in 2–17-year-old patients (pts) with pcJIA, comprising rheumatoid-factor (RF)-positive and RF-negative polyarticular and extended oligoarticular JIA. **Objectives:** Evaluation of pharmacokinetics (PK), pharmacodynamics (PD), safety, and efficacy of 3 subcutaneous (SC) sarilumab doses in pcJIA.

Methods: A 12-week dose-finding study was performed to identify an appropriate sarilumab dose for use in the pcJIA population. Pts were divided by body weight into 2 groups: A (30–60 kg) and B (10–<30 kg), and received sequential ascending doses of sarilumab, Dose 1 (Group A/B): 2.0/2.5 mg/kg q2w; Dose 2 (Group A/B): 3/4 mg/kg q2w; and Dose 3 (Group A/B): 2.0/2.5 mg/kg qw. pcJIA doses were targeted to achieve similar exposure to adult RA doses (150 mg q2w, 200 mg q2w, and 150 mg qw). Primary outcome was PK; secondary outcomes were safety, PD, and efficacy of sarilumab.

Results: 42 pts enrolled (20/22 in Groups A/B); mean age was 13.0/5.2 years. At baseline, mean pcJIA duration, number of active joints, and JADAS27-CRP were 4.6/1.7 years, 17.2/11.0, and 22.2/19.1, in Groups A/B, respectively. As in adult pts, sarilumab exhibited nonlinear PK with target-mediated drug disposition (TMDD). Following repeated SC administrations, exposure increased in a greater than dose-proportional manner and accumulated 1.9–4.5-fold over 12 weeks. Sarilumab exposure was similar in both weight groups for each dose (Figure), and comparable to corresponding adult doses. Treatment-emergent adverse events (AEs) were reported in 36/42 (85.7%) pts (comparable across dose and weight groups); infections (28/42, 66.7%) were the most frequently reported AE. 12 grade 3/4 neutropenias were identified, mostly in Dose 3 (n=6) and in Group B (n=8). None was associated with infection; all resolved in a few days. Overall, 4 pts discontinued due to neutropenia and 1 due to alanine aminotransferase increase. There were no serious AEs, no cases of GI perforation, and no deaths. By Week 12, as observed while on-treatment: all pts attained JIA ACR30; 50%, 62%, and 100% of pts attained JIA ACR70 with Doses 1, 2, and 3, respectively; JADAS27-CRP mean % changes from baseline in Doses 1, 2, and 3 were -74.6%, -73.1%, and -87.9%, respectively.

Figure. Mean (CV%) individual sarilumab exposure, following first SC dose, and after repeated SC administration at Weeks 10–12 or Weeks 11–12, in patients with pcJIA/First

pcJIA treatment		First SC administration		Repeated SC administration (Weeks 10–12 or Weeks 11–12)	
Patient weight group	Sarilumab dose	N	C _{0-12h} , mg/L (CV%) AUC _{0-12h} , day mg/L (CV%)	N	C _{0-12h} , mg/L (CV%) AUC _{0-12h} , day mg/L (CV%)
10–<30 kg (Group B)	2.5 mg/kg q2w	6	0.54 (48) 63 (30)	5	1.83 (101) 118 (37)
	4.0 mg/kg q2w	7	3.77 (43) 167 (26)	7	11.90 (41) 310 (26)
	2.5 mg/kg qw	9	5.22 (39) 54 (36)	5	25.10 (29) 203 (25)
30–60 kg (Group A)	2.0 mg/kg q2w	7	0.63 (63) 53 (46)	5	1.99 (86) 114 (18)
	3.0 mg/kg q2w	7	1.84 (69) 123 (24)	6	8.46 (68) 269 (34)
	2.0 mg/kg qw	6	8.07 (32) 61 (22)	6	30.40 (28) 250 (24)

AUC, area under the serum concentration versus time curve, calculated using trapezoidal method during a dose interval; C_{0-12h}, serum concentration observed before treatment administration during repeated dosing; CV, coefficient of variance; N, number of patients; pcJIA, polyarticular-course juvenile idiopathic arthritis; qw, every week; q2w, every 2 weeks; SC, subcutaneous.
Dose interval (q) was 2 weeks for q2w, or 1 week for qw regimen.

