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Pediatric Rheumatology

MEETING ABSTRACT

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Abstracts of the 35th Meeting of the German Society for Pediatric and Adolescents Rheumatology (Gesellschaft für Kinder- und Jugendrheumatology (GKJR)

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Abstract
The 35th Meeting of the German Society for Pediatric and Adolescents Rheumatology (Gesellschaft für Kinder- und Jugendrheumatology (GKJR) will be held from March 12th to March 15th 2025, at Hotel Badersee, Grainau, Germany.
All abstracts have been reviewed by two experts.
For detailled information concerning the conference please visit:
https://www.gkjr.de/gkjr-jahrestagung/
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We gratefully acknowledge the intensive work on the collection and editing of the abstracts done by Birgitt Huber, Martina Niewerth and Gabriele Berg. Thanks to our reviewers, all experts in the field of pediatric rheumatology, who kindly evaluated the abstracts. Finally thanks to the GKJR in financing the publishing process.

A1

Rates of infections in children and adolescents with rheumatic diseases: analysis of German nationwide health insurance data

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Pediatric Rheumatology 2025, **23(1):**A1

Introduction: Infections might be more frequent in children and adolescents with rheumatic diseases compared to the general population due to disease-inherent immune dysregulation and/or required medication. Studies upon this topic are scarce and show conflicting results.
Objectives: Compare rates of selected infections, hospitalization because of infection and antibiotic therapies among children and adolescents with different rheumatic diseases and matched controls using nationwide health insurance data.
Methods: Nationwide data from the statutory BARMER health insurance company for 2018–2022 were analyzed. The study included individuals aged 0–18 years with an ICD-10-GM diagnosis of juvenile idiopathic arthritis (JIA), juvenile systemic lupus erythematosus (jSLE), juvenile dermatomyositis (jDM) or chronic non-bacterial osteomyelitis (CNBO) in at least two quarters. Rates of selected infections, identified by ICD-10-GM codes (all infectious and parasitic diseases, 41 individual infections), hospitalization for infection, and annual antibiotic

prescription rates (identified by Anatomical Therapeutical Chemical [ATC] code) were assessed and compared to sex- and age-matched controls.
Results: On average, 1,354 patients with rheumatic diseases and 6,759 controls were identified annually. In 2022, 1,265 patients were included (JIA: 1219; jSLE: 21; jDM: 14; CNBO: 11). Among patients, 42% of those with JIA, 81% with SLE, 57% with jDM, and 27% with CNBO were on DMARDs (cs-, b- or tsDMARDs), while 8%, 62%, 21% and 9%, respectively, were on glucocorticoids.
Over the 5-year period, patients experienced an average of 1.4–1.6 different infections per year, compared to 1.4–1.5 in controls. In 2022, at least one infection was recorded in 19% of JIA patients, 38% of jSLE patients, 29% of JDM patients and 18% of CNBO patients, versus 13%, 9%, 14% and 9% of controls, respectively.
Hospitalization rates due to infection were 1,4% for JIA patients vs. 0,6% in controls, 4,8% for jSLE vs. 0%, 0% for jDM vs. 1,4%, 0% for CNBO vs. 5,5%. Antibiotic prescriptions were more frequent in patients than controls: 18% vs. 12.5% for JIA, 33.3% vs. 8.6% for jSLE, 28.6% vs. 12.9% for jDM and 18.2% vs. 12.7% for CNBO.
The most common infections were upper respiratory tract infections, including tonsillopharyngitis (2022: 6.2% in JIA vs. 4.1% in controls), acute bronchitis (2.2% vs. 1.9%), acute sinusitis (0.9% vs. 0.6%) or acute bacterial otitis media (0.7% vs. 0.6%). Except for herpes zoster (0.2% in JIA vs. 0.03% of controls), no opportunistic infections were observed.
Conclusion: Patients with rheumatic diseases, particularly jSLE and JDM, seek medical attention for infections more frequently than age-matched controls. While hospitalizations for infections are relatively uncommon, children and adolescents with rheumatic diseases receive antibiotic treatment more often than controls. Detailed analyses will follow.

Patient Consent: Not applicable (there are no patient data).
Funding: The study was funded by the Sabine Löw Foundation for Pediatric Rheumatology, Münster, Germany. Mirjam Freudenhammer was supported by the IMM-PACT Clinician Scientist Programme, Faculty of Medicine, University of Freiburg, Freiburg, Germany.
Disclosure of Interest: The authors declare that they have no conflict of interest.

A2

Need for information on disease and treatment in adolescents with juvenile idiopathic arthritis (JIA)

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Pediatric Rheumatology 2025, **23(1):**A2

Introduction: Upon reaching adulthood, adolescents with juvenile idiopathic arthritis (JIA) face the transfer to adult care. It is crucial that they possess knowledge about their disease and treatments. This knowledge empowers them to take responsibility for managing their condition, which can improve treatment adherence and satisfaction.
Objective: The study aims to explore information needs regarding disease and treatment among young people with JIA.
Method: As part of the "InfoTrans" project, all adolescents with JIA aged 16 and older who participated in the National Pediatric Rheumatologic Database (NPRD) in 2022 and 2023 were offered a structured report summarizing their disease and treatment history from the NPRD. Additionally, the adolescents were surveyed using the "Transition-KompAZ" (1) to assess their transition competency and unmet needs. Two groups were formed: Group 1 (no report requested) and Group 2 (report requested). Differences in sociodemographic and disease-related characteristics as well as transition competencies were analyzed.
Results: Data from 1,610 adolescents (median age: 17 years) with JIA were available, with 91 (6%) requesting a report. Patients who requested a report were more often female as those who did not request a report. For the other socio-demographic and disease-specific parameters, the two groups did not differ significantly. There were no obvious differences in their self-reported knowledge about their health and treatments and their disease self-management. However, patients who requested a report were more familiar with the website for young rheumatics by the German Rheumatism League. Nethertheless, their information needs, particularly regarding medications and disease progression, tended to be higher than that of those who did not request a report (see Table 1).
Conclusion: Despite self-reported knowledge gaps and unmet needs related to disease understanding, only a minority of young people with JIA requested a report detailing their disease and treatment history. Longitudinal analyses will assess whether receiving the report and accompanying links to additional resources enhances their health literacy.

Patient Consent: Yes, I received consent.
Funding: The InfoTrans project is supported by the Innovation Fund (01VSF20012).
Disclosure of Interest: None.

Reference

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Table 1 (Abstract A2). Characteristics of patients and their transition skills

	Group 1	Group 2
Number of cases	1,519	91
Gender female, %	67.9	73.3
Age in years, mean	17.3	17.4
JIA category, in %		
- Oligoarthritis	39.9	49.0
- Rheumatoid factor-negative polyarthritis	22.8	18.7
- Enthesitis-related arthritis	16.2	11.0
- Rheumatoid factor-positive polyarthritis	5.4	5.5
- Psoriatic arthritis	8.9	5.5
- Systemic JIA	3.6	7.7
- Unclassified JIA	2.9	2.2
cJADAS (0–30), mean	4.5	4.6
Overall well-being (NRS 0–10), mean	2.4	2.8
Information search via websites, apps, %	16.0	18.2
Knowledge of the website of the German Rheumatism League, %	24.8	32.2

	Group 1	Group 2
Patients with a need for information, %		
- on the disease	24.4	24.7
- on medication	20.2	26.2
- Influence of your lifestyle on your illness	28.6	31.8
- on the influence of lifestyle	24.0	32.9
- on the influence of alcohol, drugs and nicotine	30.4	32.9
- on the connection between the disease and contraception/pregnancy	34.8	40.0
- on the course of the disease on the impact on work	31.2	32.9
- on self-help services	11.3	11.9
- on socio-legal support	17.7	13.3

A3

The risk of long-term glucocorticoid use in juvenile idiopathic arthritis

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Pediatric Rheumatology 2025, **23(1):**A3

Introduction: Juvenile idiopathic arthritis (JIA) patiente can suffer from comorbidities at onset or during their disease course. Numerous targeted DMARDs have been approved for treating juvenile idiopathic arthritis (JIA) over the last two decades. Despite these advancements, co-medications with glucocorticoids (GC) are still used alongside DMARDs. However, long-term side effects such as short stature, osteoporosis or hypertension may occur.
Objectives: This study aimed to determine the frequency of hypertension, osteoporosis, and short stature in young adults with JIA and to investigate the association between duration of GC use and the onset of selected comorbidities.
Methods: We analyzed data collected until June 2024 from the JIA register BiKeR (Biologics in Pediatric Rheumatology Registry) cohort and its follow-up register JuMBO (Juvenile arthritis Methotrexate/Biologics long-term Observation). JIA patients enrolled in the pediatric register BiKeR with start of a DMARD were subsequently monitored into adulthood in JuMBO. The treating physicians half-yearly reported on patients' disease activity, treatments, and adverse events/comorbidities. Hypertension and osteoporosis were identified using the MedDRA (Medical Dictionary for Regulatory Activities) SMQs (standardized medical query) "Hypertension" and "Osteoporosis/osteopenia", respectively. Short stature in adulthood was defined according to the German society of endocrinology (<1.53 m for female, <1.67 m for male).
Results: For this analysis, 2026 JIA patients were included, with a mean age of 13.2±3.8 years at BiKeR inclusion and 23.8±4.4 years at the last JuMBO visit, and an average follow-up period of 10.5±4.5 years. The most common JIA categories were rheumatoid factor-negative polyarthritis (28%), extended oligoarthritis (19%) and enthesitis-related arthritis (19%). Hypertension, osteoporosis, and short stature were reported in 2.9%, 3.6%, and 4.7% of patients, respectively. Patients with JIA onset before 2000 were more likely to have these comorbidities than those with JIA onset after the introduction of bDMARDs (Table 1). The use of systemic GC also significantly varied between patients with JIA onset before and after bDMARD approval. Prolonged GC use was significantly associated with higher risks of hypertension, osteoporosis, and short stature in young adulthood, adjusted for JIA categor y, sex and bDMARD treatment. The shorter the duration between JIA onset and DMARD start was, the lower the rate of hypertension.
Conclusion: The use of GC in the long-term is associated with higher risks of hypertension, osteoporosis, and short stature in adulthood. The introduction of bDMARD treatment in JIA has notably reduced the long-term use of GC, but one in fourteen young adults still receives this therapy. Given the potential impact on long-term health, GC should be prescribed for as short a time as possible.

Patient Consent: Yes, I received consent.
Funding: BiKeR: Supported by an unconditional grant from Pfizer, Roche,Chugai, MSD, and Novartis; JuMBO: Supported by an unconditional grant from Pfizer, Roche, and Biogen.
Disclosure of Interest: Kirsten Minden: received honoraria from Pfizer, Novartis and medac; Gerd Horneff: Advisory Speaker: Pfizer, Novartis, Sobi; Consultant MSD, Lilly; Grants Novartis, MSD, Roche; Speakers bureau: Pfizer, Roche, MSD, Sobi, GSK, Sanofi, AbbVie, Chugai, Bayer, Novartis, Grant/research support from: Pfizer, Roche, MSD, AbbVie, Chugai, Novartis; Ariane Klein: Speakers fee: Novartis, Lilly.

Reference

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Table 1 (Abstract A3). Use of systemic glucocorticoids and rates of selected comorbidities

	Total (*n*=2026)	JIA onset before 2000 (*n*=468)	JIA onset in 2000 and later (*n*=1558)
Glucocorticoids at first BiKeR visit	682 (33.7%)	225 (48.1%)	457 (29.3%)
Glucocorticoids at last BiKeR visit	52 (2.6%)	20 (4.3%)	32 (2.1%)
Glucocorticoids at first JuMBO visit	208 (10.3%)	100 (21.4%)	108 (6.9%)
Glucocorticoids at last JuMBO visit	198 (9.8%)	90 (19.2%)	108 (6.9%)
Hypertension, n(%)	58 (2.9%)	34 (7.3)%	24 (1.5%)
Osteoporosis, n(%)	72 (3.6%)	29 (6.2%)	43 (2.8%)
Short stature, n(%)	95 (4.7%)	47 (10.4%)	48 (3.1%)

A4

Same but different: Kawasaki Disease and MIS-C – a comparative longitudinal cohort analysis

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Pediatric Rheumatology 2025, **23(1):**A4

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# These authors contributed equally to this work and share first authorship

Introduction: Although MIS-C and Kawasaki share inflammatory characteristics, they differ significantly in etiology, demographics, epidemiology, clinical and laboratory findings, and pathology.
Methods: A single-center study was conducted on consecutive pediatric Kawasaki and MIS-C patients from January 2021 to January 2024. Patients were included if they 1) met diagnostic criteria for MIS-C or Kawasaki, 2) were followed longitudinally. The analysis encompassed clinical characteristics, laboratory findings, treatment approaches, outcomes, and the evaluation of a new scoring system.
Results: The study included 80 patients: 51 with MIS-C and 29 with Kawasaki. The median age was 6.8 years for MIS-C and 2 years for Kawasaki, average hospital stays were 8.4 days and 5.6 days, respectively. Kawasaki patients more commonly presented with rash (93% vs. 45%), mucous involvement (76% vs. 49%), conjunctivitis (86% vs. 37%), hand and feet erythema/edema (51% vs. 33%), and cervical lymphadenopathy (69% vs. 45%). MIS-C patients had higher rates of respiratory (33% vs. 3%), neurological (10% vs. 0%), and renal involvement (6% vs. 0%), as well as myocarditis (89% vs. 10%) and shock (24% vs. 3%). Coronary artery dilatation was more prevalent in Kawasaki (49% vs. 5%). MIS-C patients required more high-dose steroids (60% vs. 17%), anakinra (35% vs. 3%), inotropes (14% vs. 0%), ICU admission (22% vs. 3%), and mechanical ventilation (12% vs. 0%). They also had significantly lower lymphocyte counts, platelet counts, and albumin levels, but higher creatinine, NT-proBNP, Serum Amyloid A, IL-2R, and Ferritin levels. NT-proBNP, with a cut-off of 205.5, showed 81.1% sensitivity and 82.4% specificity. The new scoring system effectively differentiated MIS-C from acute appendicitis, with a median score of 6.2 indicating MIS-C in most cases. At the last visit, fewer MIS-C patients required aspirin for coronary dilation compared to Kawasaki (18% vs. 31%), indicating risk for potential long-term cardiovascular disease.
Conclusion: Meticulous clinical examination and laboratory studies are warranted to distinguish these inflammatory syndromes, initiate appropriate therapy and improve patient outcomes.

