patients (75%), presented by polyarthritis in 7/9 (77.8%), and oligoarthritis in 2/9 (22.2%). Two patients (16.7%) had cataract, one (8.3%) had bilateral uveitis, and one (8.3%) had optic atrophy. Sensorineural hearing loss was observed only in 3/12 (25%). Hydrocephalus was detected in 3/12 (25%). Delayed mental and psycho-speech development was observed in 6/12 (50%) patients. In 3/12 (25%), the development of MAS was recorded.

All patients had nucleotide variants in *NLRP3* gene. According to NGS results and clinical characteristics, 8/12 (66.7%) patients were diagnosed with MWS and 4/12 (33.3%) had CINCA/NOMID syndrome. In children with MWS, heterozygous variant c.2113C>A in *NLRP3* gene was the most common (5/8 (62.5%) patients). One of 8 (12.5%) patients with novel heterozygous variant c.2861C>T was detected; also one child (12.5%) have heterozygous variant c.598G>A and one (12.5%) – heterozygous variant c.943A>G. Four patients with CINCA/NOMID syndrome also had heterozygous variants in *NLRP3* gene: c.598G>A, c.2173C>A, c.1991T>C and c.796C>T.

Prior to genetic testing, 12/12 (100%) patients received NSAIDs; 6/12 (50%) were treated with oral glucocorticoids (GC), 3/12 (25%) – with intravenous GC, 2/12 (22.2%) – with methotrexate. Biologics treatment included: 5/12 (41.7%) CAN, 4/12 (33.3%) tocilizumab, and 1/12 (8.3%) etanercept. After genetic testing, 7/12 (58.3%) patients were successfully switched to CAN. Only 1/12 (8.3%) child with MWS developed secondary inefficiency on CAN treatment.

Conclusion: Systemic manifestations were detected in 91.6% of children, while active arthritis was observed in 75% of patients, which can cause difficulties in the diagnosis and treatment of CAPS. The effectiveness of canakinumab therapy was estimated in 91.6% of patients. The most frequent variant of the *NLRP3* gene in MWS was c.2113C>A. In patients with CINCA/NOMID syndrome all nucleotide variants were individual.

Disclosure of Interests: Meyri Shingarova: None declared, Ekaterina Alexeeva Grant/research support from: Roche, Pfizer, Centocor, Novartis, Speakers bureau: Roche, Novartis, Pfizer., Tatyana Dvoryakovskaya: None declared, Kirill Savostyanov: None declared, Aleksander Pushkov: None declared, Evgeniya Chistyakova: None declared, Ksenia Isaeva: None declared, Aleksandra Chomakhidze: None declared, Olga Lomakina: None declared, Rina Denisova: None declared, Anna Mamutova: None declared, Anna Fetisova: None declared, Marina Gautier: None declared, Dariya Vankova: None declared, Elizaveta Krekhova: None declared, Ivan Kriulin: None declared, Natalia Zhurkova: None declared, Rustam Tepaev: None declared, Alina Alshevskaya: None declared, Andrey Moskalev: None declared

DOI: 10.1136/annrheumdis-2020-eular.5814

FRI0465 TOFACITINIB POPULATION PHARMACOKINETICS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A POOLED ANALYSIS OF DATA FROM THREE CLINICAL STUDIES

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Background: Tofacitinib is an oral JAK inhibitor that is being investigated for juvenile idiopathic arthritis (JIA).

Objectives: To describe tofacitinib pharmacokinetics (PK) in patients with JIA, identify potential covariates accounting for variability in exposure, assess the formulation effect of oral solution vs tablet and propose a simplified dosing regimen.