Conclusion: Sarilumab exhibited nonlinear PK with TMDD. Doses tested in pcJIA yielded similar exposure in both weight groups and were comparable to equivalent doses in adults with RA. All dose regimens proved effective for decreasing disease activity. Safety profile was consistent with class effects; higher incidences of neutropenia were observed with Dose 3, and in pts weighing 10–<30 kg.

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FR10550

JIA DISEASE ACTIVITY OUTCOMES ACROSS A MULTI-CENTER COHORT: ANALYSIS OF THE PEDIATRIC RHEUMATOLOGY CARE AND OUTCOMES IMPROVEMENT NETWORK (PR-COIN) REGISTRY

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Background: Clinical remission is widely accepted as the primary target outcome for juvenile idiopathic arthritis (JIA). PR-COIN is a quality improvement collaborative that serves as a sample of pediatric rheumatology centers in North America. By measuring disease activity in practice using the ACR provisional criteria for Clinical Inactive Disease (CID), variation in patient outcomes has been previously observed between centers. **Objectives:** The objective of this study was to evaluate differences in patient-level factors that may be driving center-level variation in JIA outcomes.

Methods: This study used cross-sectional data provided by PR-COIN that was collected by PR-COIN centers from March 2015 to May 2016. For each patient, sociodemographic, clinical, patient-reported, disease activity, and medication variables were extracted from the most recent encounter. Patients with disease duration less than 9 months were excluded. Patients were grouped by CID status (inactive vs active disease) and then compared using descriptive statistics, chi-square for categorical variables, and independent t-tests for continuous variables. Missing data were excluded with each analysis. Analyses were performed using R software.

Results: There were 2751 patients eligible for analysis from 14 centers, with 33 to 394 patients per center. We identified 1249 patients with inactive disease (47%) and 1428 patients with active disease (53%). Patients with inactive disease were younger (12 vs 13 years), more likely to have persistent oligoarticular subtype (33% vs 23%), and less likely to have enthesitis related arthritis (9% vs 14%). Patients with active disease had higher patient-reported measures of global assessment of disease activity, pain, and functional disability, as well as disease activity measures per definition. More medication usage was observed in patients with active disease compared to inactive disease across multiple categories, including both non-biologic DMARDs (45% vs. 32%) and biologic DMARDs (48% vs 35%).

Conclusion: This study demonstrates differences in sociodemographic, clinical, and medication factors between patients with inactive and active JIA. Further analysis is needed to adjust center-level measures of JIA disease activity using the observed differences in patient case-mix. By using population data to identify predictors of inactive disease in JIA, there is potential to develop and implement targeted clinical interventions to directly impact care and improve outcomes.

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IDENTIFYING RESEARCH PRIORITIES FOR JUVENILE IDIOPATHIC ARTHRITIS TOGETHER WITH PATIENTS, CARERS AND CLINICIANS THROUGH THE JAMES LIND ALLIANCE METHOD: PRELIMINARY RESULTS

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Background: Research on Juvenile Idiopathic Arthritis (JIA) should have the primary goal to ultimately improve the lives of the affected patients, and help health professionals provide the best care for them. Therefore, these end users of research evidence – patients, carers (parents/caregivers) and clinicians – should be included in the process of identifying research priorities. Importantly, patients and carers can use their unique experiential knowledge from living with the disease to give vital input to researchers in designing a study. Combining this input with the goal of research(ers) to make a true impact on patients' lives, will result in research that is more effective and meaningful, and thereby increases research value [1]. To this end, we initiated the project of establishing a research agenda for JIA jointly by patients, carers and clinicians [2].