Patient Consent: Yes, I received consent.
Funding: Infrastructural funding was provided by the University Hospital Tübingen. No other funding was received for this study.
Disclosure of Interest: JKD has received research grants and speaker's fees from Novartis and SOBI. The other authors declare no conflicts of interest.

A5

Sensorineural hearing loss in Cryopyrin-Associated Periodic Syndrome (CAPS)

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Pediatric Rheumatology 2025, **23(1):**A5

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Introduction: CAPS, caused by NLRP3 gain-of-function mutations, leads to excessive IL-1β production and progressive sensorineural hearing loss, especially in moderate-to-severe cases. Early detection via high-frequency hearing assessments is crucial for timely intervention.
Methods: A single-center longitudinal study (2006–2024) included 36 pediatric and adult CAPS patients with hearing loss. Data on demographics, genotype, phenotype, and treatment were analyzed. Hearing loss was assessed using 4PTA and HF-PTA, graded per WHO standards.
Results: The study included 36 patients (13 children, 23 adults). Median age at disease onset was 11.8 years, with diagnosis at 35 years and hearing loss identified at 40 years. Median follow-up was 8.2 years. MWS was the predominant phenotype (86%), with CINCA/NOMID at 14%. NLRP3 mutations were classified as pathogenic or likely pathogenic (78%), with E311K (30%) and T348M (16%) being most common. At baseline, 86% of patients exhibited hearing loss (median 4PTA: 34.5 dB), with HF-PTA abnormalities in all cases. HF-PTA demonstrated 100% sensitivity compared to 66% for 4PTA. Adults had more severe WHO impairment grades (III–IV), while children often presented with no impairment (Grade 0). Severity correlated with pathogenic mutations and treatment delays exceeding 10 years, which were associated with WHO Grades III–IV.Ten patients required therapy escalation for progressive hearing loss: five with severe and five with moderate phenotypes. Following escalation, hearing stabilized or improved in 60% of cases. Tinnitus and vertigo, reported in isolated patients, resolved completely after therapy adjustment.
Conclusion: CAPS patients develop progressive hearing loss influenced by genotype, phenotype, and treatment timing. HF-PTA outperforms 4PTA for early detection. Regular high-frequency assessments and timely therapy escalation can stabilize or improve hearing outcomes.

Patient Consent: Consent for publication was obtained from all participants.
Funding: Infrastructural funding was provided by the University Hospital Tübingen. No other funding was received for this study.
Disclosure of Interest: JKD has received research grants and speaker's fees from Novartis and SOBI. The other authors declare no conflicts of interest.

A7

The influence of therapeutic play on the treatment of children and adolescents with rheumatic diseases

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Pediatric Rheumatology 2025, **23(1):**A7

Introduction: Anxiety and negative experiences in hospitals can have lifelong effects on patients' psychological well-being and can continue into adulthood[1]. One way to prevent this vicious cycle is through therapeutic play.
Objectives: This study aims to examine whether which positive effects therapeutic play can have in the everyday care of children and adolescents with rheumatic diseases.
Methods: Since 2023 we have a special ward named "Eckbauer", designed for nursing-trainees and provided with pedagogically trained nurses. Based on the findings of a systematic review, the use of the mascot "Ecki" from the Eckbauer training station was planned for this purpose (Figure 1).
After the end of the first cycle of the training station, the practice instructors were asked about their experiences using a dichotomous questionnaire. Commenting was allowed. Insights from patient feedback were also taken into account.
Results: Of a total of 11 practice-instructing nurses, 9 participated in the survey and 6 have integrated Ecki into their daily work. All of them used "Ecki" for therapeutic instructions and 50% used it for introducing therapeutic games as well. The technique of dramatic therapeutic playing was not integrated (0% use). All 9 practice instructors perceived positive effects, in particularly in reducing fears, awakening positive emotions, and/or facilitating easier access to the patients. One practice instructor had critical remarks about the time required for this, although 83% did not mentioned this issue.
The evaluations of patient feedback were consistently positive.
Conclusion: Therapeutic playing may have positive effects in the treatment of children and young people suffering from rheumatic diseases. In the protected setting of a training ward and conducted by pedagogically trained nurses, the positive effects described in the literature were consistently evident.

Patient Consent: Not applicable (there are no patient data).
Funding: Not applicable.
Disclosure of Interest: Leadership and employees of German centre for pediatric and adolescent rheumatology, Garmisch-Partenkirchen, Germany.

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Fig. 1 (Abstract A7). "Ecki" the hand-made mascot in the design of a caprocorn

A8

Pediatric case of severe gpa with large vessel involvement

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Pediatric Rheumatology 2025, **23(1):**A8

Background: Granulomatosis with polyangiitis (GPA) is an ANCA-associated necrotizing vasculitis that affects small- to medium-sized vessels. The clinical picture is variable and is caused by granulomatous inflammation, most commonly of the respiratory tract and the kidneys. The pathogenesis is driven by the presence of anti-neutrophilic cytoplasmic antibodies (ANCA) targeted against proteinase 3 (PR3) in neutrophils. Large vessel involvement (LVI) is rare in GPA patients and, to our knowledge, has not yet been reported in pediatric patients.
Case: In March 2024, a 16-year-old female patient, with no family history of rheumatic diseases, was admitted to our clinic with presumed vasculitis. She presented with polyarthritis, cutaneous papules (granulomas on histology) pulmonary infiltrates (on X-ray and chest CT) and pauci-immune glomerulonephritis (on histology). ANCA and anti-PR-3 antibodies were positive. The diagnosis of GPA with involvement of the respiratory tract, kidneys, skin and joints was made.
The patient was initially treated with methylprednisolone pulse, rituximab, and avacopan, a C5aR antagonist for complement inhibition. There was a rapid response of the small vessel vasculitis with resolution of arthritis, regression of the pulmonary infiltrates and normalization of proteinuria and renal dysfunction.
In week one of treatment, the patient reported increasing pain in the right foot the pulses in the A. tibialis anterior und A. dorsalis pedis were not palpable anymore. Sonography revealed occlusion of the right popliteal artery and laboratory tests showed severe coagulation activation. Therefore, lysis therapy and interventional thrombectomy were performed immediately. Another steroid pulse, a single i.v. dose of cyclophosphamide and plasmapheresis therapy were started. The lysis and a subsequent low molecular heparin therapy was only partially successful, however, the right A. dorsalis pedis remained irreversible completely occluded. This resulted in ischemic myositis with necrotic demarcation in the dorsal forefoot and toes I-III, which required forefoot amputation.
The patient is currently receiving 6-monthly B-cell suppression by rituximab for at least 2 years and avocaban for at least 12 months. Her PR3-levels are within normal limits.
Conclusion: We present a case of a GPA with severe large vessel involvement requiring forefoot amputation. LVI in GPA is very rare manifestation, predominantly affecting the aorta and its branches. The risk factors for LVI, are still unclear and especially for pediatric patients there is no pediatric-specific cohort reported or consensus for the therapeutic management.

Patient Consent: Yes, I received consent.
Funding: No funding.
Disclosure of Interest: No disclosures.

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A9

Use of biologic disease-modifying antirheumatic drugs and Janus kinase inhibitors in juvenile idiopathic arthritis: data of the biker-registry 2000–2024

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Pediatric Rheumatology 2025, **23(1):**A9

Introduction: Biologic disease-modifying antirheumatic drugs (bDMARDs) have revolutionized the treatment of juvenile idiopathic arthritis (JIA), providing targeted therapies for children with moderate to severe disease. This study investigates the evolving role of biologics and Janus kinase inhibitors (JAKi) in pediatric rheumatology over the past 25 years in Germany using data from the BIKER-Registry [1].
Objectives: This study aims to analyze trends in the utilization of bDMARDs and JAKi in JIA in Germany (2000–2024), comparing usage across JIA categories, including polyarticular JIA (pJIA), systemic JIA (sJIA), enthesitis-related arthritis (ERA), and juvenile psoriatic arthritis (jPsA),
Methods: We conducted a retrospective cohort analysis using data from the BIKER-Registry (2000–2024), focusing on the use of bDMARDs and JAK Inhibitors across different JIA categories. The analysis covered 6,263 treatment initiations among 4,195 patients. Temporal trends in therapy utilization were assessed with descriptive statistics and graphical representations.
Results: Etanercept dominated the bDMARD market for many years, accounting for over 90% of therapies until 2007. It was surpassed by Adalimumab in 2023, which accounted for 29% of usage compared to 26.1% for Etanercept. Since Adalimumab belongs to the TNF inhibitors (TNFi) as Etanercept, this shift reflects a change in the specific medications used rather than a departure from TNFi as the dominant treatment class. Over the past five years, TNFi still accounted for an average of 72.4% of the total bDMARD usage. Newer treatment options, such as IL-6 inhibitors (16.6%) and JAK inhibitors (6.1%), emerged in smaller proportions (Figure 1).
For pJIA, TNFi remained the primary treatment. Abatacept accounted for a small proportion of initiations and JAK inhibitors peaked at 24% of initiations in 2022 (Figure 2).
TNFi transitioned from being the sole treatment option for sJIA to no new initiations. In 2009, TNFi still accounted for 54% of new starts, but usage steadily declined as IL-1 and IL-6 inhibitors became the preferred therapies, alternating in utilization over time (Figure 3).
In ERA/PsA, TNFi continued to dominate, while JAK inhibitors and IL-17 inhibitors collectively accounted for an average of 23.2% of new treatments (Figure 4).
Conclusion: Over the past 25 years, TNF-alpha inhibitors have remained the cornerstone of JIA treatment, with newer biologics like IL-6 inhibitors, JAK inhibitors, and IL-17A inhibitors expanding treatment options, particularly for complex JIA categories.

Patient Consent: Yes, I received consent.
Funding: The data accumulation, analysis and publication is not influenced by the sponsors and lay in the full and only responsibility of the authors.
Disclosure of Interest: The BIKER registry has been supported by unrestricted grants from Abbvie, Chugai, MSD, Novartis, Pfizer, Roche. GH: Abbvie, Boehringer, Celgene, Chugai, GSK, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, Sobi, AK: Speakers fee: Novartis, Lilly; AZ: Travel grands: Novartis, Lilly; Speakers bureau: Lilly, Glaxo-Smith-Kline, CH: nothing to disclosure.

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1. Horneff G, Schulz AC, Klotsche J, Hospach A, Minden K, Foeldvari I, Trauzeddel R, Ganser G, Weller-Heinemann F, Haas JP. Experience with etanercept, tocilizumab and interleukin-1 inhibitors in systemic onset juvenile idiopathic arthritis patients from the BIKER registry. Arthritis Res Ther. 2017 Nov 22;19(1):256. doi: https://doi.org/10.1186/s13075-017-1462-2. PMID: 29166924; PMCID: PMC5700562.

