wings of the nose and other parts of the face in most children appeared 2-3 times a year, in some cases up to 7-8 times a year. The most prone to relapse of this viral infection were patients with systemic onset JIA. Urinary tract infection was observed in 13 (18.3%) children with oligoarticular JIA, in 10 (20.8%) children with polyarticular JIA, and in 5 (25%) children with systemic JIA. The incidence of urinary tract infections in children with JIA treated with methotrexate and adalimumab was 5.5% when using methotrexate, 11.1% when using adalimumab. Among children receiving tocilizumab, urinary tract infection was noted in 13.6%.

Conclusion: Conclusion The data obtained indicate first of all the importance of infection in the initiation of a number of JIAs and the need for a thorough history taking in children with JIA, which will allow them to identify comorbid infectious diseases that complicate the course of the underlying disease and choose the optimal treatment regimen.

Disclosure of Interest
None declared

P106

Evaluation of hepatitis B vaccine response in patients with JIA

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Pediatric Rheumatology 2020, **18(Suppl 2):**P106

Introduction: Juvenile Idiopathic Arthritis (JIA) is a heterogeneous, idiopathic, chronic inflammatory disease of unknown cause which begin before 16 years of age. Vaccination is the most effective way to prevent infectious diseases. In the literature, there is limited data regarding hepatitis B vaccine response in patients with the recent diagnosis of JIA.

Objectives: With this study; we aimed to evaluate and compare the presence of antibodies against hepatitis B vaccine at the time of diagosis of JIA with the healthy peers.

Methods: Between January 2015 and January 2020, patients referred to three pediatric rheumatology outpatient clinic with the recent diagnosis of JIA were evaluated for the presence of antibody titers against hepatitis B vaccine. A response to the HBV vaccine was accepted as the production of an anti-HBs antibody level $\geq$ 10 IU/L. The results were compared with the age and sex matched control group consisting of patients without any chronic disease but prepared for surgery, their blood tests anti-HBs ab levels were obtained before surgical operations.

Results: The study included 262 patients with JIA and 275 healthy controls. The most common JIA subtypes were 98 (37.4%) oligoarticular followed by 49 (18.7%) enthesitis related arthritis, 33

(12.5%) polyarticular, 11 (4.1%) systemic, 6 (2.2%) psoriatic arthritis and 4 (1.5%)unclassified. Of the cohort, 262 patients diagnosed with JIA 135 were boys and 127 were girls, 147 of the control group were boys, 128 were girls. There was no difference between the patient and control groups in terms of age and gender (p> 0.03, p> 0.028) The mean age at diagnosis of patients was 10.9 ± 4.6 years and the mean follow-up duration was 16.1 ± 5.8 months. While anti-HBs ab positivity was present in 59.1% (n = 155) of JIA patients, it was positive in 73% (n = 201) of the control group (p <0.002). HbsAg positivity was not detected in neither in any of the patients nor the controls. Thirty-seven patients of the JIA cohort had antinuclear antibody (ANA) positivity. Of those with ANA positivity, 28 (75.6%) had anti-HBs ab positivity, while in ANA negative (n = 78) patients this rate was 53.8% (n = 42) (p <0.02).
Conclusion: This study had shown that hepatitis B vaccine response was lower in patients with recent diagnosis of JIA even before starting medications. At the time of diagnosis with JIA, hepatitis B vaccine response assessment should be routinely performed and booster dosing should be considered in cases without any response.

Disclosure of Interest
None declared

P107
Obesity impairs achievement of Clinical Inactive Disease (CID) in patients with Juvenile Idiopathic Arthritis (JIA) treated with TNF inhibitors

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Introduction: Obesity has been associated with more severe disease activity and reduced response to TNF-inhibitors (TNFi) in obese patients with rheumatoid arthritis (RA) or with psoriatic arthritis (PsA).
Objectives: to assess prevalence and disease features associated with obesity in juvenile idiopathic arthritis (JIA) and to evaluate the impact of obesity on the achievement of clinical inactive disease (CID) at six months from the start of treatment with TNFi.
Methods: retrospective analysis of demographic, clinical and laboratory features and body mass index (BMI) collected at the start of TNFi treatment in patients with oligoarticular and rheumatoid factor (RF)-negative polyarticular JIA. Patients were divided into obese and non-obese; demographic, clinical and disease features were compared in the two groups. The distribution of obese, overweight, healthy-weight and underweight patients according to the achievement of CID at 6 months was investigated.
Results: 234 patients with JIA (39% RF-negative polyarthritis, 25% extended oligoarthritis, 36% persistent oligoarthritis) were enrolled in the study. Obesity (BMI $\geq 95^{th}$ percentile for age and gender) was present in 31 patients (13.2%). Obese patients compared to non-obese patients, had an older age at disease onset (p=0.020), lower frequency of antinuclear-antibody positivity (p=0.043), a higher number of active joints at baseline (p=0.0048) and higher C-reactive protein at baseline (p=0.043). Obese JIA patients achieved clinical inactive disease (CID) at 6 months with a lower frequency compared to non-obese patients (p= 0.005). In multivariate regression analysis obesity at baseline was confirmed as an independent risk factor for non-achievement of CID at 6 months from starting TNFi (OR 2.42 [95% CI 1.04-5.61]; p=0.040).
Conclusion: obesity negatively affects response to TNFi in oligo- and RF-negative polyarticular JIA, independently from other disease-associated variables.

