Results: Of the 519 enrolled pts, 504 (with complete data on the FiRST questionnaire) were analyzed at M3. A positive screening for comorbid FM was found in 192 pts (38%) at M0 and in 127 (25%) pts at M3. Correlation between FiRST at M0 and M3 was weak with a Kappa coefficient correlation of 0.4 [0,3 - 0,5].
Four groups were identified: group [+/+] with comorbid FM at M0 and M3: N=93 (18%; group [+/-] with comorbid FM at M0 but not at M3: N=99 (20%); group [-/-] without comorbid FM at M0 and M3: N=278 (55%); group [-/+] without comorbid FM at M0 but at M3: N=34 (7%)
Changes in the status of comorbid FM (disappearance or appearance) was observed in 134 pts (26%). In the 193 pts with baseline comorbid FM, after 3 months of anti-TNF treatment, comorbid FM was no longer found in 99 (51%)%.Efficacy at M3 was significantly better, according to BASDAI 50, in patients without comorbid FM at M3 (Table).

	FM status according to the FIRST questionnaire at M0/M3 (N total=504)			
	+/+	+/–	–/–	–/+
Number of patients	93	99	278	34
Number of patients reaching BASDAI 50 at M3	26 (28%)	61 (61.6%)	162 (58.3%)	8 (25.5%)

Conclusions: There is a high frequency of comorbid FM screened by the FiRST in active axSpA, decreased by 51%f after 3 months of anti-TNF treatments. Persistence of FM after 3 months of anti-TNF treatment is associated with lower anti-TNF response. Further studies are required to analyze the impact of screening FM before starting anti-TNF therapy in axSpA.
References:
[1] Perrot S, et al. Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain. 2010;150:250–6.
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Disclosure of Interest: None declared
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THU0483 CHARACTERISTICS OF PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS AND COMORBID FIBROMYALGIA. DIFFERENCES ACCORDING TO FIBROMYALGIA SCREENING (FIRST QUESTIONNAIRE) AND FIBROMYALGIA CLASSIFICATION (ACR1990)

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Background: Fibromyalgia (FM) can be a comorbid condition in axial spondyloarthritis (axSpA). FM screening questionnaires and classification criteria fulfillment may demonstrate different prevalence and patients' characteristics may differ.
Objectives: To evaluate frequency of comorbid FM, and the differences between axSpA patients with/without comorbid FM according to screening (FiRST) and classification tools (ACR1990 FM criteria).
Methods: A multicenter national study involving 39 rheumatology centers in France included 519 patients with axSpA starting an anti-TNF treatment (PredictSpA study; ClinicalTrials.gov: NCT03039088). Patients (pts) were screened for FM with the FiRST questionnaire and classified as FM by ACR 1990 criteria. Demographic characteristics, comorbidities, axSpA characteristics, CRP and imaging were recorded in all patients. Kappa coefficient (and its 95% CI) was calculated to compare FiRST and ACR1990 criteria. Baseline characteristics associated with FM were evaluated by univariable and multivariable logistic regression (including the variables with a p value$<$0.20 in the univariable analysis).
Results: In the 519 pts (females: 46%, age: 42±12 years, mean BASDAI 5.7±2.0, mean ASDAS-CRP 3.3±0.9), a comorbid FM was screened in 38% and diagnosed in 16% of pts. Agreement between FiRST and ACR1990 was poor, with a Kappa coefficient of 0.2 [0.2–0.3].
In the multivariable analysis, comorbid FM (by the FiRST questionnaire) in axSpA patients was independently associated with a lower education level, more sick leave, more heel pain, more frequent second line anti-TNF. Comorbid FM defined by the ACR1990 classification criteria was independently associated with heel pain and inversely associated with B27 haplotype. (Table)

Table 1

Number of patients	Fibromyalgia according to FiRST questionnaire		Odds-ratio [95% CI]
	yes (199)	no (320)	
Education level (> high school)	72 (37%)	163 (51%)	0,6 [0,4- 0,9]
Sick leave (yes)	108 (54%)	134 (42%)	1,5 [1,0 - 2,2]
Heel pain (yes)	127 (64%)	151 (47%)	1,6 [1,1–2,5]
Etanercept at baseline (yes)	63 (32%)	137 (43%)	0,6 [0,4–0,9]