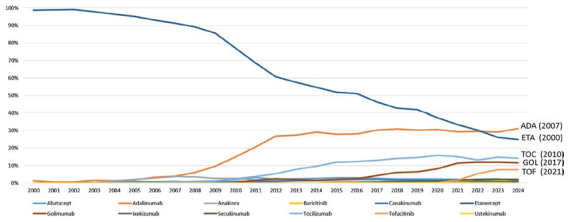

Fig. 1 (Abstract A9). Percentage of JIA Patients receiving Biologic DMARDs in the respective year and dates of first approval in Europe (2000–2024)

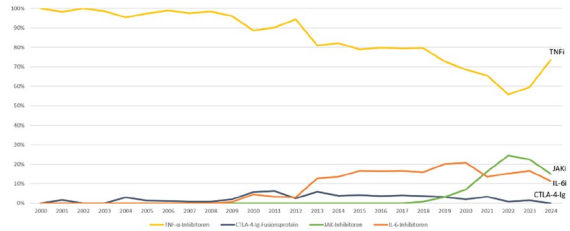

Fig. 2 (Abstract A9). Initiations of Biologic DMARDs in pJIA: TNFα Inhibitors, JAK Inhibitors, IL-6 Inhibitors, CTLA-4-Ig Fusion Protein (%)

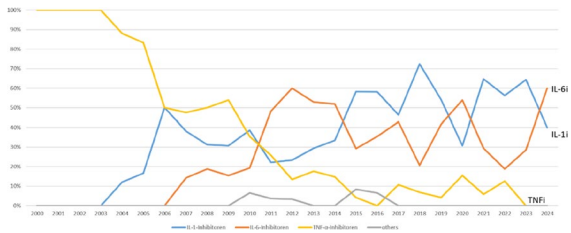

Fig. 3 (Abstract A9). Initiations of Biologic DMARDs in sJIA: IL-1 Inhibitors, IL-6 Inhibitors, TNFα Inhibitors and other Biologics (%)

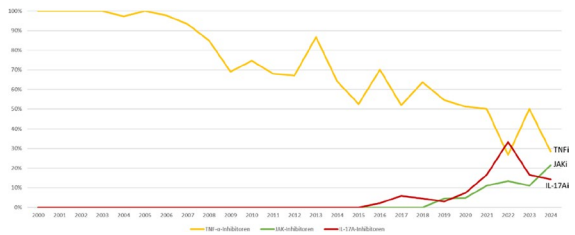

Fig. 4 (Abstract A9). Initiations of Biologic DMARDs in ERA/PsA: TNFα Inhibitors, JAK Inhibitors, IL-17A Inhibitors (%)

A10

Juvenile idiopathic arthritis in infancy – a multicenter retrospective study in Germany

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Pediatric Rheumatology 2025, **23(1):**A10

Introduction: Juvenile idiopathic arthritis (JIA) in infants is a very rare disease and diagnosis may be challenging.
Objectives: This study aims to characterize JIA in infancy in terms of initial symptoms, diagnostic delay, JIA categories, drug treatment and clinical outcomes, and to compare these features with those of patients with later onset of JIA.
Methods: Patients with JIA onset in infancy were included if they were enrolled in the National pediatric rheumatology database (NPRD) between 2011 and 2020 and had at least one follow-up visit within the first 5 years after disease-onset. Information on demographics, family history, disease activity (cJADAS-10), joint involvement, concomitant diseases, treatment and outcomes was collected prospectively via the NPRD and retrospectively via an infant-onset JIA module. Disease characteristics (except for distribution of JIA categories) were compared with those NPRD patients with JIA onset >1 and <6 years of age (for comparison of JIA categories and gender), and additionally matched at a ratio of 1:5 according to age and JIA category (toddler cohort, n=447, for comparison of clinical parameters). The mean follow-up time was 35.4±15.8 months for infants and 34.0±17.8 months for toddlers.
Results: A total of 90 infants with JIA (62.2% female) from 18 pediatric rheumatology centers throughout Germany were identified. JIA in infancy manifested at a mean age of 9.5±2.64 months. In comparison to JIA with later onset, infants were more likely to have systemic JIA (20.0% vs. 4.3%, p<0.001; Figure 1).
The time to first contact with a rheumatologist was significantly longer for infants than for toddlers (3.1±3.5 vs. 2.3±3.1 months, p=0.025). At follow-up, 66.3% of infants and 58.9% of toddlers received disease-modifying anti-rheumatic drugs (DMARD, p=0.178), of which 34.3% (infants) and 27.4% (toddlers) were treated with biologic DMARDs (p=0.156). Although disease activity at onset did not differ between the two groups, it was significantly higher at follow-up in the infant compared to the toddler cohort (cJADAS-10 3.0±4.4 vs. 2.1±3.5, p=0.034). Parent-reported health status was considered worse at the time of follow-up for infants as compared to toddlers (p=0.037).
Conclusion: JIA with very early onset is often diagnosed late. This inflammatory disease occurs in a highly vulnerable growth phase. Our study emphasizes the need for improved and timely diagnosis in infants with non-infectious arthritis, as well as prompt treatment. We are currently expanding the cohort to include European patients from the *Juvenile Inflammatory Rheumatism* (JIR) cohort.

Patient Consent: Yes, I received consent.
Funding: Between 2011 and 2020, the NPRD was funded by the German Pediatric Rheumatism Foundation, Pfizer, Abbvie, Chugai, GSK and Novartis.
Disclosure of Interest: None of the authors report any conflict of interest.

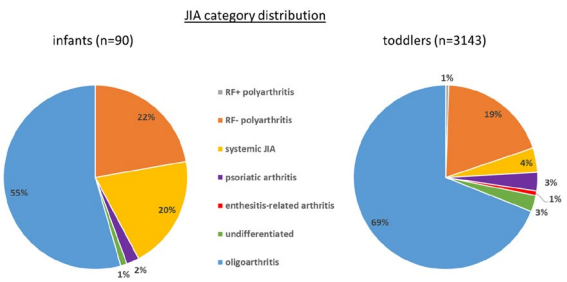

Fig. 1 (Abstract A10). Comparison of JIA categories (ILAR classification) in infants and toddlers recorded in the National pediatric rheumatology database in Germany between 2011 and 2020. RF+ = rheumatoid factor positive; RF- = rheumatoid factor negative

A11

Challenging wound management of calcinosis cutis in juvenile dermatomyositis

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Pediatric Rheumatology 2025, **23(1):**A11

Introduction: Juvenile dermatomyositis (JDM) is the most common chronic autoimmune disease in children. In general, JDM manifests with proximal muscle weakness and characteristic skin rashes, but other organs may also be affected. Approximately 35% of patients treated with the diagnosis at the Pediatric Center for Child and Adolescent Rheumatology in Garmisch-Partenkirchen present with calcinoses of the skin. Despite this relative frequency, there is no official guideline or standard of care. Treatment depends on the current focus of treatment. A case report presents the challenges of treatment calcinoses of the skin in children. The importance of individualized, needs-oriented wound management is discussed.

Case report: The case patient developed juvenile dermatomyositis at the age of 2 years and showed skin lesions of calcinosis cutis at the age of 4 years. The main symptoms of calcinoses were swelling, pain, inflammation and epidermal plaque breakthroughs.
During her stay, the numerous wounds, especially on the legs, which were infected with Pseudomonas aeruginosa and Staphylococcus aureus, were treated. These situations required sophisticated wound management with a special wound treatment concept, the use of the most modern wound dressings and intensive care of the child and her relatives.
In the treatment of calcinoses, special attention was given to reducing the risk of infection and atraumatic dressing changes. Silver-containing or antibacterial dressings were used to control infection. Silicone plasters were used for exudate management and atraumatic dressing changes. Advice and guidance on maintaining and improving quality of life and promoting self-management were also important.
Individualized, modern, flexible and yet continuous wound care can improve the management of these chronic wounds, even in the absence of standardization or guidelines.
Conclusion: Current management of calcinosis wounds is based on years of experience and experiments with different wound treatment concepts. The choice of therapy depends on the wound status and the patient's current focus. Therefore, the treatment plan must always be drawn up individualized and adjusted as necessary. Patient's ability to self-manage also plays a crucial role in the success of the treatment.

Patient Consent: Yes, I received consent.
Funding: Not applicable.
Disclosure of Interest: Leadership and employees of German Centre for Pediatric and Adolescent Rheumatology, Garmisch-Partenkirchen, Germany.

A12

Case report: Golimumab treatment in a patient with chronic nonbacterial osteomyelitis

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Pediatric Rheumatology 2025, **23(1):**A12

Introduction: Golimumab has been used only in a small number of patients with chronic nonbacterial osteomyelitis (CNO) so far. A review has shown a favourable outcome in 18 pediatric or adolescent patients. [1]
Methods: We report the case of a 10-year old boy who had been diagnosed with CNO at the age of 7 years, who had multifocal involvement of both lower limbs. He showed no improvement under therapy with etanercept and pamidronate, respectively. Adalimumab was efficient, but caused severe perioral skin disease, which we interpreted as paradoxical psoriasis. After 12 months, adalimumab was discontinued, although MR imaging did not show complete resolution. After stopping the medication, the skin gradually improved, but the CNO relapsed three months later.
Results: With golimumab, we were able to achieve clinical remission again in this patient. Under continued treatment the patient is well. No adverse effects were seen so far, especially concerning the skin.
Conclusion: Golimumab is an alternative in CNO patients, who do not respond or do not tolerate other TNF alpha inhibitors.

Patient Consent: Yes, I received consent.
Funding: No funding.
Disclosure of Interest: No conflicts of interest.

Reference

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A13

Pyoderma gangrenosum as a rare complication of chronic recurrent multifocal osteomyelitis successfully treated with upadacitinib as steroid-sparing agent

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Pediatric Rheumatology 2025, **23(1):**A13

Background: Pyoderma gangrenosum (PG) is a rare, inflammatory skin disorder, particularly uncommon in childhood. It is often associated with chronic inflammatory conditions, most notably inflammatory bowel diseases, rheumatoid arthritis and myelodysplastic disorders. In adults, treatment of PG typically involves corticosteroids and increasingly biologics such as TNF inhibitors and others (AWMF guidelines 2020). Chronic Recurrent Multifocal Osteomyelitis (CRMO) is an autoinflammatory bone disorder that can present with extraosseous manifestations, including skin conditions like psoriasis. Management of CRMO is challenging, especially in cases with extra-articular manifestations, where classical disease-modifying antirheumatic drugs (DMARDs) and TNF inhibitors may be used.
Case Report: We present the case of a young girl with complicated and intermittently therapy-refractory CRMO, who had undergone several previous treatments, and who also had severe psoriasis and arthritis. During treatment with the IL-12/23 inhibitor ustekinumab, the patient developed pyoderma gangrenosum. At the time of presentation, she had significant bone and joint pain, multiple skin ulcerations in addition to her pre-existing psoriasis, elevated inflammatory markers, and MRI findings indicative of active multifocal osteomyelitis. Upon discontinuation of ustekinumab, methotrexate (MTX) was reintroduced. As a bridging therapy, upadacitinib, a Janus kinase (JAK) inhibitor, was used once daily in a dose of 15 mg as a steroid-sparing agent for 4 weeks. Within a few days of initiating upadacitinib, the patient's skin lesions showed dramatic improvement, without any worsening of the underlying osteomyelitis or psoriasis. The patient developed no infections or other side effects during upadacitinib treatment.
During subsequent follow-up, the patient remained stable on MTX monotherapy, with both her CRMO and psoriasis under control. Comprehensive diagnostic workup, including evaluation for underlying genetic disorders, immune deficiencies, and malignancies, yielded no significant findings.
Conclusion: This case demonstrates the successful off-label use of upadacitinib as a bridging therapy in a pediatric patient with CRMO and pyoderma gangrenosum. The patient achieved stabilization of both her osteomyelitis and psoriasis after multiple disease flares, and the combination of methotrexate and upadacitinib allowed for effective disease control without the risk of steroid-depending rebound. While upadacitinib is not approved for use in children, this case highlights the potential of JAK inhibitors as a valuable therapeutic option in complex cases involving autoinflammatory diseases with extraosseous manifestations and complications.

Patient Consent: Yes, I received consent.
Funding: CR was supported by the Faculty of Medicine Tübingen (TÜFF program No. 3050-0-0).
Disclosure of Interest: The authors declare no conflicts of interest.

A14

Diagnosing autoinflammatory diseases: Insights from an interim analysis of the PRO-AID study

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Pediatric Rheumatology 2025, **23(1):**A14

Introduction: Uncontrolled disease activity in autoinflammatory diseases (AID) can cause morbidity and mortality. Familial Mediterranean Fever (FMF), NOD-like receptor protein 3 (NLRP3)-AID, Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) and Mevalonate Kinase Deficiency (MKD) are effectively treatable following accurate diagnosis. Early diagnosis is critical to mitigate disease burden and improve patient outcomes.
Objectives: To explore the diagnostic journey of children and adolescents with FMF, NLRP3-AID, TRAPS and MKD.
Methods: The multicenter, prospective PRO-AID cohort study, embedded in the National Pediatric Rheumatologic Database, enrolled children and adolescents ≤18 years diagnosed with FMF, NLRP3-AID, TRAPS, or MKD. At enrollment, demographic data and diagnostic journey details (e.g., number of clinicians consulted, hospitalizations) were collected from parents. The subjectively perceived disease burden was indicated by parents and adolescents (e.g., disease activity, overall well-being, fatigue, pain, each on a numerical rating scale (NRS) of 0–10). Treating physicians provided information on diagnosis and disease characteristics, including disease activity (NRS 0–10). Time to diagnosis (TtD) was defined as the interval between symptom onset and confirmed diagnosis.
Results: The study included 124 patients (45% female) with a mean disease duration of 7.4±4.1 years. Diagnoses included FMF (n=95; 76%), NLRP3-AID (n=18; 15%), MKD (n=6; 5%), and TRAPS (n=5; 4%). The mean age at symptom onset was 2.8±3.1 years, with a mean TtD of 16.9±16.1 months. TtD was longest for TRAPS (26.5±3.5 months) and NLRP3-AID (20.8±16.7 months), followed by FMF (16.2±16.2 months) and MKD (14.2±18.1 months). Almost half of the patients experienced delays in diagnosis of ≥12 months, which was associated with higher physician-reported (1.5±2.1 vs. 0.7±0.9) and patient-reported (3.2±3.1 vs. 1.7±2.6) disease activity at the time of documentation compared to patients with earlier diagnosis.
Hospitalization rates in the year prior to diagnosis were 33% for FMF, 56% for NLRP3-AID (9/16), 50% for TRAPS (2/4), and 50% for MKD (3/6). Additionally, 39% of patients received antibiotics in the year before diagnosis. On average, 3.1±3.9 clinicians were consulted during the diagnostic process, with most diagnoses made by pediatric rheumatologists (59%; 57/97), although FMF was frequently recognized by pediatricians prior to referral (44%).
Conclusion: Diagnoses of FMF, NLRP3-AID, TRAPS and MKD remain significantly delayed, hindering timely access to effective treatment. Raising awareness among primary care providers and promoting early referral to pediatric rheumatologists are critical for improving diagnostic timelines and optimizing care.