Objectives: The objective of this project is to bring patients, carers and clinicians together to identify research priorities and create a research agenda for JIA, such that future research into JIA is guided to the issues that matter most.

Methods: The method for research priority setting developed by the James Lind Alliance (JLA) is used [3]. This method consists of several steps with the end goal of creating a top 10 list of research priorities agreed on by all parties. First, a steering group with equal representation of patients, parents and clinicians was assembled. We are now in the process of collecting research questions through an online survey. Focus groups are being held to ensure the inclusion of younger patients. Questions will be clustered and checked against the evidence. Next, the process of interim priority setting will follow, in which a shortlist of up to 30 questions will be assembled. During a final workshop in which all parties are equally represented, the top 10 research priorities will be established. This workshop is scheduled for the end of 2019. A process evaluation is conducted to monitor ethical aspects in the decision-making process.

Results: The first step of collecting research questions is performed until the end of March 2019. We will be able to present preliminary results on the questions gathered from the online survey and focus groups by June 2019. Furthermore, we will discuss the effects of our efforts to be inclusive and representative of every party involved.

Conclusion: Through this project, patients, carers and clinicians are brought together to define the most important unanswered questions for JIA. Engaging patients and stakeholders in this crucial phase is the next step in performing more meaningful and effective research.

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PERFORMANCE OF NEWLY PROPOSED PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS AND CERVICAL ADENITIS (PFAPA) SYNDROME CRITERIA IN REGIONS ENDEMIC FOR FAMILIAL MEDITERRANEAN FEVER (FMF)

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Background: The periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome is an autoinflammatory condition characterized by regularly recurrent episodes of high fever lasting 3 to 6 accompanied by aphthosis, cervical adenitis, and pharyngitis, in the absence of upper respiratory tract infections. A relevant number of patients with monogenic periodic fevers also meet the diagnostic criteria for PFAPA syndrome. Especially in regions endemic for familial Mediterranean fever (FMF), it would be important to avoid useless genetic testing and to be able to identify PFAPA patients by using clinical classification criteria. Despite the high specificity, widely used Marshall's criteria have been shown to have low specificity. An international consensus among experts has been established recently, in order to define a set of classification criteria for PFAPA syndrome with a better performance in term of sensitivity and specificity.

Objectives: We aimed to evaluate the performance of recently proposed PFAPA criteria, in order to assess their utility in regions endemic for FMF.

Methods: Patients diagnosed with PFAPA syndrome, FMF and juvenile idiopathic arthritis (JIA) were consecutively included in the study. PFAPA diagnosis has been established by Marshall's criteria. Patients with FMF and JIA were diagnosed according to Turkish pediatric FMF criteria and ILAR criteria, respectively. Two investigators blindly evaluated all of patients for the newly proposed PFAPA criteria.

Results: A total of 321 PFAPA, 118 FMF and 45 JIA patients with mean age of 7.23±2.9, 14.7±3.09, 13.5±4.6 years, respectively, were included in the study. A 45% (146/323) of PFAPA, 50% (59/118) of FMF and 58% (23/45) of JIA patients were female. We found quite high sensitivity (90%) of newly proposed PFAPA criteria: 289 out of 321 (90%) patients followed up as PFAPA syndrome fulfilled newly proposed PFAPA criteria, as well. When applied to patients diagnosed with FMF and JIA, 46 out of 118 (39%) FMF and 10 out of 45 (22%) JIA patients also fulfilled newly proposed PFAPA criteria. Specificity of recently proposed PFAPA criteria was found to be 61% and 77%, among FMF and JIA patients, respectively. Positive predictive value was 86% and 97%, negative predictive value was 69% and 50% for FMF and JIA patients, respectively.

Conclusion: Recently proposed PFAPA criteria have satisfactory high sensitivity. Specificity of recently proposed criteria is still under expectation in regions endemic for FMF. Multicentric studies with higher patients' number in different regions are needed in order to provide more relevant data on performance of newly proposed PFAPA criteria.

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