Disclosure of Interest
None declared

P108
Use of telemedicine in pediatric rheumatology in one Russian center

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Pediatric Rheumatology 2020, **18(Suppl 2):**P108

Introduction: The pediatric rheumatology workforce is committed to a mission of providing children with access to care and superior clinical outcomes. With a limited number and distribution of pediatric rheumatologists, telemedicine has been proposed as one way to meet this mission, yet the adoption of this modality has been slower than expected.
Objectives: The main goal of the department of Telemedicine is to organize and conduct effective assistance with the remote interaction of doctors in the regions of Russia with the Center's consultants to assess the patient's health status, clarify the diagnosis, determine the prognosis and tactics of the diagnostics and optimal treatment, correct the previously prescribed treatment, and in difficult cases to transfer the patient to Federal Center. Provide an overview of the use of telemedicine consultations in rheumatology department at the Federal Center.
Methods: The telemedicine consultations department was established on the basis of the Federal Center on 7^{th} of September in 2018. It is equipped with all the necessary equipment for organizing telemedicine consultations in real time, as well as holding deferred consultations on documents and selecting for hospitalization.
Results: In 2018 43 applications were received (8 - emergency, 13 - urgent, 22 - planned), rheumatic diseases were excluded in 4 patients, 39 patients were hospitalized (4 of them in the ICU). In 2019 268 requests were received (75 - emergency, 48 - emergency, 145 - planned), rheumatic diseases were excluded in 43 patients, 92 patients received the recommendations of diagnostics and correction of therapy, 133 patients were hospitalized (11 of them in the ICU). In 2020 (3 months) - 85 applications (16- emergency, 27 - emergency, 42- planned), rheumatic diseases were excluded in 5 patients, 33 patients were hospitalized in the rheumatology department (2 of them in the ICU). In 2020 (from January to March) the number of applications increased 3.5 times in comparison with 2019.
Conclusion: Telemedicine increased acceptability of providing children professional care. Outreach clinics were acceptable to a majority. In telemedicine setting, physicians face various difficulties and challenges, requiring special expertise, qualities and skills. Special measures are needed to obtain proper diagnosis and decisions and decrease the number of hospitalizations.

Disclosure of Interest
E. Alexeeva Speaker Bureau of: Novartis, Pfizer, Sanofi, MSD and Roche, T. Dvoryakovskaya Speaker Bureau of: Novartis, Pfizer, MSD and Roche, A. Fetisova: None declared, R. Denisova Speaker Bureau of: Novartis, MSD and Roche, A. Babayan: None declared, A. Mirzaeva: None declared

P109
Clinical spectrum of childhood arthritis: experience from a single centre in sub- Himalayan region in north west India

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Pediatric Rheumatology 2020, **18(Suppl 2):**P109

Introduction: Arthritis is one of the commonest presentations of rheumatological illnesses in children.It is often accompanied by fever,rash,uveitis,hepatosplenomegaly,lymphadenopathy and

serositis.Growing up with arthritis is often challenging. With optimal care and treatment,most children with arthritis live life to full potential.
Objectives: To present clinical,laboratory characterstics and treatment in patients with Childhood -Arthritis followed up in Pediatric -Rheumatology- Clinic(PRC) at DR .Rajendra Prasad Government Medical College ,Tanda, Himachal Pradesh ,India
Methods: A Retrospective Chart Review was conducted for all patients who attended PRC with a musculoskeletal complaint.International-League-of-Associations-for-Rheumatology(ILAR)criteria were used to diagnose Childhood-Arthritis. Data collected included:gender,age at onset of symptoms,initial manifestations,clinical and laboratory-parameters, final diagnosis,treatment,follow-up and duration before attending PRC.
Results: Total of 44 children with arthritis were included.There was male predominance(male:female=1.3:1),mean age at onset of symptoms was 10.14±3.89years.Median-interval between onset of symptoms and diagnosis was 2 months. Various subtypes of arthritis identified are shown in figure 1.Commonest joint involved is Knee followed by Hip and elbow joints.Fever at time of presentation was present in 6(13.63%) patients.One child with Systemic-JIA had splenomegaly.One with Camptodactyly-Arthropathy-Coxavara-Pericarditis-Syndrome(CACP) had panserositis.Mean hemoglobin was 11.33± 1.60 g/dl.ANA which was done by Indirect-Immunofluorescence on Hep-2 cell line was positive in 10(22.72%), of which 5 had Oligoarthriitis.HLA-B27 which was done by PCR was positive in 7(15.90%) patients. Uveitis was observed in 4(9.09%) patients and all had oligoarthritis.11(25.00%)patients were treated by NSAIDS only and 12(27.27%),7(15.90%),3(6.81%) patients were given Methotrexate,Intra-Articular-Corticosteroid-Injection and Sulfasalazine respectively. Cyclophosphamide was started in 1 patient with SLE arthritis and 1 patient with systemic-JIA is on Tocilizumab.16(36.36%) patients are on regular follow-up with mean duration of 93.92 person-months.
Conclusion: We highlighted various clinical and labortary characterstics in children with arthritis.Oligoarthritis-JIA is the commonest subtype in our study.Unusual causes like CACP and SLE arthritis were seen among study population.Childhood musculoskeltal pain is still a dilemma among pediatricians.Knowledge of clinical spectrum will increase the awareness for early referral,diagnosis and treatment .