Patient Consent: Yes, I received consent.
Funding: Stiftung "Kindness for Kids".
Disclosure of Interest: ÖS, KT, MN, JK, ML, NB: none. KM received honoraria from Amgen, Biogen, medac, Novartis. TW has given invited talks for Novartis (no personal honoraria). FD received honoraria from Abbvie, Novartis und Pfizer und Adboards von Fresenius, Mylan und Novartis. PO received honoraria from Novartis. MH received study funding from Novartis. Tkr received honoraria from Novartis, Pfizer.

A15

Belimumab in the treatment of juvenile systemic lupus erythematodes- safety and efficacy data from the BiKeR registry

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Pediatric Rheumatology 2025, **23(1):**A15

Introduction: The inhibition of B-cell activation is of great importance in the treatment of systemic lupus erythematosus (SLE). Belimumab inhibits this by blocking the activity of BLYSS and has been approved as the first biologic for the therapy of juvenile SLE (jSLE) from the age of 5 years.
Objectives: To investigate use, efficacy and tolerability of Belimumab therapy in jSLE patients in clinical practice.
Methods: In this ongoing non-interventional study, data from the Biologics in Pediatric Rheumatology (BiKeR)-registry are collected from patients who meet the EULAR/ACR criteria for jSLE and fulfill the indication for Belimumab-therapy. Therapeutic efficacy is assessed using the Systemic Lupus Disease Activity Index-2K (SLEDAI-2K), laboratory parameters (ds-DNA antibodies, complement-C3 and -C4), as well as clinical parameters (physician/patient global assessment of disease activity (0–100)), evaluated at months 0, 6, 12, 18, and 24. Reported adverse events (AEs) are analyzed to assess

safety data. All data are compared with a control group of jSLE patients who had not received Belimumab.

Results: At data cut off (11/21/2024), 19 patients with 25.4 treatment years undergoing Belimumab therapy and 12 control patients with 12.6 observation years have been enrolled. The baseline patients' and clinical characteristics are shown in Table 1. Data on clinical progression are available for 10 patients/12 months and 6 patients/24 months, showing a decrease in SLEDAI-2K, the physician global assessment of disease activity, ds-DNA antibody levels, and an increase in C3-complement. In two patients, initially highly elevated dsDNA antibodies became negative with normalization of C3 and C4 levels and disappearance of clinical signs of disease activity (Figure 1). Regarding AEs, 28 in 9 patients (47.4%) were reported in the Belimumab cohort (rate 1.08;0.75–1.56,CI95%)/patient year), compared to 13 AEs in 6 patients (50.0%) of the control cohort (rate 1.02;0.8–1.6,CI95%/patient year). No therapy discontinuations or serious adverse events have been reported to date under Belimumab therapy. Two patients with three events of the Belimumab cohort have so far shown a disease flare or a new organ manifestation (one lupus nephritis, one hepatitis in the same patient) versus two patients with two events of the control cohort.

Conclusion: Data regarding jSLE patients undergoing Belimumab therapy in childhood with a longer follow-up concerning efficacy and safety is yet insufficient. Our results indicate so far both, good efficacy and safety. As the observation continues, the inclusion of additional patients in the BiKeR-Belimumab registry would be highly appreciated.

Patient Consent: Yes, I received consent from the patients/ their legal guardians.

Funding: There is no pharmaceutical company funding for the Belimumab study arm of the BiKeR-registry.

Disclosure of Interest: Angela Zimmer: Travel grands: Novartis, Lilly; Speakers bureau: Lilly, Glaxo-Smith-Kline; Ariane Klein: Speakers fee: Novartis, Lilly; Normi Brueck: none; Jasmin Kuemmerle-Deschner: none; Frank Dressler: Advisory Boards by Novartis and Mylan, Speakers bureau: Abbvie, Novartis, Pfizer, Advisory Boards Novartis and Mylan; Anton Hospach: Consulting fees: Novartis, SOBI; Speakers bureau: Novartis and SOBI; Jens Klotsche: none; Kirsten Minden: received honoraria from Pfizer, Novartis and medac; Ralf Trauzeddel: none; Prof. Haas: none declared; Gerd Horneff: Advisory Speaker: Pfizer, Novartis, Sobi; Consultant MSD, Lilly; Grants Novartis, MSD, Roche; Speakers bureau: Pfizer, Roche, MSD, Sobi, GSK, Sanofi, AbbVie, Chugai, Bayer, Novartis, Grant/research support from: Pfizer, Roche,MSD, AbbVie, Chugai, Novartis

Table 1 (Abstract A15). Patient and clinical characteristics at baseline

	Belimumab-cohort, $N = 19$	Control, $N = 12$
Female sex, n(%)	**15 (78.9)**	**10 (83.3)**
Age at disease onset, years (median, IQR)	13.2 (9.5–14.8)	11.4 (5.7–13.3)
Disease duration at baseline, years (median, IQR)	1.4 (1.1–3.0)	1.1 (0.1–1.9)
Antinuclear antibody (ANA)-/ dsDNA-antibody-positive (%)	84.2%/84.2%	91.7/66.7
Reduced C3-/C4-complement levels (%)	42.1/31.6	58.3/25.0
Antiphospholipid-antibodies (%)	21.1	50
Lupus-nephritis, n(%)	1 (5.3)	2 (16.7)
Lupus-encephalitis n(%)	0	1 (8.3)
Hematologic manifestations n(%)	6 (31.6)	7 (58.3)
Skin manifestations (excluding butterfly-rash) n(%)	2 (10.6)	0
Physician global assessment disease activity (scale 0–100), (median, IQR)	31 (18–60)	37 (0–54)
Patient global assessment disease activity (scale 0–100), (median, IQR)	31.5 (0–53)	27 (10–44)
Ds-DNA antibodies (IU/ml)	167.5 (12–229)	24 (6–161)
Complement-C3 levels (mg/dl)	97 (76–105)	77 (63–99)
Complement-C4 levels (mg/dl)	13 (5.5–17)	11.5 (3.3–17)
Selena-SLEDAI score (points)	7 (4–8)	7 (2–14)
Steroids (%)	100	75
Hydroxychloroquine (%)	94,7	83,3
Azathioprine/ methotrexate/ mycophenolate mofetil (%)	10.5/15.8/47.4	8.3/0/58.3

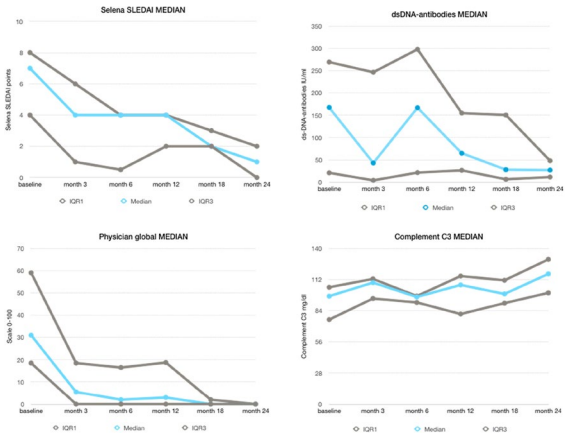

Fig. 1 (Abstract A15). Belimumab cohort, selected efficacy data

A16

Simultaneous occurrence of A20 haploinsufficiency and a possibly GOF-STAT3 variant: challenges in diagnosis and therapy

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Pediatric Rheumatology 2025, **23(1):**A16

Background: Monogenic disorders of immune dysregulation are characterized by impaired immune tolerance, leading to autoimmune, autoinflammatory, and immunodeficiency phenotypes. A20 haploinsufficiency (HA20), caused by heterozygous *TNFAIP3* loss-of-function variants, disrupts NF-κB regulation, resulting in unchecked inflammation with recurrent fevers and organ-specific autoinflammatory features (1). In contrast, heterozygous *STAT3* gain-of-function (STAT3-GOF) variants enhance STAT3 activity, causing widespread immune dysregulation with prominent autoimmunity, lymphoproliferation, short stature, and developmental delay (2). Although these conditions share features such as polyendocrinopathy and enteropathy, their distinct molecular mechanisms result in differing clinical presentations. This distinction is crucial for tailoring management strategies.

Case Report: We present a family with co-occurring *TNFAIP3* and STAT3-GOF genetic variants. The 9-year-old girl exhibits severe early-onset enteropathy, failure to thrive, neurodevelopmental delay, prediabetes,

and lymphadenopathy. Persistent gastrointestinal ulcers and Food Protein Induced Enterocolitis Syndrome (FPIES) significantly impair her quality of life. Her 6-year-old brother developed symptoms at 52 months, including recurrent fevers, type 1 diabetes mellitus, hepatosplenomegaly, pulmonary involvement, mucocutaneous ulcers, arthritis, and erythema nodosum. Both children experience Chronic musculoskeletal pain, arthralgia, arthritis, erythema nodosum and soft tissue swelling unresponsive to current therapies. The father's symptoms included failure to thrive, fever, arthralgia, and oral ulcers during childhood, resolving in adolescence except for alopecia. The immunological evaluation revealed no definitive evidence of cellular or humoral immunodeficiency, with both children displaying normal leukocyte and lymphocyte counts. In the girl, B- and T-cell differentiation appeared unremarkable. The boy demonstrated normal B-cell differentiation but showed a mildly increased frequency of TCRγδ+ cells within the T-cell compartment. Current treatment regimens - Tocilizumab, Pregabalin, NSAIDs, Infliximab - partially alleviate symptoms but fail to fully sufficiently disease activity.
Conclusion: The coexistence of *TNFAIP3* and STAT3-GOF variants represents a novel and complex dual-pathology immune dysregulation with significant rheumatologic involvement. Persistent arthritis, chronic musculoskeletal pain, gastrointestinal disease and autoimmune polyendocrinopathy dominate the clinical phenotype and the need for both precision medicine and multidisciplinary care. Since conventional immunomodulatory therapies have proven insufficient, hematopoietic stem cell transplantation (HSCT) is being considered. The simultaneous presentation of two independent monogenic immune dysregulation syndromes provides valuable insight into the interplay of their molecular mechanisms. Effective management requires precision medicine to address the complexities of this dual-pathology phenotype.

Patient Consent: Yes, I received consent.
Funding: SLK was competitively selected for "CORE100Pilot", which is an advanced clinician-scientist program co-funded by the Else Kröner Fresenius Foundation and the Ministry for Science and Culture of the State of Lower Saxony.
Disclosure of Interest: The authors declare no conflicts of interest relevant to this work.

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A17

Side effects of 1st Bisphosphonate Administration in children

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Pediatric Rheumatology 2025, **23(1):**A17

Introduction: Bisphosphonates are standard of care in the treatment of osteogenesis imperfecta. They are also used in rheumatic diseases such as NSAID- refractory CRMO with good results.[1–7]
Objectives: Survey of side effects after 1st iv bisphosphonate (neridronate) administration.
Methods: Questionnaire for all patients/caregivers with osteogenesis imperfecta at first administration of neridronate (over a period of 3 years). A total of 65 children (43 male, 22 female; age 12d to 15,9 years, median 2,9 years) were included.
Results: Fever occurred in almost half of the cases (n=27, 60% within 24h). Age proved to be the most significant variable with regard to developing a fever, as the incidence of fever was significantly lower with increasing age. In older patients, intensity and duration of fever were lower/less prolonged and the onset tended to be later.
An initial increase in pain was found to be another side effect. However, pain was rated significantly lower in the weeks following bisphosphonate treatment than before treatment.
Conclusion: A decrease of severity of fever as reaction to first iv bisphosphonate treatment was seen with increasing age. As this was a patient group with primary bone diseases, it might be useful to evaluate possible side effects in children with rheumatic diseases/autoinflammatory dispositions in regard to the severity of acute phase reaction after initial treatment.
An increase in pain after treatment was observed in most patients. However, after the initial increase, the pain decreased to significantly lower levels than before treatment.

Patient Consent: Not applicable (there are no patient data).
Funding: None.
Disclosure of Interest: None.

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A18

Case report: Pediatric IgG4 – related disease

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Pediatric Rheumatology 2025, **23(1):**A18

Background: Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated systemic condition characterized by elevation of the IgG4 as well as infiltration of various organs by IgG4-positive plasma cells. In affected individuals, the disease was initially recognized in the pancreas but has meanwhile been described in almost every organ: the biliary tree, salivary glands, periorbital tissues, kidney, lungs, lymph nodes, hypophysis, meninges, aorta, thyroid gland, pericardium and skin. The clinical picture is highly heterogeneous and the symptoms are related to involvement of the specific organ. The disease typically occurs in elderly males, but pediatric cases have also been described. The pediatric phenotype might be different from the adult one, in terms of organ involvement.

Case Report: We report the case of a 14-year-old patient with IgG4-RD involving of salivatory glands, lymph nodes as well as renal and ocular manifestations. The patient first presented with sialadenitis and cervical lymphadenopathy accompanied by eye dryness und eye swelling. Serum IgG4 was elevated, without evidence of ANA, ds-DNA, SSA and SSB antibodies or hypocomplementemia. The histopathological feature of the submandibular gland showed fibrosis and lymphoplasmacytic infiltrates with an elevated IgG4: IgG ratio. The cranial MRI showed an accentuated hypophysis, without any hormonal abnormalities. The abdominal MRT displayed bilateral parenchymal hypointensities with diffusion restriction, suggestive of a renal involvement, without any sign of proteinuria. The rest of the extensive work-up revealed no signs of further organ involvement. The patient received low dose corticosteroids. Due to the xerosis a local therapy with intraocular azathioprine was initiated.
Conclusion: The pediatric IgG4-RD is a rare entity and differs from adult IgG4-RD. Only about 20% of published cases met IgG4-RD classification criteria. Exclusion of mimickers is crucial for the diagnosis. Lack of recognition is associated with a delayed treatment and poorer outcomes. As in this case, corticosteroids remain the first-line therapy but severe forms respond to rituximab, with a remarkable reduction of mass lesions and a variable regression of fibrosis even in a steroid-free regimen.