Methods: This was a pooled analysis of data from 3 tofacitinib clinical studies in patients with JIA aged 2–<18 years: a Phase 1, open-label (OL), non-randomised study (NCT01513902); a Phase 3, randomised, double-blind, placebo-controlled, withdrawal study (NCT02592434); and an OL long-term extension study (NCT01500551). Tofacitinib was dosed at 5 mg twice daily (BID) in patients ≥40 kg or at body weight (BW)-based lower doses BID in patients <40 kg, to achieve average concentrations (C_{avg}) comparable with those in patients receiving 5 mg BID. A sparse PK sampling scheme was applied, and the plasma samples were assayed using a validated, sensitive and specific high-performance liquid chromatography tandem mass spectrometric method (lower limit of quantification = 0.100 ng/mL). A nonlinear mixed-effects modelling approach was used for the population PK model, and population parameter variability was assumed to be log-normally distributed. Covariates relating to patient demographics, disease characteristics, concomitant medications and formulation (oral solution vs tablet) were selected using a stepwise covariate modelling approach, and parameter-covariate relationships were evaluated using stepwise forward-inclusion ($p < 0.05$) backward-deletion ($p < 0.001$) procedures. The effect of time-varying BW on oral clearance (CL/F) and apparent volume of distribution (V/F) was characterised using an allometric model. Final model quality was assessed by Visual Predictive Checks (VPCs).

Results: Of 246 patients in the analysis, 74.0% were female; 87.8% were white, 2% were black, 10.2% were 'other' races and no patients were Asian. Median (range)

BW was 46.3 (11.1–121.8) kg. Initially, 100 patients received oral solution and 146 patients received tablets; 11 patients switched formulations during the studies. A one compartment disposition model with first-order absorption and a lag time sufficiently described the data. Final estimates for CL/F, V/F and the first-order absorption rate constant (k_a) for tablets were 26.1 L/hr, 89.2 L and 2.78 hr⁻¹, respectively. The only statistically significant covariate was a formulation effect on k_a . All parameters were estimated adequately. Estimated allometric exponents were 0.310 for CL/F and 0.537 for V/F. Absorption was described with an estimated lag time of 0.186 hr, and the oral solution had a 1.64-fold faster absorption rate vs the tablet. VPCs sufficiently described the observed data over time, across BWs and ages. Given the PK characterisation and variability in patients with JIA, a simplified dosing scheme was proposed, targeting C_{avg} values equivalent to those in patients receiving 5 mg BID: 3.2 mg BID solution in patients 10–<20 kg; 4 mg BID solution in patients 20–<40 kg; and 5 mg BID tablet or solution in patients ≥40 kg.

Conclusion: Tofacitinib population PK in patients with JIA were adequately described by a one compartment model parameterised in terms of CL/F, V/F and first-order absorption with a lag time. Drug absorption from the oral solution was faster than from the tablet. Tofacitinib does not require dose modification or restrictions for any covariates, except BW, to account for differences in C_{avg} . Based on the results of this analysis, a simplified BW-based dosing regimen was proposed.

Acknowledgments: Study sponsored by Pfizer Inc. Medical writing support was provided by Sarah Piggott of CMC Connect and funded by Pfizer Inc.

Disclosure of Interests: Camille Vong Shareholder of: Pfizer Inc, at time of analysis, Employee of: Pfizer Inc, at time of analysis, Xiaoxing Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Anasuya Hazra Shareholder of: Pfizer Inc, at time of analysis, Employee of: Pfizer Inc, at time of analysis, Arnab Mukherjee Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Timothy Nicholas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Cheng Chang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2020-eular.400

FRI0466

NO DISEASE PROGRESSION AFTER 36 MONTHS FOLLOW UP IN THE JUVENILE SYSTEMIC SCLERODERMA INCEPTION COHORT

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Background: Juvenile systemic sclerosis (JSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. There is rare longitudinal prospective follow up data of patients with JSSc. In the international juvenile systemic sclerosis cohort (JSScC) patients are followed with a standardized assessment prospectively.

Objectives: To assess the changes regarding organ involvement pattern and patients related outcomes after 36 months follow up in the JSScC.