Disclosure of Interest
None declared

P110

Dermatologic adverse events associated with Juvenile Idiopathic Arthritis treatment

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Introduction: Steroids and disease-modifying anti-rheumatic drugs (DMARDs) are widely used in the treatment of juvenile idiopathic arthritis (JIA). Dermatologic adverse events including psoriasis have been reported in treatment of various inflammatory diseases (1-3). However, data regarding the occurrence of dermatologic adverse events in JIA patients are scarce (4-6).
Objectives: To determine the prevalence of dermatologic adverse events in JIA patients treated with systemic steroids and DMARDs. To investigate an association between drugs and dermatologic adverse events and the association between anti-TNF treatment and psoriasiform lesions.
Methods: Data from the international, observational registry Pharmachild were used. It includes patients with JIA who were treated with NSAIDs, steroids and/or synthetic and biological DMARDs. Pharmachild started in 2011 and data on adverse events were collected. Treatment of patients with and without a dermatologic adverse event was compared. The start date of the drug had to be at least one day before the adverse event date and the end date needed to be similar or later than the adverse event date.
Results: Among 8841 patients, 439 (5.0%) patients had at least one dermatologic adverse event and in total 492 dermatologic adverse events were reported. Median follow-up time was 3.9 years. Erythema, rash and pruritus occurred in 65 of 492 (13.2%) dermatologic adverse events, other dermatologic adverse events in 46 (9.3%), eczema in 34 (6.9%), hair disorders in 33 (6.7%), and psoriasisform lesions in 30 (6.1%). Several drugs were used more often in patients with such an event than patients without. In five of eight patients with psoriasiform lesions during anti-TNF treatment the lesions disappeared with the discontinuation, reduction or interruption of the dose.
Conclusion: A wide range of dermatologic adverse events was reported in this cohort underlining the importance to be aware of such adverse events.

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Trial registration identifying number: ClinicalTrials.gov Identifier: NCT01399281

Disclosure of Interest
None declared

P111

Estimation of the vitamin D status and its correlation with clinical activity in children with JIA

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Pediatric Rheumatology 2020, **18(Suppl 2):**P111

Introduction: JIA is the most common rheumatologic disease and these patients suffer from the condition with difficult pathogenesis and as well other underestimate conditions - microelement and vitamin deficiency. Vitamin D deficiency in pediatric population plays a leading role according to WHO reports.
Objectives: The aim of our study was to evaluate status of vitamin D and its correlation with clinical activity of the disease in patients with JIA.
Methods: We did complete clinical and laboratory investigation of 83 children with JIA, at the age range from 3 to 16 years and middle duration of the disease 14 months. Estimation of the vitamin D

status was done with classification approved by experts of International endocrine society, concentration of the serum hydroxyvitamin D was done without connection with child's age, osteocalcin level was measured. For characteristic of the clinical activity we took into account amount of the active joints, results of CHAQ, VAS, CRP, IL-1β, IL-6 in serum by using of the ELISA method.
Results: Laboratory activity of the inflammatory response was presented by enlarged concentration of CRP (6,9±2,7g/l), IL-1β (5,8± 4,2 pg/ml; N ranges <5 pg/ml), IL-6 (10,2±2,4pg/ml; N ranges <9 pg/ml). Concentration of CRP, IL-1β was slightly increased through all patients in different subtypes of JIA, IL-6 was significantly higher in patients with polyJIA. Patients with anamnesis of the JIA in more than 18 months had slightly lower laboratory activity ($p < 0,05$). We figured out that half of the patients were detected with vitamin D deficiency (40 cases (48,19 ± 5,17) %), that exceeded frequency of vitamin D insufficiency (31 cases (37,35 ± 4,68) %, $p> 0,05$) and observed more often than number of them with normal amount (12 cases (14,45 ± 4,21) %, $p< 0,01$). Children with JIA had concentration of 25(OH)D in serum ((21,13 ± 2,64) ng/ml, 95% CI: 16,02 – 27,44 ng/ml). Vitamin D deficiency was more often found in kids with high disease activity (23 children (57,5 ± 9,05) %, $p<0,05$; OR = 0,51, S = 0,56, 95% CI: 0,17 – 1,58), than in kids with mild or moderate process. As well, we found that increasing of the inflammatory activity in patients influence on decreasing of 25(OH)D in serum ($r = – 0,43$, $p < 0,01$). Rising of the vitamin D deficiency followed by significant decrease of the osteocalcin in serum ($p < 0,05$). We estimated correlation between osteocalcin amount and hydroxyvitamin D in serum of the children with mild and moderate activity ($r = 0,51$, $p < 0,01$), and high disease score ($r = 0,6$, $p < 0,01$).
Conclusion: So, patients with high activity of the JIA have lowest concentration of 25(OH)D in serum ((19,33 ± 2,17) ng/ml, 95% CI: 14,55 – 23,84 ng/ml) and low intensity of bone metabolism accoding to serum osteocalcin ((52,27 ± 3,74) ng/ml; 95% CI: 46,19 – 61,36 ng/ml).