Table 2

Number of patients	Fibromyalgia according to ACR 1990 criteria		Odds-ratio [95% CI]
	yes (84)	no (435)	
HLA B27 (positive)	27 (32%)	272 (63%)	0.39 [0.22–0.68]
Heel pain (yes)	61 (73%)	217 (50%)	2.03 [1.16–3.56]

Conclusions: FM is frequently associated with active axSpA, with poor correlation between screening (FiRST) and diagnosis (ACR1990) test. Several characteristics are associated with comorbid FM, depending on FM classification and screening tools.
References:
[1] Perrot S et al. Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain. 2010;150:250–6.
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THURSDAY, 15 JUNE 2017

Basic science in paediatric rheumatology

THU0484 RO60 EXPRESSION DECREASES WITH AGE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF CHILDREN AND ADOLESCENTS AND CORRELATES WITH TLR7 STIMULATION IN PDCS OF PREPUBERTAL CHILDREN

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Background: Auto-antibodies to the RNA binding protein Ro60 are present in patients with autoimmune disorders such as systemic lupus erythematosus (SLE). In addition to its established role as an auto-antigen, Ro60 has been found to bind Alu RNA retroelements whereby it may target Alu retroelement RNA for degradation suggesting a novel putative function of this auto-antigen. If Ro60 modulates the amount of cellular RNA then one may hypothesise an association with toll-like receptor (TLR) 7 stimulation threshold.
Objectives: To measure the physiological levels of intracellular Ro60 protein in healthy children and adolescents and investigate a possible link between Ro60 protein expression and interferon-α (IFN-α) production after TLR7 stimulation.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from blood from 48 healthy children and adolescents (age range 6.7–17.9 years old). Cell lysates from thawed PBMC samples were tested for Ro60 expression by Western blot. PBMCs were also stimulated for 20 hours with TLR7/8 agonist R848, at 1ug/ml in the presence of brefeldin A, and plasmacytoid dendritic cell (pDC) IFN-α expression was measured using flow cytometry. Statistical tests to measure correlation between IFN-α expression in (pDCs) and PBMC Ro60 expression were performed using SPSS.
Results: Ro60 expression in PBMCs correlated negatively with age (Spearman's rho = -0.317, p=0.032). When participants were divided into two groups based on their self-reported puberty status, Ro60 expression was higher in the pre-pubertal group (p=0.02). There was, however, no difference in Ro60 expression between males and females (p=0.44) or when sexes were stratified according to pubertal status. pDC IFN-α production after TLR 7 stimulation, did not correlate with ex vivo PBMC Ro60 expression overall (Spearman's rho =0.159, p=0.302) however a moderate positive correlation was observed in pre-pubertal samples only (Spearman's rho =0.554, p=0.021).
Conclusions: Ro60 expression decreases with age in healthy young people. These findings need to be confirmed in a larger cohort and further studies are necessary to investigate the link between Ro60 expression and TLR7 signalling across different age groups as well as in patients with SLE.
Disclosure of Interest: None declared
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THU0485 POLYMORPHISM OF SOME GENES INVOLVED IN IMMUNE AND INFLAMMATORY RESPONSES IN BELARUSIAN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND OTHER ARTICULAR PATHOLOGY

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Background: Etiology and pathogenesis of juvenile idiopathic arthritis (JIA), which prevails among pediatric rheumatic diseases, are insufficiently clear. The study of molecular-genetic basis of JIA is of great interest for revealing genetic predisposition and early diagnosis.
Objectives: The present study aimed to analyze seven SNPs in five genes involved in immune and inflammatory responses: *TNFα* (rs1800629, rs361525), *PTPN22* (rs24766012), *MIF* (rs755622, rs5844572), *CTLA4* (rs5742909), *STAT4* (rs7574865), as well as in two DNA repair genes *XPD* (rs1799793) and *XRCC1* (rs25487) in different conditions.