Methods: Patients diagnosed according to 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 Interests: Ivan Foeldvari Consultant of: Novartis, Jens Klotzsche: None declared, Ozgur Kasapcopur: None declared, Amra Adrovic: None

declared, Maria T. Terreri: None declared, Rolando Cimaz: None declared, Maria Katsikas: None declared, Dana Nemcova: None declared, Maria Jose Santos Speakers bureau: Novartis and Pfizer, Juergen Brunner Grant/research support from: Pfizer, Novartis, Consultant of: Pfizer, Novartis, Abbvie, Roche, BMS, Speakers bureau: Pfizer, Novartis, Abbvie, Roche, BMS, Mikhail Kostik: None declared, Kirsten Minden Consultant of: GlaxoSmithKline, Sanofi, Speakers bureau: Roche, Anjali Patwardhan: None declared, Kathryn Torok: None declared, Nicola Helmus: None declared
DOI: 10.1136/annrheumdis-2020-eular.2271

FRI0467

DRUG SURVIVAL AND SAFETY OF BIOLOGICAL THERAPIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Biological treatment (BT) has changed perspectives of JIA patients. Increasing data from real life experience have been reported.

Objectives: To compare drug survival, safety and efficacy of BT in patients with Juvenile Idiopathic Arthritis (JIA).

Methods: A retrospective observational study was conducted on JIA patients followed in a referral hospital and who had received at least one BT between 1999 and 2019.

Results: 218 BT in 130 JIA patients were analyzed. 67.7% were women with a median age at diagnosis of 8 years old IQR (3-13) and a median age at the beginning of the BT of 15 years old IQR(7.8-21). 21.5% of the patients had uveitis during follow-up. BT were indicated due to: arthritis(73.9%), uveitis(10.1%), arthritis and uveitis(2.7%), systemic activity(8.3%) and macrophage activation syndrome (1.8%). There were 130 BT started in 1st line, 55 in 2nd line, 20 in 3rd line, 10 in 4th line and 3 in 5th line.

The 1st line BT most frequently indicated was Etanercept(ETN) up to 40%, followed by 30% Adalimumab(ADA) and 16.2% Infliximab(INF). The median duration of the 1st line was 51 months IQR (14-109,3). However, 53.8% of the 1st line BT were switched: 28.3% due to adverse events, 25.7% due to 1st failure and 25.7% due to 2nd failure. The BT that were discontinued were: INF (76.2%) and Anakinra (ANAK) (75%) due to adverse events and ETN (59.6%) due to 1st and 2nd failure. 55 patients started a 2nd BT: 43.6% received ADA and 20% Tocilizumab (TCZ) with a median duration of 43 months IQR (12-90). 22 of 55 BT required a change: 75% of ETN and 59% of INF prescribed in 2nd line were discontinued. The causes were: 40% 1st failure, 28% 2nd failure and 12% remission. In 1st line 87.6% of patients received TNF inhibitors, 74% maintained the target in 2nd line. In 3rd line TCZ was the most frequent BT. 71.5% of patients continue on BT. BT was withdrawn in 20 of 130 patients due to remission (40%), adverse events (30%), and pregnancy (10%).

In the analysis by decades, 80 BT (36.7%) were started from 1999 to 2008 and 138 BT (63.3%) from 2009 to 2019. In the 1st decade ETN and INF were the most frequently prescribed and in the 2nd decade, ADA and TCZ ($p < 0.0001$). The 1st BT in the 2nd decade were indicated sooner compared to the 1st decade (1st decade: mean 119.5months SD(109.2); 2nd decade: mean 53.9 months SD(99.7); $p < 0.0001$). In 1st line BT, the BT prescribed in the 2nd decade had a shorter duration than those in the 1st decade (1st decade: mean 84.1 months SD(71.8); 2nd decade: mean 51.7 months SD(5); $p < 0.0001$).

In the survival analysis, TCZ and ADA were the BT with the highest survival ($p=0.001$). Of the 31 patients that started TCZ, 61.3% continue on TCZ, with a median duration of 46 months IQR(25-99) and 36/68(52.9%) still on ADA with a median duration of 61,5 months IQR(30.5-98).