Disclosure of Interest
None declared

P112

Inaugural hip involvement in Juvenile Idiopathic Arthritis

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis of childhood. Hip involvement often represents a turning point in the course of the disease.
Objectives: The aim is to study the epidemiological, clinical, radiological and therapeutic characteristics of hip involvement during JIA.
Methods: Retrospective study over 13 years (2006-2019) enrolling patients followed for JIA meeting the criteria of the International League of Associations for Rheumatology (ILAR) and presenting a hip involvement.
Results: Among the 25 cases of JIA collected, 14 patients had hip involvement with a sex ratio of 1. The average age at the onset of the disease was 11 years. The average time to diagnosis of JIA was 25 months. Subtypes of JIA according to The ILAR were: enthesitis-related arthritis in 7 cases, seropositive polyarticular JIA in 2 cases, seronegative polyarticular JIA in 2 cases, oligoarticular JIA in 2 cases and juvenile psoriatic arthritis in one case.
Hip involvement was bilateral in 12 cases. Examination revealed lower limb inequality in 5 cases, limited hip mobility in all planes in 12 cases and irreducible hip flessum in 4 cases. Lequesne algofunctional index averaged 8.5.
Standard radiographs showed minimal to moderate pinching in 9 cases and destructive hip disease in 5 cases.
All patients were initially treated with a combination of non-steroidal anti-inflammatory drugs (NSAIDs) and rehabilitation. Disease modifying anti-rheumatic drugs were initiated in 11 patients (salazopyrine in 2 cases and methotrexate in 9 cases). Hip joint injection of steroid has been indicated in 11 cases with improvement in clinical symptoms in 9 cases.
Total hip replacement (THR) was necessary in 2 cases. The average duration of progression of JIA at the time of THR was 9 years and 6 months. No patient had any post-surgical complications.
Conclusion: Hip involvement is common and estimated to occur in approximately 35–63% of children with JIA. It is a predictor of disease severity because of the disability it can cause. Hence the need for early diagnosis and management to delay the progression of the disease and the use of THR.

Disclosure of Interest
None declared

P113

Juvenile Idiopathic Arthritis and growth pattern in Egyptian patients.

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Pediatric Rheumatology 2020, **18(Suppl 2):**P113

Introduction: Juvenile idiopathic arthritis (JIA) is one of the most common rheumatic diseases in childhood and is frequently associated with growth retardation. Along, vitamin D is critical to the growth and development of the skeleton as well as to bone mineral metabolism.
Objectives: We aimed to evaluate growth pattern and vitamin D level in patients with JIA and its different subtypes.
Methods: 80 JIA patients and 80 healthy controls were included. For all patients and controls we assessed body weight, standing height, body mass index (BMI), Serum 25(OH) D3. Thyroid function tests were assessed to exclude patients with hypothyroidism or autoimmune thyroiditis, liver and renal function tests, calcium, phosphorus, alkaline phosphatase, fasting blood sugar were done to evaluate other causes of short stature.
Results: JIA patients' mean height, weight, and BMI were significantly lower compared to controls (135.4±22.1 vs. 145.7±21.8, p=0.042 for height), (34.6±13.6 vs. 39.8±11.4, p=0.039 for weight) and (18.52±3.96 vs. 21.73±5.43, p= 0.041 for BMI). Mean serum 25(OH) D3 level was significantly lower in JIA patients than controls (15.69±6.6 ng/ml vs. 31.62±4.9 ng/ml, p<0.0001), patients with systemic onset and seropositive polyarthritis (RF positive) have the lowest 25(OH) D3 level compared with other JIA subtypes. There was significant negative correlation between steroid dose, duration and JIA patients' height (r= -0.456, p=0.017 and r=-0.776, p=0.001 respectively). Serum 25 (OH) D3 level was significantly correlated with patients' height and BMI (r=0.33, p= 0.029 and r=0.32, p=0.043).
Conclusion: the nutritional status of JIA patients is multi-factorial. Onset subtype and low level of vitamin D were found to have an effect on growth parameters as height and body mass index in patients with JIA.

Disclosure of Interest
None declared

P114

Musculoskeletal complaints of children with psoriasis and ultrasonographic evaluation of subclinical achilles enthesopathy

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Pediatric Rheumatology 2020, **18(Suppl 2):**P114

Introduction: Psoriasis (Pso) is an immune-mediated inflammatory skin disease displaying several presentations such as plaque, nail, guttate, inverse, pustular and erythrodermic . Pso may be complicated with systemic features including arthritis, uveitis and metabolic syndrome. Various musculoskeletal manifestations, such as peripheral arthritis, enthesitis, dactylitis and spondylitis may accompany Pso. According to adult studies, the prevalence of Pso is approximately 2% to 3% of general population, whereas psoriatic arthritis (PsA) is present in 30% of patients with Pso. However, there are no studies evaluating the subclinical musculoskeletal findings of juvenile Psos patients.
Objectives: To evaluate the presence of articular/extra-articular inflammatory conditions and enthesis thickness by ultrasonographic imaging in pediatric Pso patients.
Methods: Pso patients without known musculoskeletal features and healthy peers were evaluated with standardized forms and physical examination by pediatric rheumatologist. Both patients and controls underwent ultrasonographic evaluation for Achilles tendon thickness in order to define subclinical enthesopathy.
Results: A total of 55 pediatric Pso and 46 age and gender matched selected healthy children were included in the study. Of patients with Pso 56.4% had arthralgia, 25.5% had lower back pain, 18.2% had heel pain, 12.7% had hip pain, and 10.9% described morning stiffness. Arthritis of knee was detected in 7.3%, sacroiliac tenderness in 12.7% and enthesitis in 9.1% of the patients. Arthralgia, lower back pain and heel pain were significantly frequent in Pso group than healthy children (p=< 0.001, p=0.02 and p=0.03 respectively). None of the healthy children had inflammatory lower back pain, arthritis, morning stiffness, sacroiliac tenderness and enthesitis. Median left and right Achilles tendon thicknesses of Pso patients were significantly greater than that of healthy controls (p=0.03 and p=<0.001). Prevalence of psoriatic arthritis (PsA) among Pso patients was 7.3 %.
Conclusion: Evaluation of a child with Pso regularly for the musculoscelatal complaints is critical for early recognition of PsA. Collaboration between dermatologists and pediatric rheumatologists should be provided for preventing diagnostic delay in PsA. Ultrasonography is a useful technique for screening Pso patients in order to detect subclinical enthesopaty early.