Methods: 94 patients diagnosed with JIA (mean age 8.78±5.21), 95 children with articular syndrome (mean age7.90±4.81) and 164 hospital controls without any signs of autoimmune or inflammatory diseases (mean age13.99±2.68) were included in the study. The JIA patients were divided into subgroups according to IIAR classification criteria; among them 63 patients were diagnosed with oligoarthritis and 16 with RF- polyarthritis. Genomic DNA was extracted from blood samples by means of phenol-chloroform method. SNPs were genotyped using PCR-RFLP or fragmental analysis.
Results: The allele frequencies for all SNPs in the hospital control group were similar to those characteristic of other Europeans. No differences were found between the frequencies of the TNFα risk alleles across all three groups. Hence, both SNPs in the TNFα locus were not associated with JIA and other articular pathologies in our study. The same is true for -318C>T *CTLA4* polymorphism. Unlike these genes, *PTPN22* C1858T polymorphism influenced developing arthritis in children since heterozygous CT genotype was associated with articular pathology (rather than JIA) in the total group (OR=1.87, 95% CI [1.06–3.30], p=0.04), especially in males (OR=3.50, 95% CI [1.61–7.63], p=0.0016). In the latter case, it was effective even being combined with any genotypes in the -308G>A TNFα locus (OR=2.73, 95% CI [1.19–6.24], p=0.018). When analyzing *MIF* polymorphisms (rs755622 and rs5844572), the evident trend to increased carrying genotypes containing the risk allele *MIF*-173C was observed in females with JIA as compared to controls and significantly elevated frequency of this risk allele in females with RF- polyarthritis as compared to males (p =0.037). In females with JIA, increased frequency of heterozygous *MIF*-794 $CATT_{7,8}$ genotype as compared to the controls (OR =7.78, 95% CI [0.95 – 63.8], p=0,056) was also revealed. *STAT4* polymorphism (rs7574865) demonstrated subtype-related association with JIA due to increased frequency of the minor allele in patients with polyarthitic form of JIA as compared to both hospital controls (p=0.01; OR =2.45; 95% CI [1.19–5.04]) and other articular pathology (p=0.001; OR =3.37; 95% CI [1.56–7.28]). The same SNP was also associated with developing arthritis in females. As to role of DNA repair genes, carriers of *XPD* heterozygous Asp/Asn genotype had an enhanced risk of JIA in females (OR=2.14; 95% CI [1.05–4.35]; p=0.05).
Conclusions: Thus, the gender- and subtype-specific associations of some SNPs studied with developing joint pathologies including JIA are found in the Belarusian child population.
Disclosure of Interest: None declared
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Paediatric rheumatology

THU0486 ANGIOPOETIN-2 AS A NEW VALUABLE MARKER OF DISEASE ACTIVITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Angiopoetin-2 (ANG-2) is one of the main angiogenesis modulators. As synovial angiogenesis is considered to be an important early step in the course and pathogenesis of juvenile idiopathic arthritis (JIA), it may be a valuable marker of activity of the disease.
Objectives: To evaluate ANG-2 serum and synovial fluid levels in JIA patients and its possible correlation with disease activity and the degree of ultrasound-detected synovial angiogenesis.
Methods: Serum levels of vascular markers were measured in 63 patients with JIA (aged 1,5–17) and 31 age-matched healthy controls. Synovial fluid was collected from 17 JIA patients. Disease activity (low, medium and high) was assessed by JADAS-27 scale. Ultrasound examination of inflamed joints was performed in each JIA patient and synovial angiogenesis was evaluated by means of Power Doppler ultrasonography (PDUS) and the 4th grade vascularity scale (0–3).
Results: ANG-2 serum levels were higher in children with JIA comparing to the healthy controls (5,5±1,2 ng/ml vs. 1.9±1.4 ng/ml). Serum concentration of ANG-2 in JIA children increased with disease activity (1,4±0,9 ng/ml vs. 1,4±1,0 ng/ml vs. 1,8±2,2 ng/ml), whereas Ang-2 levels in the synovial fluid were the highest in the high disease activity (3,4±2,5 ng vs. 12,5±9,5 ng/ml vs. 26,4±9,0 ng/ml, $p<0,05$). Concentration of ANG-2 in serum correlate with the synovial vascularization obtained by PDUS (0–3, accordingly 1,5±0,8 ng/ml vs. 1,3±0,9 ng/ml vs. 1,5±1,0 ng/ml vs. 13,2±8,7 ng/ml, $p<0,01$) The same pattern was observed for ANG-2 levels in synovial fluid and PDUS grade (0–3, accordingly 3,8±1,0 ng/ml vs. 5,1±4,1 ng/ml vs. 13,5±2,0 ng/ml, $p<0,01$).
Conclusions: ANG-2 might be a valuable marker in JIA children with high disease activity. Together with ultrasound examination, it may add more information about disease severity, what may be helpful in introducing the correct therapy.
Disclosure of Interest: None declared
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THU0487 REAL-LIFE TREATMENT WITH CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS – FIRST EXPERIENCE FROM THE BIKER REGISTRY