Conclusion: 42.3% of patients required more than one BT. Since the onset of the BT there has been a change in prescription, probably related to the emerge of new targets and the evidence provided by clinical trials and guidelines. TCZ and ADA were the BT with the highest survival rate. On the other hand, INF and ANAK were the ones with the lowest survival rate. The most common causes of BT change in 1st line were adverse events in relation to INF and ANAK. In 2nd line there was a high rate of change in those patients who maintained TNFi, related to 1st failure.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4655

FRI0468

SYSTEMIC AND CUTANEOUS POLYARTERITIS NODOSA IN COLOMBIAN PEDIATRIC PATIENTS: CUTANEOUS POLYARTERITIS IS NOT SO BENIGN

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Background: Polyarteritis nodosa (PAN) is the third most frequent vasculitis in pediatrics. Cutaneous PAN (CPAN) being more common than Systemic PAN (SPAN). CPAN is frequently described as a benign disease. In children, PAN onset is frequent between 9 and 11 years of age, with no sex differences, and its clinical features may be nonspecific.

Objectives: To characterize pediatric patients who were diagnosed with CPAN and SPAN and to compare their clinical features, treatments, and outcome.

Methods: A descriptive study was conducted in two centers from Medellín - Colombia, using retrospective data from January 2010 to December 2019. Patients under 18 years of age classified as PAN according to EULAR/PRINTO/PRES(1) criteria were included. CPAN patients were defined according to EULAR/PRES definition (2). Data from medical records were registered, and were expressed in median and ranges and mean and standard deviation (SD) according to their distribution. A univariate analysis was carried out by comparing signs, symptoms, and treatment between CPAN and SPAN, and a p -value $< 0,05$ was considered as significant.

Results: Twenty patients were included. The median age at diagnosis was ten years. 60% were boys. The median follow-up period was 27 months. CPAN was diagnosed in 11 (55%) and SPAN in 9 patients (45%). The most frequent symptoms were cutaneous manifestations (95%), fever (60%) and Calf Pain (55%). Mucosal ulcers were described in four patients; 3 of them were defined as CPAN. Lingual necrosis was present in two CPAN, and peripheral nervous system involvement was found in one SPAN and two CPAN patients in skin affected with lesions; even though, no significant statistical differences between CPAN and SPAN were found in constitutional, cutaneous, muscle-skeletal symptoms, and acute phase reactants. Arteriographic anomalies as hepatic and renal microaneurysms, carotid aneurysms without aortic involvement, and renal infarction were found in one patient each. Skin Biopsy was performed in 18 patients, being compatible with PAN in 16. All PAN patients (CPAN and SPAN) required treatment with glucocorticoids. None of the patients died during the follow-up period.

Conclusion: In this Colombian pediatric cohort of PAN patients, the disease was more common in boys than girls, and CPAN was more frequent than SPAN, as already been described. As is evident in this cohort, although CPAN has been considered a benign disease, these patients may be severely ill, requiring glucocorticoid treatment. Pediatric CPAN patients should be strictly followed with particular attention to identify systemic involvement, considering that constitutional, cutaneous, and muscle-skeletal features may be very similar between CPAN and SPAN.

References:

- [1] Ozen S, Pistorio A, Lusan S, et al. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. *Ann Rheum Dis.* 2010 May;69(5):798–806.
- [2] Ozen S, Ruperto N, Dillon M, et al. EULAR/PreS endorsed consensus criteria for the classification of childhood vasculitides. *Ann Rheum Dis.* 2006;65(7):936–41.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6512

FRI0469

TO DISTINGUISH BETWEEN DISEASE FLARE AND ACTIVE INFECTION IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: SLE is the autoimmune disease involving multiple systems. Infections might mimic SLE flare, leading to confusion over the diagnosis and appropriate treatment. To distinguishing acute infection from active flare always remains a clinical challenge.

Objectives: We aim to explore the potential parameters in identifying active infection and disease activity in pediatric SLE.