Patient Consent: Yes, I received consent.
Funding: Infrastructural funding was provided by the University Hospital Tübingen. No other funding.
Disclosure of interest: No conflict of interest.

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A19

Case report: treatment of dermatomyositis with JAK inhibitor Baricitinib

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Pediatric Rheumatology 2025, **23(1):**A19

Background: Juvenile dermatomyositis (jDM) is a rare, idiopathic autoimmune disorder characterized by inflammation of both muscle and skin, often leading to significant morbidity and, in severe cases, mortality. Transcriptomic analyses in adult and juvenile forms of dermatomyositis (DM and jDM) have consistently demonstrated the upregulation of interferon (IFN)-regulated genes, suggesting a central role for the IFN pathway in the pathogenesis of the disease. Given the essential role of the JAK-STAT pathway in the pathophysiology of jDM, JAK inhibitors have emerged as a promising therapeutic option. Few case reports demonstrate the efficacy of JAK inhibitors in refractory jDM. Only a few patients treated with JAK inhibitors received Baricitinib.
Case report: We describe the successful use of JAK kinase inhibition in a 4-year-old boy presenting with positive Mi2-alpha and MDA-5 antibodies, manifesting with muscle weakness, arthritis and skin involvement.
The patient presented with typical crusted lesions on the hands, feet, nose, and ears, as well as inversed Gottron´s lesions, polyarthritis and muscle weakness. Laboratory investigations demonstrated the presence of Mi2-alpha and MDA-5 antibodies. MRI revealed widespread myositis, predominantly in the gluteal region, alongside synovitis and tenosynovitis in the elbows, hands, knees, and ankles. There were also inflammatory changes in the skin and subcutaneous tissue, hepatosplenomegaly, and lymphadenopathy, but no pulmonary involvement or vasculitis.
The patient showed a highly elevated interferon signature (892.89, Ref. range: <12.49), which led us to explore treatment options targeting the interferon pathway. In addition to standard therapies with IVIG, single course of steroid pulse and hydroxychloroquine, we introduced the JAK kinase inhibitor, Baricitinib (2mg/d).
Under this combined treatment, the patient experienced fast improved, by resolution of the skin lesions, polyarthritis and normalization of the muscle strength without any significant side-effects.
Conclusion: This case highlights the potential role of JAK kinase inhibition in managing patients with juvenile dermatomyositis and an elevated interferon signature, particularly in patients with MDA-5 antibodies, who display a high risk for pulmonary disease. In our case, the use of JAK kinase inhibitor in the therapeutic regimen contributed to rapid resolution of symptoms and persistent disease control.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: The authors declare no conflicts of interest relevant to this work.

A20

Salivary gland ultrasound in primary and secondary juvenile Sjögren`s Syndrome – longitudinal view over a 24 months period

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Pediatric Rheumatology 2025, **23(1):**A20

Introduction: Salivary Gland Ultrasound (SGUS) has become an important tool to visualize morphological changes in pediatric patients with primary or secondary Sjögren`s Syndrome (SS).It can show the degree of inflammatory infiltrates in four major salivary glands (1,2,5). This study analyses SGUS observations longitudinal according to the OMERACT and Doppler semi-quantitative scoring systems (3, 4) over 24 months performed in a cohort of primary and secondary juvenile SS patients (jSS).
Methods: Longitudinal examinations in n=20 patients were performed in a single center SS cohort over 24 months by two experienced observers. Time-line: T0= first visit, t1= within the following 6 months, t2= within 12 months, t3= within 24 months. Inclusion criteria: (a) primary or secondary jSS and (b) any present glandular symptoms. A Canon Aplio® 800 US-system with a linear high-frequency transducer was used. The exams were scored after OMERACT semi-quantitative -scoring system, including Colour Doppler. Chart data, medication and ESSDAI were collected at every examination.
Results: 17 female and 3 male patients were included, mean disease duration of 3.7 years at t 0 and a mean age at disease onset 10.5 years. Diagnosis: pSS in 6 and sSS in 14 patients, ESSDAI values from 0 to 18. Highest score of SGUS B-mode (within a patients course) found in 35% at t3, and only in 25% at t0. Doppler highest scoring in 35% at t3 and only in 20% at t0. Sum scoring in B mode showed a decrease over the 24 months period in n=5 , while n=15 sum scores persisted or increased. In n=6 one glandula developed morphologic fibrosis over time. Parotid gland vascularization was

graded 0 preprandial in 60,5% (63 of 104 scans) parotidal scans and in only 28% (27 of 97 scans) submandibular scans . No correlation between medication / activity and scoring results or Doppler findings.
Conclusion: Within the whole period no improvement of typical morphologic lesions were detected (Fig 1). There was no correlation between scores and disease-duration or medication. According to the results of the OMERACT reliability exercise (5) we found differences in SGUS images pre-, and postprandial. In general the mean blood flow scoring was higher in submandibular glands. A decrease in Doppler scoring might represent a late fibrotic state. We confirm SGUS as a diagnostic tool in suspected SS, but also as a monitoring tool in the course of the disease (2).

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: None.

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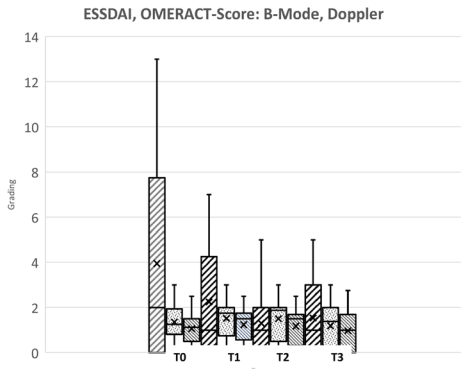

Fig. 1 (Abstract A20). ESSDAI, Omeract and Doppler scores (mean) over time line t0-t3

A21

Unraveling Juvenile Recurrent Parotitis (JRP): a decade of clinical and therapeutic observations

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Pediatric Rheumatology 2025, **23(1):**A21

Introduction: Juvenile Recurrent Parotitis (JRP) is a chronic, non-obstructive, non-suppurative inflammation of the parotid gland in children with an unclear etiology. It manifests as recurrent painful swelling of the parotid gland, often accompanied by fever. Characteristic findings include turbid discharge from the Stensen duct and a "Swiss cheese" pattern on ultrasound. Despite being the second most common pediatric salivary gland disorder after mumps, JRP is underdiagnosed, with no standardized diagnostic or therapeutic algorithms. This leads to prolonged patient suffering and inconsistent management strategies.
Objectives: This study evaluates clinical-demographic parameters, diagnostic modalities, and treatment pathways in children with JRP, identifying gaps and areas for further research.
Methods: A retrospective, single-center study reviewed data from 224 pediatric sialadenitis cases between 2015 and 2024. Of these, 50 met JRP diagnostic criteria. Statistical analyses used descriptive methods and Welch's t-test.
Results: Among 50 children with JRP, 48% initially sought care from pediatricians, 46% from otorhinolaryngologists, and 6% from pediatric surgeons. Gender distribution was balanced (56% male). Symptoms began at a mean age of 4.6 years, with an average diagnostic delay of 1.9 years. Patients experienced a mean of 6.7 episodes, even with no gender differences.
Key symptoms included parotid swelling (96%; 60% unilateral, 40% bilateral), pain (80%), and fever (54%). On examination, 70% had parotid tenderness, 73% cervical lymphadenopathy, and 28% turbid or purulent discharge from the Stensen duct. Further diagnostics included imaging, primarily ultrasound (47 cases) and MRI (3 cases), and general blood tests (24 cases), but advanced immunological diagnostics were rare (9 cases).
Therapeutic strategies focused on supportive care, including analgesics, antipyretics, sialogogues, and gland massages for all patients. Antibiotics were prescribed in 64% of cases but did not significantly reduce recurrence rates (p=0.89). Only one child underwent sialendoscopy with steroid application.
Conclusion: JRP is under-recognized, with diagnostic delays and inconsistent management due to a lack of standardized protocols. Antibiotics showed no measurable benefit, and advanced diagnostics were underutilized. Prospective studies are needed to establish evidence-based diagnostic and therapeutic guidelines, with a focus on immunological factors.

Patient Consent: Yes, I received consent.
Funding: n/a.
Disclosure of Interest: No conflicts.

A22

An increase in invasive infections of the musculoskeletal system caused by streptococci or staphylococci in a tertiary German hospital?

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Pediatric Rheumatology 2025, **23(1):**A22

Background: From January 2023 until December 2024 we perceived an increasing number of hospitalizations due to invasive musculoskeletal infections caused by staphylococci or streptococci species in our tertiary hospital in Germany, counting 47 inpatient beds in the children's department. Recent literature on invasive Group A streptococcal (iGAS) disease highlights an ongoing rise in severe cases, particularly after COVID-19. Studies have documented an increase in hospitalizations and admissions in intensive care units (ICU) related to iGAS in both children and adults across Europe and the United States

of America. The increased incidence of scarlet fever and iGAS infections is attributed partly to pandemic-related immunity shifts and possibly to emergent bacterial strains [1]. In 2024 a German group also showed that children were at higher risk for iGAS infections post-pandemically than before. The surge of post-pandemic iGAS infections was not accompanied by increased iGAS-associated morbidity and mortality [2] yet alone an increase in ICU admissions due to iGAS infections was registered post-pandemically [3].
Objective: To compare and analyse numbers and distribution of invasive musculoskeletal infections in the pre- and post-pandemic years.
Methods: Comparison and analysis of patients being hospitalized due to invasive musculoskeletal infections, i.e. bacterial osteomyelitis or septic arthritis or both in the pre-pandemic years (2018 to 2019) and the post-pandemic years (2023 to 2024).
Results: In the years 2018 and 2019 a total of 23 patients were hospitalized due to invasive musculoskeletal infections (2018: 10, 2019: 13). In contrast, in the post-pandemic years there was a total of 13 patients (2023: 8, 2024: 5), who hospitalized and treated in our hospital due to one or both diagnosis (bacterial osteomyelitis, septic arthritis).
Conclusion: Although there was a perceived increase in invasive musculoskeletal infections in the last two years, compared to the pre-pandemic years, this assumption could not be confirmed. Interestingly these findings do not correlate with the published literature.

Patient Consent: Yes, I received consent.
Funding: None.
Conflicts of Interest: None.

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A23

Subjective evaluation of an exercise program for patients with juvenile idiopathic arthritis

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Pediatric Rheumatology 2025, **23(1):**A23

Introduction: Studies on physical activity in patients with juvenile idiopathic arthritis (JIA) show reduced activity levels, particularly in moderate to vigorous intensities compared to healthy peers [1, 2]. Well-planned and individualized exercise programs conducted 2-3 times/week, for 30-50 minutes over a period of 12-24 weeks could help to reduce pain and enhance functional capability and quality of life in patients with JIA [3, 4]. Due to the heterogeneity of JIA caused by a varying number of affected joints and disease flares, it is challenging to provide general exercise recommendations for these patients. Therefore, the "AktiMiRh (Aktiv mit Rheuma)– program" was developed.
Objectives: AktiMiRh contains exercises for home use, tailored to the patient's condition and based on the "Rheuma und Sport Kompass (RSK)" [5], which is an individualized recommendation for sports participation.
The primary objective of this randomized controlled intervention study (https://drks.de/search/en/trial/DRKS00027043) was to improve physical activity in young JIA patients (aged 6–18 years) through a web-App based, customizable exercise program. A secondary objective adresses the safety of using the program assessed by a structured evaluation.
In addition, acceptance of this exercise program and the potential long term use have been evaluated.
Methods: For the evaluation, a questionnaire consisting of 8 questions was used. A 5-point Likert scale ranging from 1 = strongly disagree to 5 = strongly agree as well as free-text responses were applied. The questionnaire was analyzed descriptively using percentage values.
Results: 19 patients out of the initial 30 participants in the intervention group took part at the survey. The following percentage values include all ratings $\geq$4:
94% had no problems performing the exercises, 80% understood the exercises well. 58% of the patients stated that the exercises were enjoyable, as well as 58% could imagine continuing the program. 47% felt motivated to be more active and 63% liked the design. All patients reported to have no joint problems after the exercises (0% scored <3).
Conclusion: The results show that no participant reported significant joint issues, suggesting that the program is safe to implement. Overall, the program appears to have been well received. However, the opportunity for patients to independently select exercises to create their own training program proved to be more of a challenge than a perceived benefit.
For the further development of the digital exercise program, it will be important to pre-structure training programs and address individual deficits in more detail.

Patient Consent: Yes, I received consent.
Funding: The study was funded by the Dr. Melitta-Berkemann Foundation.
Disclosure of Interest: None.