Disclosure of Interest
None declared

P115

Screening for depression in a single pediatric rheumatology centre using the BDI-fast screen

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Introduction: Depression is a known comorbidity in juvenile idiopathic arthritis (JIA) and has an impact on quality of life and therapy outcome. In clinical routine, depression is probably underdetected.
Objectives: Prevalence of depressive symptoms, manifest depression and suicidal ideation was evaluated and associations with patient characteristics, disease activity and treatment were analysed in a cross sectional study.
Methods: Patients aged 10-18 years from a pediatric rheumatology centre were screened with the BDI-FS. An abnormal score of ≥4 points (out of 21) led to psychologically evaluation.
Results: 148 JIA patients (72% female) were evaluated. 19 (13%) had an abnormal BDI-FS score.. Frequent statements were sadness (n=31, 21%), lack of joy (n=43, 29%), hopelessness (n=23, 16%) and self-blame (n= 26, 18%). Suicidal ideation was present in 9 (6%). 4 (3%) patients had a previously diagnosed depression, 10 (7%) were newly diagnosed with depression. Patients with an increased BDI FS score more frequently presented with a diagnosis in JIA subcategories RF-negative and -positive polyarthritis and psoriatic arthritis but rarely with extended oligoarthritis or enthesitis related arthritis. There was an association between an increased BDI FS score and pain experienced by patients in both the patient reported pain visual analogue scale (VAS) (p= 0.002) and in the number of painful joints (p=0.017). Patients with a BDI-FS ≥4 also had significantly higher scores concerning disease activity as measured by physician and patient global assessment of disease activity and by the JADAS 10. A significantly higher percentage of patients with a normal BDI FS were in remission and had minimal disease activity. Patients with an abnormal BDI-FS score also had a significantly higher disability index as measured by the CHAQ (p=0). More patients with a BDI-FS ≥4 were taking NSAR, steroids, biologicals or a combination of biologicals and DMARDs as well as an overall higher number of different drugs.

	Total n= 148	Score <4 n= 129 (87%)	Score ≥4 n=19 (13%)	p
Age, median (1./3. quartile)	14,7 (13/ 16,2)	14,6 (12,8/ 16,1)	15,5 (14,2/ 16,6)	n.s.
Disease duration [y], median (1./3. quartile)	4 (2/7)	4 (2/7)	2,5 (1,75/ 6,25)	n.s.
Sex female, n (%)	106 (71,6%)	89 (69%)	17 (89,5%)	n.s.
Diagnose				
JIA, n (%)	148 (100%)	129 (87%)	19 (13%)	n.s.
RF - polyarthritis	44 (29,7%)	34 (26,4%)	10 (52,6%)	**0.019**
RF + polyarthritis	3 (2%)	1 (0,8%)	2 (10,5%)	**0.005**
Oligoarthritis	29 (19,6%)	28 (21,7%)	1 (5,3%)	n.s.
Extended Oligoarthritis	25 (16,9%)	24 (18,6%)	1 (5,3%)	n.s.
ERA	24 (16,2%)	22 (17,1%)	2 (10,5%)	n.s.
Psoriatic arthritis	16 (10,8%)	13 (10,1%)	3 (15,8%)	n.s.
Active Joints, median (1./3. quartil)	0 (0/1)	0 (0/1)	0,5 (0/2,5)	n.s.
Tender joints				
Pat. Global Asessment	1 (0/2)	1 (0/2)	2 (0,5/4)	**0.017**
Physician Global Assessment	1 (0/3)	0,7 (0/2,5)	3,5 (1/6)	**0.002**
CHAQ-DI	0 (0/1,5)	0 (0/1)	1 (0/3)	**0.026**
JADAS 10, med. (1./3. quartil)	0 (0/0,4)	0 (0/0,4)	0,4 (0/1)	**0.00**
JADAS ADA, n (%)	2 (0/6)	2 (0/5)	5 (2/10)	**0.008**
JADAS MDA, n (%)	101 (73,2%)	92 (76%)	9 (52,9%)	**0.044**
JADAS-remission, n (%)	76 (55,1%)	71 (58,7%)	5 (29,4%)	**0.023**
	56 (40,6%)	53 (43,8%)	3 (17,6%)	**0.04**

Conclusion: The BDI-FS is a convenient tool for detecting depression during routine checkups as it is simple in execution and evaluation. A high percentage of the patients showed signs of depression and suicidal ideation was detected. Patients with JIA especially with polyarthritis (RF negative and positive) and psoriatic arthritis have an increased risk for depressive symptoms. Increased scores were associated with pain, disability and higher disease activity especially if present despite intensified drug therapy. Only 26% of patients with an abnormal BDI-FS were already receiving psychological treatment. Screening for depressive symptoms in clinical practice is highly recommended to ensure adequate psychological support

Disclosure of Interest
None declared

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Switching patterns of biologic drugs among children with Juvenile Idiopathic Arthritis: a single center experiences

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Pediatric Rheumatology 2020, **18(Suppl 2):**P116