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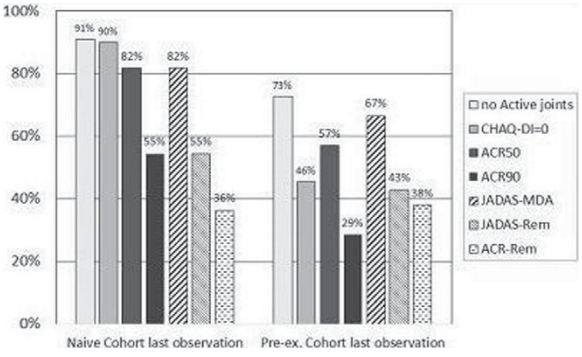
Background: Canakinumab (CAN) had demonstrated its efficacy and safety in SJIA pts (1).
Objectives: To report on the experience with CAN treatment in SJIA in the clinical practice in Germany.
Methods: Data on patients' and disease characteristics, disease activity and safety reports from the German BIKER registry were analysed.
Results: Until Dec. 2016, 37 pts exposed to CAN were identified. In 12 pts used CAN as first biologic, 25 pts were pretreated: Tocilizumab 15, Anakinra 11, Etanercept 9, Adalimumab 9. 3 patients in the pre-exposed cohort had experienced a macrophage activation syndrome. Pts' and disease characteristics are outlined in table 1. Pts pretreated were older, had a longer disease duration and more comorbidities than naïve patients. The proportion of pts with active arthritis, active systemic features and both were comparable. Disease activity at baseline was higher in the naïve cohort suggesting some clinical benefit from pretreatment. Dosing of CAN was comparable (*3.9+/-0.4 vs. 3.5+/-0.7mg/kg)* as well as the median treatment duration (0.8vs.1year). Treatment efficacy at last follow up was better in the naïve cohort with more pts reaching a PedACR 30/50/70/90 response while JADAS- or ACR-remission rates were comparable. Treatment was discontinued by 42% in the naïve and 48% in the exposed cohort. Reasons were inefficacy (n=7;19%), intolerance (n=2;5%) and remission (n=7;19%) of the disease and other (n=2;5%).

Table 1. Baseline characteristics

	Biologics naive	Biologics pre-exposed
N (female gender)	12 (17%)	25 (52%)
Age at JIA onset (years); mean ± SD; Median (IQR)	4.4±4.0; 3.0 (2.0–4.9)	6.0±4.8; 3.7 (2.6–7.1)
Age start of Canakinumab (years); mean ± SD; Median (IQR)	7.1±4.9; 5.6 (3.1–10.2)	9.8±4.8; 10.6 (5.5–14)
Disease duration (years); mean ± SD; Median (IQR)	2.8±4.1; 0.7 (0.3–3.9)	3.8 ± 4.2; 1.9 (0.6–8.7)
Concomitant treatment at baseline: NSAIDS/Steroids/MTX	6 (50%)/6 (50%)/3 (25%)	10 (40%)/11 (44%)/4 (16%)
Patients with active joints	7 (58.3%)	10 (47.6%)
Patients with active systemic features	7 (58.3%)	10 (47.6%)
Patients with active arthritis and systemic features	4 (36.4%)	4 (19.1%)
Active joint count	1.8±1.7; 2.5 (0–3)	2.1±3.3; 0 (0–3)
Physician global VAS (0–10)	5.2±2.8; 6.2 (3.2–7.2)	3.8±3.4 ; 3.7 (0.7–6.3)
Patient Global VAS (0–10)	4.8±2.9; 4.6 (2.7–7)	3.3±2.9; 2.6 (0.6–5.1)
CHAQ-DI (0–3)	0.71±0.65	0.65±0.84
ESR (mm/h)	28.2±22.8	15.4±20.1
CRP (mg/l)	70.5±58	12±23
JADAS10	15.7±8.3	10.5±7.9



Conclusions: First experience with CAN for treatment of sJIA in clinical practice is presented. A high proportion of pts gained significant improvement. JADAS remission was reached by about 50% and ACR remission by 25–57% in both biologics pre-exposed and naïve pts while few pts discontinued treatment in remission so far. Intolerance was rare. The further long term surveillance of sJIA pts exposed CAN is intended by the registry.
References:
[1] Ruperto N, Brunner HI, Quartier P, et al. Two randomized trials of canakinumab in systemic juvenile idiopathic arthritis. N Engl J Med 2012;367(25):2396–406.
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