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A24

Recurrent fever, headache, abdominal pain and aphthous lesions in a 7-year-old boy

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Pediatric Rheumatology 2025, **23(1):**A24

Background: Autoinflammatory syndromes in children often represent a diagnostic challenge. Genetic testing as whole exome sequencing (WES) can help to make a diagnosis. For new or variants of unknown significance, functional testing may confirm the diagnosis and result in patient -tailored treatment.
Case report: We report the case of a now 7-year-old boy of Caucasian, non-consanguineous, healthy parents who presented with recurrent, self-limiting fever from the age of 18 months. Fever occurred every 2 −4 weeks, lasted 2 - 4 days, and was accompanied by oral aphthous lesions, episodic headache, and abdominal pain (without diarrhea or vomiting) as well as flu-like limb pain. The febrile episodes were not accompanied by lymphadenopathy, skin, muscle or joint involvement. Laboratory tests revealed elevated inflammatory markers during fever, without evidence of infection or autoimmune disease. At the age of 6 years, the boy initially presented to us for immunologic-rheumatologic evaluation, and a Behçet's-like disease was suspected. HLA-B51 was negative. WES was performed and revealed a truncating, likely pathogenic, de novo heterozygous variant in the RELA gene c.1114C>T, p.(Gln372*). The variant was not found in either parent. Functional tests showed increased TNF-alpha secretion during fever, type I IFN signature was only weakly increased.
RELA encodes a subunit of the NF-κB transcription factor complex, which is critical for immune regulation and inflammatory responses. RELA haploinsufficiency is a recently identified monogenic cause of early-onset autoinflammatory disease resembling Behçet's disease. The patient's clinical presentation, combined with the genetic findings and supported by functional testing, confirmed the diagnosis of RELA-associated disease (RELAD). A single dose of prednisone (1.5 mg/kg) at the beginning of each febrile episode led to prompt resolution of fever whithin hours, but over time the intervals between episodes shortened to 1–2 weeks. As functional tests revealed increased TNF-alpha secretion, compassionate treatment with a tumor necrosis factor (TNF) inhibitor (etanercept) was started.
Summary: This case demonstrates the importance of considering monogenic autoinflammatory syndromes in children with unexplained non-infectious recurrent fever accompanied by non-specific systemic symptoms. RELA-associated inflammatory disease should be considered in patients with early-onset Behçet's -like disease or other autoinflammatory syndromes. Early genetic diagnosis facilitates access to targeted treatment and has the potential to prevent long-term complications. Further research is needed to delineate the full phenotypic spectrum and optimize therapeutic strategies for RELA-associated diseases.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure **of Interest:** None.

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A25

Pamidronate in CRMO: advantages of early treatment?

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Pediatric Rheumatology 2025, **23(1):**A25

Introduction: Chronic recurrent multifocal osteomyelitis (CRMO) primarily affects long bones and spine. Symptoms include pain, swelling, restricted movement, and vertebral fractures. Pamidronate is an established second-line treatment, particularly in spinal involvement while less commonly used in peripheral CRMO [1,2]. Due to a lack of prospective randomized trials, timing and management of treatment in CRMO remain unclear.
Objectives: This study adresses the effects of pamidronate treatment in early vs. later stages of disease.
Methods: Charges of 83 patients treated with pamidronate at the DZKJR between 2016 and 2024 were analysed retrospectively. Inclusion criteria included CRMO diagnosis according to Bristol criteria [3], no prior treatment beyond NSAID, no relevant comorbidities and two MRI studies. Patients were divided into two groups: Group 1 (early treatment), with treatment initiated within one year after onset of symptoms and Group 2 (late treatment), where treatment was initiated after more than one year. Data collected were age, number of lesions and spinal involvement on MRI, number of pamidronate treatments, PedCNO scores, physician and patient global assessment, pain on VAS, prior to pamidronate and on first MRI after treatment. Demographic data were analyzed using descriptive statistics, repeated measures ANOVA and Student's T test.
Results: 22 patients were included with mean age of 10.9 years (range 5–15), 19 (86.4%) female. In Group 1, 11/12 patients had spinal involvement, compared to 4/10 in Group 2. Mean number of pamidronate cycles was 2.6 (G1) vs. 2.2 (G2). Prior to treatment, mean number of radiological lesions was 9 (G1; IQR 5–10) and 7 (G2; IQR 4–8), after treatment the number of lesions decreased to 8 (G1) and 4,8 (G2) ($F(1,40) = 0.08422$, $p = 0.7732$). G1 showed significant improvements in: physician global assessment (VAS, $p = 0.047$), patient global assessment (VAS, $p = 0.022$), and pain (VAS, $p = 0.002$). In G2, pain ($p < 0.001$) and patient global ($p = 0.001$) improved significantly while physician global did not ($p = 0.138$) (Fig. 1, Fig. 2). PedCNO scores were calculated in 21/22 patients, with G1 reaching a $PedCNO_{50}$ and $PedCNO_{70}$of 50% and 41%, and G2 40% and 30% respectively [4].
Conclusion: Pamidronate treatment led to significant improvements in both groups [3,5]. Pamidronate treatment early in the disease course can be considered, even in patients without spinal involvement. Further prospective studies are needed to refine treatment protocols and evaluate long-term efficacy.

Patient Consent: Not applicable (there are no patient data).
Funding: None.
Disclosure of Interest: None.

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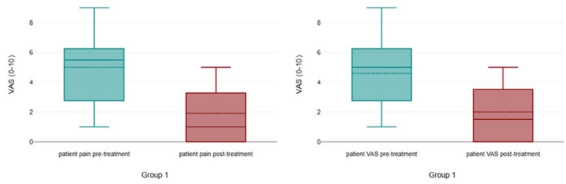

Fig. 1 (Abstract A25). Group 1 pain and patient global assessment (VAS) prior to pamidronate and after treatment

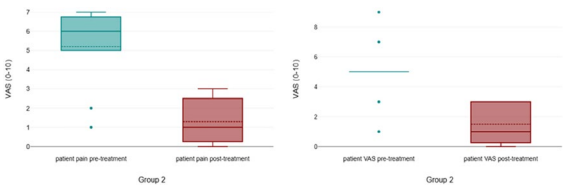

Fig. 2 (Abstract A25). Group 2 pain and patient global assessment (VAS) prior to pamidronate and after treatment

A26

Pyrin and PSTPIP1 mutations hamper cell differentiation of phagocytes, altering functional capabilities

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Pediatric Rheumatology 2025, **23(1):**A26

Introduction: Pyrin, encoded by the MEFV gene, functions as a sensor protein of the Pyrin inflammasome, responsible for the maturation of IL-1ß and IL-18, and Gasdermin D pore formation during inflammatory stimulation of innate immune cells. Mutations cause the Familial Mediterranean Fever (FMF) syndrome, characterised by disease flares with fever, serositis and arthritis, due to a pre-activated state of the Pyrin inflammasome. The Pyrin inflammasome is partly regulated by proline-serine-threonine phosphatase-interacting protein 1 (PSTPIP1), a cytoskeletal- associated protein that is mutated in the pyogenic arthritis, pyoderma gangrenosum and acne (PAPA) syndrome. Although the clinical manifestations are different, patients with either PAPA or FMF show increased levels of IL-1ß due to Pyrin-inflammasome mediated caspase-1 activation, indicating a similar but not identical disease mechanism. As Pyrin and PSTPIP1 are both mainly expressed in innate effector cells, we aim to elucidate their role in cell differentiation and function, gaining insight in the poorly understood disease mechanisms of FMF and PAPA syndrome.
Objectives: This study investigates the impact of Pyrin and PSTPIP1 on cell differentiation and functional differences in key phagocyte functions.
Methods: Murine in vitro models with knock-in/-out ER-HoxB8 cell lines were used to study the effect of the genomic alteration of related proteins. GeCKO (genome-scale CRISPR-Cas9 knockout) lentiviral pooled library screening was used to identify key drivers of phagocytic cell differentiation. Morphological aspects were assessed by spinning disc confocal microscopy. The inflammatory response was studied using ELISA. Immunophenotyping was studied using FACS analysis. Adhesion was studied using crystal violet staining. Spontaneous and chemotaxis migration were studied by fluorescence microscopy and processed via an in-house algorithm. Transcriptomic data were obtained by using next generation mRNA sequencing and validated by conventional quantitative polymerase chain reaction and immunoblotting.
Results: Genome-wide DNA sequencing indicated PSTPIP1 as a driver of phagocyte differentiation. Further characterization of PSTPIP1 KO cells revealed hampered differentiation, but no distinct different leukocyte phenotype. We obtained the same result for Pyrin KO and FMF cells. The hampered differentiation is reflected in cytokine secretion, as FMF phagocytes show increased secretion of inflammasome dependent and independent cytokines, which is not the case in PSTPIP1 KO cells. This is mirrored in Pyrin KO cells, which lack the ability to secrete not only inflammasome-dependent cytokines, but also TNF-α. Pyrin KO cells are smaller and rounder, showing a decrease in area, with an increase in roundness, while FMF cells showed the same area and roundness of the plasma membrane as WT, but had a larger perimeter. No measurable difference between WT and PSTPIP1 KO cells regarding the shape-parameters was observed. Wildtype phagocytes showed a significant increase in adhesion during five days of differentiation, which was even more pronounced in the FMF cells. However, neither Pyrin KO nor PSTPIP1 KO macrophages showed a significant increase in adhesion. LPS and PMA, increased the adhesion of wildtype and FMF macrophages whereas they had no effect on the adhesion of Pyrin KO or PSTPIP1 KO cells. A higher spontaneous migration speed of Pyrin KO to WT cells was observed. In contrast, FMF and PSTPIP1 KO cells did not differ from WT speed. A straighter motion of Pyrin KO and PSTPIP1 KO cells, compared to WT and FMF cells, was observed. The first dimension of PCA of the transcriptome analysis shows a distinct clustering of Pyrin and PSTPIP1 KO cells versus WT macrophages and further analysis of differentially expressed genes revealed Sept8 and GNA15 expression elevation in FMF macrophages and showed reduction in Pyrin KO and PSTPIP1 KO cells.
Conclusion: Pyrin and PSTPIP1 are crucial factors in phagocyte differentiation, with mutated or knockout cells showing clear alterations in their differentiation profile. This leads to impaired functional abilities in adhesion, migration and morphology and is reflected in the cell's transcriptome, where we identified Sept8 and GNA15 as differentially expressed at the protein level. Impaired differentiation may represent a missing link in the pathophysiology of FMF and PAID.

Patient Consent: Not applicable (there are no patient data).
Funding: Walter-Benjamin-Programm der DFG.
Disclosure of Interest: None.

A27

Outcome of oligoarticular patients in the German PRO-Kind cohort

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Pediatric Rheumatology 2025, **23(1):**A27

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic pediatric rheumatologic disease (incidence 34–60 / prevalence 133–168/ 100.000) in Germany. Many children have oligoarthritis (involving 4 or less joints). Oligoarticular JIA may be characterized by refractory inflammation leading to joint damage, impaired quality of life, and poor functional outcomes. Improvement and harmonisation of diagnosis, monitoring, treatment decision and outcome is the aim of the PROKIND protocols.

Objectives: Improvement and harmonisation of diagnosis, monitoring, treatment decision and prognosis is the aim of the PROKIND protocols, which are based on the treat to target concept.

Methods: Outcomes from a prospective observational study of patients with newly diagnosed oligoarticular JIA during the first year of treatment were analysed. Disease activity was assessed with the cJADAS-10. The treatment target was to achieve inactive disease (cJADAS $\leq$1,1) by month 6 after treatment initiation [1]. Treat to target was defined as DMARD escalation or change if the treatment target was not reached. Outcomes at month 12 included inactive disease and the patient-reported outcomes overall-wellbeing, pain, functional ability (CHAQ) and health-related quality of life (HRQoL, PedsQL 4.0).

Results: 272 oJIA patients from 23 paediatric rheumatology institutions in Germany and Austria were recruited, month 6 and 12 data were available for 110 of these patients. Most patients received in addition to NSAIDs intraarticular corticosteroid therapy as initial therapy, and 49% had reached the treatment goal of inactive disease at 6 months, while 51% were not. 14 % received DMARD escalation / change according to T2T approach, while 37% did not. At 12 months 52% with T2T approach had inactive disease while only 32% of the group that did not follow the T2T approach (p=0.032). Those treated according to T2T tended to have a better overall well-being (1.6$\pm$2.0 vs 2.2$\pm$2.0), less pain (1.2$\pm$2.2 vs 2.1$\pm$2.6) and a higher physical HRQoL (87$\pm$18 vs 82$\pm$19) at the 12-month follow-up compared to those not treated with T2T, but there were no significant differences. However, the patients' functional ability (0.2$\pm$0.5 vs. 0.2$\pm$0.3) and psychosocial HRQoL (86$\pm$15 vs. 86$\pm$14) were the same in both groups.

Conclusion: A treat-to-target approach achieves improvement in disease activity of oligoarticular juvenile idiopathic arthritis patients. However, after 12 months, less than half of oligoarthritis patients have inactive disease, which suggest that more aggressive treatment approaches are necessary.

Patient Consent: Yes, I received consent.
Funding: GBA innovation fond 01VSF18031.
Disclosure of Interest: None.

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A28

Autoantibody induction following SARS-CoV-2 infection in children and adolescents

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Pediatric Rheumatology 2025, **23(1):**A28

Introduction: Viral infections, including Coxsackie type 1, Influenza, and Epstein–Barr virus, are known to trigger autoimmune conditions. Similarly, SARS-CoV-2 has been linked to autoantibody production, which could also be associated with the development of Post COVID syndrome [1-3]. Proposed mechanisms include viral persistence, post-infectious tissue damage, autonomic dysfunction, and chronic inflammation [4, 5]. While most studies focus on adults, we aim to investigate autoantibody generation in the COVID KiD cohort, a pediatric population of over 1,000 children with well-defined antibody and infection status [6].

Objective: To investigate the presence of autoantibodies in pediatric patients across various SARS-CoV-2 exposure groups, including vaccinated, previously infected, and uninfected individuals.