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood with an estimated incidence of 10–20 per 100,000 children. The conventional treatment of JIA includes non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease modifying anti-rheumatic drugs (DMARDs) . However, some patients do not experience complete response to conventional first-line options and require second-line therapy with biologic agents(BA). Though the BA provide JIA patients a better disease control, knowledge concerning switching patterns of BA in JIA is scarce.
Objectives: To evaluate the clinical responses and safety profiles of patients who required switching from one biological therapy to another for any reason
Methods: Children with JIA who received at least one biologic drug were included to the study. Disease activity was evaluated by juvenile arthritis disease activity score 71 (JADAS71). Demographic, clinical and laboratory findings, switching patterns and etiology of switching were recorded.
Results: A total of 191 (91 girls, 100 boys) JIA patients receiving BA were included into study. The mean ± SD age of diagnosis was 9.1± 4.9. Biologic drugs were prescribed with a median of 14 (2-66) months after diagnosis. Among 191 patients, 37 (19.3%) patients required to switch BA with a median of 10.5 (1-38) months after first biologic initiation. Tocilizumab (n=19) was the most commonly switched drug. The main reason of switching was inadequate response (n=32). The frequency of biologic switch was higher in patients with extended oJIA and pJIA and also in patients with uveitis. Biologic drugs were switched twice in nine and three times in three patients. When compared the 1st switchers to 2nd and 3rd switchers, there were not any differences in terms of JIA subgroups whereas, 2nd and 3rd switchers had higher active joint number and JADAS71 scores at the 6th month of first biologic drug initiation.
Conclusion: Some JIA patients could not achieve remission despite to the first prescribed biologic. Therefore, the biological drug has to be replaced by a second BA in these patients. We demonstrated both patterns and etiologies for switching that may facilitate the management approach of those dealing with JIA.

Disclosure of Interest
None declared

P117

Early registration of myocardial disorders in children with Juvenile Idiopathic Arthritis using the 4th generation electrocardiography

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children and often leads to disabilities due to joint and non-joint lesions, especially cardiovascular (CV) ones. New diagnostic methods may be useful to find these lesions before clinical manifestations or even predict them.
Objectives: To evaluate the results of electrocardiography (ECG) of the 4th generation (signal-averaged ECG obtained by processing several electrocardiographic complexes except atypical) in children with JIA in early diagnosis.
Methods: 46 patients with JIA (60.9% f, 9.69±0.93 y.o., duration of the disease 1.45±0.51 y.) were examined using 4th generation hardware-software complex ECG "Cardio plus P". Disease course and activity (JADAS27) were rated. In addition to standard laboratory&instrumental markers the level of immunoglobulins (IG), IL6, TNFα in the serum of patients was determined by ELISA, a correlation analysis of clinical and laboratory parameters was made.
Results: There were no instrumental (by standard ECG and cardiac ultrasound (US)) and laboratory signs of CVS injury among observed group, 50% JIA patients had unfavorable course of the disease (UCD), 10.5% had hepatosplenomegalia, JADAS27 9.7±2.04. Serum level of IL6 was 5.19±2.21 pg/ml, ALT, AST, LDG, cholesterol were normal. Using the 4th generation ECG showed the presence of significant changes in the myocardium in the majority of patients. Following indicators of heart rhythm variability and myocardium state evaluation in patients with JIA were deviated most often: stress index was 245.96±44.33s^{-2} (69.56% cases), condition of regulation reserves 61.65±2.77 (86.96%), overall heart rate variability 2279.74±406.36 (65.21%), immediate control of condition of myocardium 51.56±3.91 (95.65%), its reserve 61.04±1.82 (95.65%), T-wave/R-wave ratio lead I was 0.67±0.11 (80%), amplitude-areas index lead I-III from 48.65±2.64 to 61,17±4,33 (up to 95.65%), Macruz index 1.39±0.76 (94%), complex indicator of condition of myocardium 56.30±2.57 (95.65%) complex indicator of functional state 66.13±2.41 (65.2%). Previously, the best combination of ECG indicators to evaluate activity was found using CART algorithm: integral indicator of form ST-T lead II (55.41±5.09), T wave symmetry based on derivatives ratio and on areas of triangles (1.78±0.71, deviation in 100%) & T amplitude lead II (112.23±71.96 uV, in 86.36%), heart ratio, alpha QRS angle in the frontal plane. Some correlations between these parameters and other data were found: immediate control of the regulation with serum IL6 (r=-0.73, p<0.05), and with UCD (r=-0.53, p<0.05); heart ratio with ESR (r=0.53, p<0.05), hepatosplenomegalia (r=0.57, p<0.05), cholesterol serum level (r=0.58, p<0.05); integral indicator of form ST-T with serum IgG (r=-0.55), IgA (r=-0.55); T wave symmetry based on derivatives ratio had correlations with metabolic myocardial changes (r=-0.68, p>0.1), IgA (r=0.85, p>0.1), DMARD replacement (r=0.51, p>0.1); T wave symmetry based on areas of triangles with hepatosplenomegalia (r=0.67, p<0.05), US reactive changes of parenchymal organs (r=-0.96, p>0.1), IgM, IgA (r=0.74 and 0.98), serum TNFα (r=-0.59, p>0.1); T amplitude, lead II with IgG total (r=-0.72, p>0.1), TNFα (r=0.99, p>0.1); alphaQRS angle with ALT (r=-0.72, p<0.05), cholesterol (r=0.49, p<0.05), NSAIDs (r=0.82, p<0.05); complex indicator of condition of myocardium with cholesterol (r=-0.62, p<0.05).
Conclusion: With the help of "Cardio-Plus P" the changes in CVS and latent heart rhythm disorders in children with JIA can be found more frequently by evaluating complex indicators than using standard 12channel ECG. Most of registered changes had no other clinical, laboratory or instrumental signs, in accordance with the obtained correlations they may be due to immune inflammation.