Methods: Autoantibodies targeting antigens linked to autoimmune diseases were quantified in 500 children and adolescents from the COVID KiD cohort in Northeastern Germany [7], screened from December 2020 to March 2023. Serum samples were pooled and treated with DNase I, diluted 1:100, and hybridized onto Coronavirus-associated Autoimmune Antigen Arrays (120 antigens, OmicsArray™ PA012). Detection utilized Cy3-conjugated anti-human IgG, and imaging was performed with a GenePix 4000B scanner. Data analysis included generating heatmaps from net signal intensity (NSI) values and extracting specific patterns using Cluster software. For further analysis, an in-house antigen-bead array is currently under development to assess the complete cohort.
Results: Our preliminary screening of pooled patient samples demonstrates the presence of autoantibodies in individuals infected with SARS-CoV-2, specifically in those without a documented history of chronic diseases. Notably, autoantibodies such as GAD-65, dsDNA, CENP-A, La/SS-B, RNP/Sm, Ro52, and TPO (see Figure 1: Heatmap of IgG autoantibodies, and Figure 2: Autoantibody production against GAD-65 across SARS-CoV-2 exposure groups) — markers associated with autoimmune diseases — were observed at higher frequencies compared to pre-pandemic and non-infected controls.
Conclusion: This study reveals an increased frequency and diversity of autoantibodies in pediatric patients following SARS-CoV-2 exposure, even in the absence of chronic diseases. These findings underscore the virus's unique potential to induce autoantibodies beyond conventional infectious disease patterns.
To investigate further, we are using an in-house antigen array to analyze all patients from the COVID KiD cohort individually, including those with pediatric Post COVID syndrome.

Patient Consent: Yes, I received consent.
Funding: Start-up funding 2024: Research Network for Molecular Medicine, University Medicine Greifswald Gerhard Domagk Early Career Development Program, Clinician Scientist Program, University Medicine Greifswald.
Disclosure of Interest: No financial interests.

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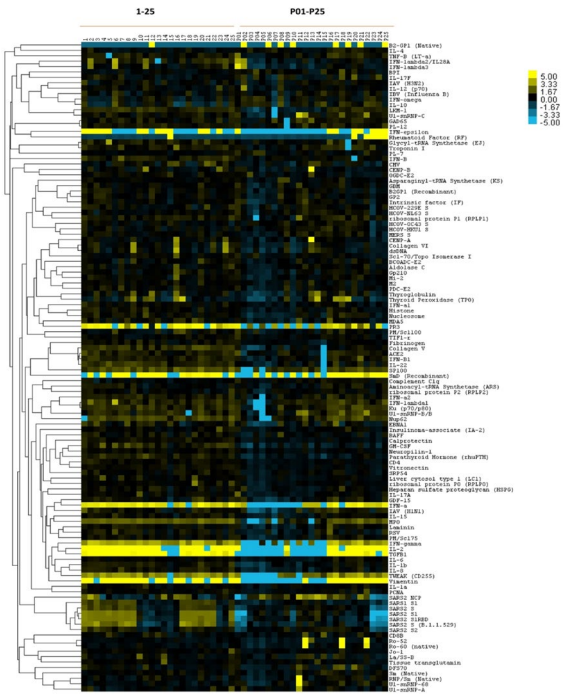

Fig. 1 (Abstract A28). Heatmap of IgG autoantibodies: Columns represent pooled samples, rows correspond to antigens, with yellow indicating the highest interaction levels and blue the lowest

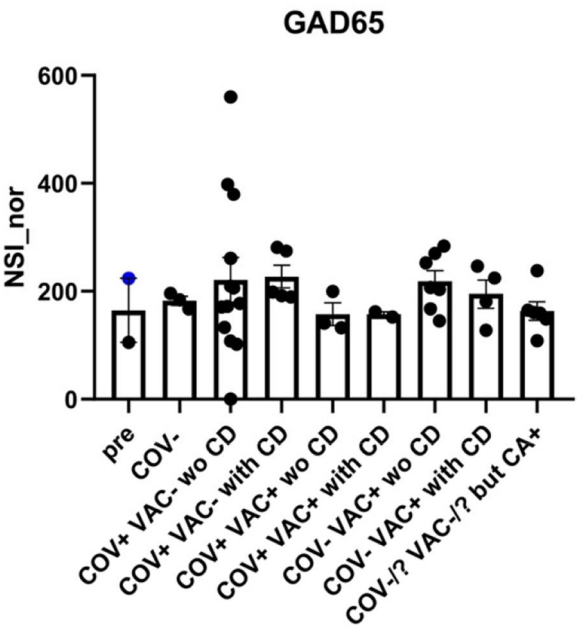

Fig. 2 (Abstract A28). Autoantibody production against GAD-65 across SARS-CoV-2 exposre groups: comparison of uninfected and vaccinated individuals with prepandemic controls. Blue dot represents ANA-positive prepandemic controls. The groups are defined as follows: Pre-pre-pandemic individuals; COV- uninfected individuals; COV+ VAC± (infected, vaccinated/ unvaccinated)- individuals infected with SARS-CoV-2, vaccinated or unvaccinated, with or without chronic diseases (CD); COV-VAC+ (uninfected, vaccinated)- uninfected but vaccinated individuals, with or without chronic diseases; COV? VAC? CA+- individuals with unknown infection and vaccination status but positive corona array results

A29

Safe sports participation through individualized sports promotion for patients with Juvenile idiopathic arthritis

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Introduction: Even with standard care, Juvenile idiopathic arthritis (JIA) can lead to irreversible limitations, joint damage, decreased physical inactivity and poor patient-reported outcomes (PRO) [1].
Objectives: The objectives were to investigate whether individualized sports promotion in the early JIA disease state based on clinical status, PROs and functional analyses, including three-dimensional movement analyses (3DMA) and a motor function test (Deutscher Motorik-Test, DMT [2]) could encourage safe physical activity and improvements in motor skills. Partial results will be presented.
Methods: Patients' inclusion took place according to defined criteria at the time of moderate or high JIA disease activity (t0) and of minimal disease activity (t1). The assessment of clinical status, PROs, 3DMA and DMT were scheduled at three time points (t0, t1, t2). An exploratory approach was chosen to identify functional deficits. To investigate the effects of individualized sports promotion (intervention) in comparison to standard care (control), a mixed-methods approach with randomized controlled trial was used (http://drks.de/search/en/trial/DRKS00017272). The DMT strength (primary outcome) and total score, global walking function, concerning kinematics (Gait Deviation Index, GDI [3]), and health related quality of life (PedsQL [4]) were analyzed before (t1) and 3–9 months after (t2) intervention.
Results: 125 newly diagnosed JIA-patients (female 75 / male 50; ∅ age=11yrs) were included. During the observation period (t0-t2), the total group had significant better walking function (GDI) at t1 compared to t0 ($p<0.001$). At t2 significant improvements were mainly found in DMT (except the task forward bend) compared to t1. Despite an inactive disease level, more than 50% of patients showed functional deficits in walking and in endurance at t1 and t2.
Intervention and control group had no significant differences in motor skills (DMT strength: $p=0.683$ and total score: $p=0.994$) and walking function (GDI: $p=0.485$) at t2. Patients in the intervention group (14%) showed a lower risk for disease worsening than the control group (24%; $p=0.088$), however this difference was not statistically significant. In PROs, the intervention group reported a significant better well-being compared to patients with standard care ($p=0.037$). No statistically significant differences were found in health-related quality of life (PedsQL) ($p=0.563$).
Conclusion: With minimal disease activity, safe physical activity is possible with individualized sports promotion. Although there is no statistical evidence, the recognition of clinically invisible functional deficits by objective 3DMA seems relevant for preventive sports promotion. Based on PRO's, a guide with indication criteria for different type of sports promotion could be developed.

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Dsclosure of Interest: No.

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A30

Establishment of normative data on entheses in children and adolescents using musculoskeletal ultrasonography

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Introduction: Musculoskeletal ultrasonography is used increasingly in pediatric rheumatology to assessdisease activity. Features of arthritis are well defined and age-related normative data have been published but data on the entheses are very limited and no consensus exists on how to define pathology [1]. In adults, one of the main features of enthesitis is thickening of the enthesis and increased vascularity [2]. There is no consensus to date on how to define entheseal thickening in healthy children and adolescents.
Objectives: The aim of the study was to determine the entheseal thickness and presence of vascularity during growth in children and adolescents as a prerequisite for determining pathology.
Methods: Participants from a convenience sample of children and adolescents underwent detailed physical and ultrasonographic B-Mode and Power-Doppler examinations of the entheses of hip, knee and ankle joints. All scans were performed by an experienced examiner on the dominant side according to a standardized protocol, followed by assessment of entheseal thicknesses and intra-entheseal vascularity. Data on demographics, pubertal stage and regular physical activities were collected.
Statistical analyses were performed using compositional intraclass correlation coefficients (ICC), single regression analyses and Pearson unpaired t-test.
Results: 79 healthy participants with a mean age of 10.5 years (range 6.1 – 15.8 years, female 48%, right-handed 86%) participated in this study. Of 790 measured entheses, 8 had to be excluded due to technical problems; all 782 evaluated entheses appeared normal in B-Mode imaging. The intraobserver reliability indicated high to excellent agreement for entheseal thickening (ICC 0.91–0.98).
Significant positive correlations from 0.77 to 0.93 were found between entheseal thickness and age (Table 1). In most entheses no difference in tendon diameter between boys and girls was present except for Peroneus brevis and Rectus Femoris enthesis ($p > 0.05$). A slight Doppler activity in less than 1/3 of the area within 2 mm of the tendon insertion was detected in 0 to 40% depending on measured enthesis. Within 5 mm the percentage increased to 1 to 54% (Table 1).
Conclusion: In this cross-sectional study, the ultrasonographic characteristics of lower extremity enthesis in healthy children and adolescents were investigated. Significant correlations between entheseal thickness and demographic data were demonstrated, with no detectable gender difference for most of the entheses. Even in healthy children, mild vascular changes in the enthesis are common with signals mainly in the Sartorius-, Quadriceps- and Achilles-entheses. This data could facilitate the differentiation between normal and pathologic findings and may support the inclusion of the ultrasonographic examination of entheses and their assessment in pediatric rheumatology clinical care.

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Table 1 (Abstract A30). Correlation between entheseal thickness and age, height and weight and percent of Power Doppler signal (vascularity) in up to one third of the area within 2 and 5 mm from the tendon insertion

		Pearson correlation coefficient			Percent of vascularity	
	Enthesis	Age	Height	Weight	at 2 mm	at 5 mm
Hip	Insertion of Sartorius	0.84*	0.80*	0.76*	40	54
	Enthesis of Rectus Femoris	0.88*	0.84*	0.78*	0	1
	Gluteus Minimus at Trochanter major	0.77*	0.72*	0.66*	5	5
	Gluteus Medius at Trochanter major	0.78*	0.74*	0.70*	1	5
Knee	Distal Quadriceps enthesis	0.94*	0.87*	0.81*	24	43
	Proximal Patellar ligament enthesis	0.93*	0.87*	0.77*	18	32
	Distal Patellar ligament enthesis	0.93*	0.88*	0.78*	15	16
Ankle	Achilles enthesis	0.81*	0.76*	0.66*	35	39
	Tibialis Posterior enthesis	0.85*	0.85*	0.76*	6	14
	Peroneus Brevis enthesis	0.91*	0.89*	0.79*	1	1

*The correlation is significant at the 0.01 level (2-sided)

A31

Molecular differentiation trajectories of peripheral helper T cells in the chronically inflamed tissue of patients with ANA positive juvenile idiopathic arthritis

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Introduction: Previous research has demonstrated that antinuclear antibody (ANA)-positive juvenile idiopathic arthritis (JIA) is characterized by a synovial expansion of PD1^{high}CXCR5- peripheral T helper cells (T_{PH}) that co-express interleukin (IL)−21 and interferon (IFN)-γ and can provide efficient B cell help. (1) Similar cell populations are implicated in the pathogenesis of several autoimmune diseases. (2) However, the molecular mechanisms underlying the differentiation of this T cell population remain poorly understood.
Objectives: To elucidate the differentiation trajectories and identify key transcription factors that induce a TPH-like effector program in juvenile idiopathic arthritis.
Methods: We conducted a comprehensive analysis of T helper cells in the synovial fluid from 4 JIA patients using single-cell RNA sequencing. *In silico* perturbation simulations were performed to investigate potential key molecules driving T_{PH} differentiation. Naïve T helper cells were isolated from peripheral blood mononuclear cells and stimulated with plate-bound CD3 and CD28 antibodies in the presence of recombinant cytokines (TGFβ, IL-12, IFNα). Cell phenotype and cytokine profiles were assessed using flow cytometry and ELISA, while the transcriptome signature was investigated through bulk RNA sequencing. The CRISPR-Cas9 system was employed via electroporation to knockout potential regulators of T_{PH} differentiation.
Results: Single-cell RNA sequencing revealed distinct cell clusters with T_{PH}, cytotoxic, and regulatory transcriptome signatures. Utilizing gene regulatory networks and *in silico* perturbation (CellOracle), we identified, amongst others, BHLHE40 as a potential key molecular regulator. To validate the hypotheses derived from these computational simulations, we established an *in vitro* model to induce T_{PH} effector functions in naïve T cells.
Conclusion: We applied an unbiased single-cell RNA sequencing analysis approach to generate hypotheses about potential key regulators of T_{PH} differentiation in JIA. These hypotheses are currently being tested *in vitro* to identify potential druggable targets for ANA-positive juvenile idiopathic arthritis.