Disclosure of Interest
None declared

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A family history of autoimmunity is a risk factor for celiac disease and Juvenile Idiopathic Arthritis co-occurrence

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Introduction: Autoimmune disorders share common predisposing factors and immune pathogenic mechanisms. The prevalence of celiac disease (CD) has been reported to be consistently higher in patients with juvenile idiopathic arthritis (JIA) in comparison to the general population, however not negligible variations in the prevalence have been observed in distinct geographic locations.

Objectives: To investigate the co-occurrence of JIA and CD in southern Italy and to identify potential predisposing factors.
Methods: A single-center retrospective study was conducted. Patients diagnosed with JIA according to International League of Associations for Rheumatology criteria, admitted to the Pediatric Rheumatology Unit of the University of Naples Federico II from January 2001 to December 2019, who underwent CD serological screening at least once, were included. For each patient, demographic, clinical and laboratory data were extracted from clinical charts. Differences between patients affected by JIA with or without CD were analyzed.
Results: Three hundred twenty-nine JIA patients (246 females, 83 males; median age 12.5 years, IQR 9.1-16.1) were included in our study. Median age at JIA onset was 4 years (IQR: 2.2-7.8). Eight patients (2.4%) received a diagnosis of CD. Five were diagnosed according to the ESPGHAN guidelines. Two were diagnosed solely based on positive serology that normalized after the beginning of the gluten-free diet (GFD). One patient received a diagnosis of Potential CD (positive serology in the absence of villous atrophy). All of them started a GFD. Only in one patient CD onset preceded JIA, that occurred despite the GFD. The remaining seven developed JIA first. Most of those (5/7, 71,4%) were asymptomatic and diagnosis followed the screening for CD that all JIA patients undergo in our clinic. In our cohort the prevalence of CD was higher than that reported in the general population (2.4% vs 1%, $p<0.05$). No differences were observed in regard to JIA subtype and ongoing treatment for JIA ($p=0.59$) between patients with or without CD. Notably, 87.5% patients with JIA and CD had at least one family relative with an autoimmune disorder compared to 45.8% of those without CD ($p<0.05$). In none of those patients GFD promoted clinical improvement, nor prevented JIA relapse. Indeed, five patients required a new disease modifying antirheumatic drug (DMARD). Finally, 87.5% patients with JIA and CD required both a conventional DMARD and a biological DMARD (bDMARD) over time compared to 36.8% (118/321) of those without CD ($p=0.006$).
Conclusion: A higher prevalence of CD in patients with JIA was found in our wide southern Italian cohort in comparison to the general population. Notably, a positive family history of autoimmunity was found to be associated with a higher co-occurrence of JIA and CD, suggesting that common predisposing factors shared across autoimmune disorders may contribute to both diseases. Furthermore, our patients with JIA and CD more frequently required a bDMARD than patients without CD, suggesting that JIA course can be more aggressive in children with CD. Our findings support the need for an active screening for CD in patients with JIA, especially in those with a positive family history of autoimmunity. This is clinically relevant since the clinical course seems to be more aggressive in these patients and require a step-up therapy.

Disclosure of Interest
None declared

P119

A large proportion of patients with Juvenile Idiopathic Arthritis undergo antibiotic treatment and arthrotomy at the onset of disease

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Introduction: Acute arthritis is a common cause of consultation in pediatric emergency wards. It can be caused by septic (SA), juvenile idiopathic arthritis (JIA), or undetermined arthritis (UA). An early accurate diagnosis is essential to provide appropriate treatment and follow-up.
Objectives: To compare clinical and biological characteristics, exposure to antibiotics and invasive orthopedic management and lengths of hospital stays according to the final diagnosis of patients with JIA, SA and UA.
Methods: We retrospectively analyzed data from <16-year-old children, hospitalized between 2008–2009 or 2015–2018 at a French tertiary center for acute arthritis, who underwent a joint aspiration. Non-parametric tests were performed to compare children with JIA and children with SA or UA, respectively (Bonferonni-adjusted statistical threshold = 0.025).
Results: Among the 251 included patients, 123 (49%) had SA, 32 (13%) had JIA and 96 (38%) had undetermined arthritis (UA). Patients with JIA were older when compared to SA (2.9 years [1.9-5.3] versus 1.5 [1.1-2.7], $p<0.01$). Presence of fever and fibrinogen were not different between JIA and SA or UA. White blood cells in serum and synovial fluid were lower in patients with JIA (11.2x109/l [9.6-12.7] and 42.05x103cells/mm3 [10.5-100.0]) when compared to SA (13.2x109/l[11.0-16.6] and 105.5x103cells/mm3 [44.0-210.0], $p<0.01$ and $p<0.01$). Intravenous antibiotics were administered to 87.5% of children with JIA, 100% of patients with SA, and 91,5% of UA. Arthrotomy was performed in 43.3% of patients with JIA, 69.7% of patients with SA, and 54.1% of patients with UA.
Conclusion: At onset of acute arthritis currently used clinical and biological parameters do not allow to reliably differentiate between JIA, SA and UA. A large proportion of patients with JIA undergo antibiotic treatment and invasive surgical treatments. There is a need for the identification of new diagnosis biomarkers that allow early identification of JIA.

Disclosure of Interest
None declared

P120

Extra_articular manifestations of Juvenile Idiopathic Arthritis and their impact on health related quality of life

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Pediatric Rheumatology 2020, **18(Suppl 2):**P120

Introduction: Juvenile idiopathic arthritis (JIA) is the commonest rheumatic disease in children (1).It is associated with a range of extra-articular manifestations (EAM) (2).These EAM may have a negative impact on health related quality of life (HRQoL) in these patients .However ,this issue is not deeply studied .
Objectives: This study aimed to investigate EAM in patients with JIA and assess their impact on HRQoL among these patients.
Methods: This cross-sectional analytic study was carried out on 117 patients with JIA. EAM were identified clinically by history and examination. Sicca symptoms, peripheral neuropathy, enthesitis and skin lesions were picked up during clinical examination .Pulmonary involvement was evaluated by high resolution CT .Patients were assessed by abdominal ultrasonography to assess the size of liver and spleen. Atlantoaxial sublaxation was evaluated by cervical spine x-rays. Patients were evaluated by Pediatric Quality of Life Inventory-4 (PedsQL-4) and PedsQL arthritis module.
Results: The median age of patients was 14 years with a median disease duration 4 years ,82.9% were females .Of the studied 117 JIA patients , 85 patients (72.6%) had EAM in the form of persistent fatigue (70.6%), significant weight loss (14.1%),recurrent attacks of fever (18.8%), enthesitis (21.2%),lung disease (8.2%), rheumatoid nodules (2.4%),peripheral neuropathy (4.7%),uveitis (16.5),lymphadenopathy (80.2%),hepatomegaly (3.5%),splenomegaly (5.9%),sicca symptoms (2.4%), atlantoaxial sublaxation (2.4%),psoriasis (2.4%) and inflammatory bowel diseases (2.4%). Patients with EAM scored significantly lower in physical functioning ($p=.001$), emotional

functioning (p <.001), social functioning (p=.005), and school functioning (p=.001).Regarding PedsQL arthritis module, patients with EAM had also significantly lower scores than did patients without EAM on the domains of pain and hurt (p<.001), daily activities (p=.008) and worry (p= .001).

Conclusion: Conclusion

EAM are prevalent among JIA patients and have a negative impact on their HRQoL. So, early identification and treatment are highly recommended.

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Disclosure of Interest

None declared

P121

Joint distribution at presentation of Juvenile Idiopathic Arthritis

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Pediatric Rheumatology 2020, **18(Suppl 2):**P121

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease in childhood and includes a heterogeneous group of different forms of arthritis of unknown etiology and pathophysiology. The major clinical manifestation of JIA is persistent joint swelling that results from the combination of synovial fluid accumulation and synovial thickening. Such swelling may cause deformities of affected joints due to stretching of periarticular ligaments and tendons, with inflammation of enthesis. Any joint can be affected, although the large ones are more frequently involved.

Objectives: The aim of this study is to assess the first joint involved in patients diagnosed with JIA in a Pediatric Rheumatology Unit

Methods: We retrospectively studied patients observed between January 1st of 1987and December 31st of 2019. The diagnosis of JIA was defined by ILAR criteria.

Results: A total of 563 patients were identified: 336 (60%) girls and 227 (40%) boys (female/ male ratio 1,5:1). Mean age was 6,2 ± 4,2 years. Most of the patients had oligoarthritis by the time of the diagnosis (*n* = 299, 53%), 17% (*n* = 107) had poliarthritis (9% with positive rheumatoid factor) and 9% (*n* = 51) had systemic arthritis. A total of 404 (72%) patients had only one joint affected at the presentation of JIA. Lower limbs joints were more frequently involved (*n* = 334, 83%), followed by upper limbs joints (*n* = 42, 10%) and axial joints (*n* = 28, 7%). Among upper limbs, metacarpophalangeal and interphalangeal joints were mainly affected (*n* = 17, 40%), followed by elbow (*n* = 12, 29%), wrists (*n* = 9, 21%) and shoulder (*n* = 4, 10%). Among lower limbs, knee was the first joint more frequently involved (*n* = 236, 71%), followed by ankle (*n* = 55, 16%), metatarsophalangeal and interphalangeal (*n* = 22, 7%) and hip (*n* = 21, 6%). Cervical spine was the most affected axial joint (*n* = 14, 50%), followed by sacroiliac joint (*n* = 10, 36%), temporomandibular joint (*n* = 3, 11%) and costochondral/ sternocostal/sternoclavicular joints (*n* = 1, 3%).

Among the 404 patients, the knee was involved in 58%, ankle in 14%, metatarsophalangeal and interphalangealin 5,4% and hip in 5,2%. Proximal joints (shoulder and hip) were the first affected joints in 6% of the cases (*n* = 25). Hip was the first joint affected in 4 cases of oligoarthritis (1,3%), 3 cases of polyarthritis (3%) and 2 cases of systemic arthritis (4%).

Conclusion: This study emphasizes the frequency of the first joint involvement in different JIA subtypes with only one joint affected at presentation. Lower limb's joints are the most affected ones, specially knee and ankle. However any joint can be the first one involved in JIA. Hip's involvement is common in pediatric rheumatology, although among rheumatological disorders, JIA is a less probable diagnosis if hip is the first joint affected. Cervical spine's prolonged involvement should raise the diagnosis of JIA *ab initio*.

Disclosure of Interest

None declared

About this supplement

These abstracts have been published as part of Pediatric Rheumatology, Volume 18, Supplement 2, 2020: Proceedings of the 26th European Paediatric Rheumatology Congress (PRES 2020). The full contents of the supplement are available at https://ped-rheum.biomedcentral.com/articles/supplements/volume-18-supplement-2. Please note that this is part 1 of 2.