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Disclosure of Interest: The authors declare no conflict of interest.

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A32

RAPID-Still: a new study on accelerated biomarker-based diagnosis of Still's disease and Macrophage-activation-syndrome

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Background: Still's disease, also known as systemic juvenile idiopathic arthritis (SJIA) and adult-onset Still's disease (AOSD), is a severe systemic inflammatory condition which at disease onset is often difficult to differentiate from other conditions characterized by systemic inflammation. Furthermore, Still's disease may be complicated by life-threatening macrophage activation syndrome (MAS) at disease onset and during the disease course. Early diagnosis and initiation targeted therapy are key for treatment success. Biomarkers, including serum calprotectin (MRP8/14, S100A8/A9), interleukin (IL)−18 and CXCL9, have been identified as being highly correlated with the different Still's disease/MAS disease states. However, these biomarkers are currently not widely available to providers in Germany.
Objective: We present the RAPID-STILL study that aims to accelerate the diagnosis and improve the diagnostic accuracy of Still's disease (SJIA and AOSD) and MAS by validating and implementing novel biomarker-based diagnostic tools into routine clinical practice.
Methods: This multicenter, non-interventional diagnostic study will recruit 100 patients presenting with fever of unknown origin or fever without focus and suspected Still's disease or MAS. The study will be conducted in two phases:

Phase 1: We will establish a centralized diagnostic platform for biomarker analysis, accessible to clinicians nationwide. Biomarker measurements will utilize an advanced ELLA (Enzyme-linked Lectin Assay) methodology. Phase 2: All members of the GKJR (and DGRh) will be informed about the new diagnostic platform, which is made available on a research basis for all colleagues caring for patients with suspected Still's disease or MAS. The results for serum calprotectin (MRP8/14, S100A8/A9), IL-18 and CXCL9 are reported to the centers. We will also conduct exploratory multiplex analyses to identify and validate novel biomarker combinations for improved diagnostic accuracy.

Primary endpoints include the validation of biomarker cut-off values and the implementation of a nationwide diagnostic service. Secondary endpoints will evaluate the feasibility and clinical applicability of the diagnostic tools to facilitate the availability of biomarker measurements in routine laboratories.
Results: The study anticipates that validated biomarkers will significantly enhance diagnostic precision, enabling earlier and more reliable identification of Still's syndrome and MAS. This is expected to facilitate prompt initiation of targeted therapies, leading to better clinical outcomes and potentially reducing the risk of long-term complications.
Discussion: Still's disease and MAS remain diagnostic and therapeutic challenges due to their overlapping features with other hyperinflammatory syndromes. The RAPID-STILL study seeks to address these challenges by leveraging novel biomarker assays to create a robust diagnostic framework. By refining diagnostic tools, this research aims to reduce diagnostic delays, optimize therapeutic strategies, and ultimately improve survival and quality of life for patients with these severe autoinflammatory disorders.

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A33

Severe Kawasaki disease caused by parvovirus B19 infection?

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Introduction: Parvovirus B19 infection and Kawasaki disease may overlap. Parvovirus can cause severe (atypical) Kawasaki disease (1). Two thirds of patients with Kawasaki disease have a concomitant parvovirus infection (2). Other authors describe that parvovirus infection itself can mimic atypical Kawasaki disease with persistent fever and rash (3).
Methods: A case report of a four-year-old boy with atypical Kawasaki disease is presented. The clinical disease course and challenges are described.
Results: The four-year-old boy presented with five-week history of fever without focus, refractory to antibiotics, cervical lymphadenopathy and coronary aneurysms. Three months prior to the onset of Kawasaki's disease, the boy had a parvovirus infection, resulting in a low haemoglobin level (8.8 g/dl) at first presentation. No active infection was detected at that time. He received two courses of IVIG (2g/kg KG), which resulted in clinical and biochemical improvement. However, three weeks later, he had a relapse of fever and new erythema nodosum, haemoglobin dropped to a low of 7.7 g/dl, and haemolysis parameters increased. Leukocytes increased to 45*10^3/µl. Parvovirus DNA was again found in the blood. Treatment with prednisolone was started. Reduction of prednisolone was tried twice, resulting in flares of erythema nodosum, decrease in haemoglobin and increase in leukocytes. Differential diagnoses for hyperleucocytosis were excluded. A very slow tapering of prednisolone two months after the onset of Kawasaki disease was tolerated. The erythema nodosum resolved slowly after a total of 8 weeks.
Conclusion: Parvovirus infection in Kawasaki disease was associated with several complications in this four-year-old boy, including haemolytic anaemia, hyperleukocytosis, and erythema nodosum. Haemolytic anaemia could be due to IVIG (4) or parvovirus B19 infection/ reactivation. Erythema nodosum is rarely seen in Kawasaki disease. Erythema nodosum and hyperinflammation may be related to prolonged disease activity due to late diagnosis and have been associated with the need for prolonged steroid therapy.

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A34

Autoantibody profiles in Systemic Juvenile Idiopathic Arthritis (SJIA)

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Introduction: Classification of SJIA as an autoinflammatory or autoimmune disease has been subject of an ongoing discussion in the literature. Following the model of a disease continuum [1], SJIA is a multifactorial systemic autoinflammatory disease although mechanisms of autoimmunity have been observed as well. Analyzing the presence of autoantibodies (aAB) in SJIA our group as others found several aABs present in patients with SJIA such as increased serum antinuclear antibodies and positive rheumatoid factor [2]. Moreover aABs in SJIA seem to be related with disease activity [3]. This study presents a more detailed insight to the presence of aABs in SJIA [3].
Methods: Presence of IgG aAB against 67 antigens were analyzed in 43 patients with SJIA (acc. ILAR classification), 13 of them at three different time-points using Luminex method. The cut off value was determined using the ≥98 quantile of the fluorescence intensity values in healthy controls (n=123).
Results: The cohort included 43 patients with SJIA (acc. ILAR classification, fem. 33, male 10, mean age 6,5 yrs.). First we analyzed a cross-section of samples observing aABs in 30,23% (n=13/43) of patients with a mean duration of disease of 20.9 month in aAB pos. and 24.1 month in aAB neg. patients. The mean age of aAB pos. vs. neg. patients was 8 and 8,5 yrs. respectively. Comparing aAB pos. vs. neg. patients we observed significant higher blood values for IgG (1262,3 mg/dl vs 955.1 mg/dl; p=0,01) and ESR (53 vs. 23 mm/h, p< 0,02) and an elevation of Ferritin (1058.4 µg/l vs. 136.9 µg/l, p=0,14), and SAA (358,7 mg/l vs. 121.9 mg/l; p= 0,07) in the aAB pos. group. The aAB positive group had a higher Woo Score (0.9 vs. 0.5 points p=0,03), while there was no difference in the autoinflammatory activity index (AIDAI).

There was no specific pattern of aABs but anti-MYO18A and anti-ZXDC antibodies were observed most frequently (n=5, 11.6% each).
In 13 patients aABs have been analyzed at three consecutive time points (t0, t1, t2). The mean age of disease onset was 63,5 month. The mean patients age was 100,8 month at t0 (n=13), 119,9 month at t1 (n=13) and 193.83 month at t2 (n=6). The mean duration of disease at t0 was 36.6 month, 55.9 month at t1 and 110.8 month at t2. At t0 we found aAB in all of our patients (n=13; 100%). At t1 38.46% (n=13) and at t2 83.3% (n=5/6) patients presented aABs. SNRPF and ZXDC were observed most frequently in this longitudinal group 23.08% (n=3/13). Interestingly patients positive for aABs against CD47, FOS and PPL remained constantly positive over the observation period.
Conclusions: Analyzing the disease activity and the presence of autoantibodies (aAB) in our SJIA group we found aABs in early stages of the disease, combined with elevated blood values (IgG, ESR) and disease activity according the Woo-score. Autoimmune processes seem to have a significant role during the course of S-JIA even in early stages of disease. Although there are no SJIA specific aABs the pattern significantly differs from those found in Oligo- and Polyarticular JIA [4].

Patient Consent: Yes, I received consent.
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A35

Unraveling T cell dysregulation in chronic nonbacterial osteomyelitis

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a poorly understood autoinflammatory disease characterized by an altered innate immune system resulting in cytokine dysbalance.[1] Despite its clinical impact, validated biomarkers remain unavailable.[2] Emerging evidence links alterations in circulating lymphocyte subpopulations to SAPHO (synovitis, acne, pustulosis hyperostosis, osteitis) syndrome, which shows similarities to CNO in adulthood.[3–5]
Objectives: This study aimed to evaluate differences in circulating lymphocyte subpopulations in pediatric CNO compared to juvenile idiopathic arthritis (JIA) and healthy controls (HC), expanding upon immunophenotypic insights from SAPHO syndrome.
Methods: History and clinical data from CNO patients were collected, and cytometry of lymphocyte subpopulations was performed using an established immunophenotyping panel.[6] Comparative analyses of B, T, and NK (natural killer) cell subpopulations were conducted across groups. Statistical analysis was performed using the nonparametric paired Wilcoxon-test, with $p < 0,05$ considered statistically significant.
Results: A total of 16 CNO patients were analyzed alongside age- and sex-matched JIA patients and HC. Results revealed reduced CD56+CD16+ NK cells in CNO patients compared to HC. Additionally, increased effector memory RA+ (EMRA) T cells and increased exhausted helper T cells were observed in CNO relative to HC but not in comparison to JIA. Furthermore, regulatory T cells (Treg), including total and naïve subsets (helper and cytotoxic Treg), were elevated in CNO compared to HC but not when compared to JIA. These findings are summarized in Table 1.
Conclusion: Distinct alterations in lymphocyte subpopulations, including changes in NK and T cell subsets, suggest potential roles for T cell senescence and exhaustion in CNO pathophysiology. These findings hint at autoimmune mechanisms and potential therapeutic targets but may also represent secondary effects, given the similarities with JIA. The observed elevation of Tregs in the CNO group compared to HC was unexpected and may reflect the heterogeneity of the CNO cohort.[5] Further research is required to elucidate these pathways and validate therapeutic implications.

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Disclosure of Interest: None.
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Table 1 (Abstract A35). Circulating lymphocyte subsets in CNO patients compared to HC

Circulating lymphocyte subset	*p* value	median (range) cellnumber/µl CNO HC
EMRA T helper cells	0,002	17.8 (3.7–115.6) 5.2 (1.4–18.2)
EMRA cytotoxic T cells	0,029	65.7 (16.0–155.7) 42.9 (15.5–97.7)
Low exhausted T helper cells	0,029	161.0 (49.3–204.7) 109.8 (75.7–234.0)
CD56+CD16+ NK cells	0,049	96.0 (38.0–220.8) 115.0 (34.0–579.0)

Circulating lymphocyte subset	*p* value	median (range) cellnumber/µl CNO HC
total helper Treg	0,039	76.1 (46.1–126.3) 57.2 (31.0–106.2)
naïve helper Treg	0,021	49.7 (24.7–108.8) 35.8 (11.7–79.2)
total cytotoxic Treg	0,003	(0.3–3.5) 0.5 (0.1–1.9)
Naïve cytotoxic Treg	0,003	0.8 (0.2–3.1) 0.6 (0.2–2.2)

A36

The tree inside the knee - Bilateral lipoma arborescens of the knee in an adolescent

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Pediatric Rheumatology 2025, **23(1):**A36

Background: Lipoma *arborescens* (LA) is a benign tumor characterized by subsynovial villous proliferation of mature adipocytes, which leads to displacement of synovial tissue [1]. The etiology of LA remains unknown; however, mechanical stress and synovial inflammation are thought to be potential triggers [2]. Cases in children are rare, especially with bilateral manifestation [3]. It is often associated with effusion and synovitis of the affected joint [2].
Case Report: A 12-year-old male patient with no previous medical history, presented with increasing bilateral swelling and stress dependent pain of the knees persistent for 2 weeks following a jump. Three months prior he had noted progressive pain after playing soccer with occasional functional disability for the first time. Physical examination revealed swelling and a painless extension deficit of both knee joints. Laboratory findings did not show any signs of systemic inflammation, ANA titer of 1:640 and negative rheumatoid factor. Serologic tests ruled out *Lyme arthritis* and previous infection with *Yersinia* or *Mycoplasmas.* Plain radiograph was unremarkable. Sonography revealed a slight bilateral effusion with villous tumor-like tissue proliferation in the suprapatellar pouch and the cubital fossa. Treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) had no effects.
Looking at the characteristics of juvenile arthritis (JIA), the missing morning stiffness, painless slowly progressive joint swelling, lack of vascularization of the proliferated tissue in imaging, as well as nonresponsiveness to NSAIDs seemed unusual. The contrast enhanced magnetic resonance imaging (MRI) showed an advanced osteoarthritis of both knee joints and finger-like synovial proliferation leading to the diagnosis of LA. Tumor resection was offered for definitive treatment. At the current time the patient and his family refuse surgical treatment due to regression of symptoms.
Summary: Intraarticular synovial lipoma should be considered in the differential diagnoses when young patients present with atypical arthritis. The LA is characterized by a slowly progressive tissue swelling in an arbor-like pattern affecting bigger joints. The specific appearance allows diagnosis from imaging alone [1,2]. In uncertain cases a biopsy should be performed. Symptomatic cases can be effectively treated with synovectomy [2,3]. In cases with underlying JIA a conservative approach including TNF inhibitors can be attempted [4].

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: None.

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A37

Juvenile idiopathic arthritis in children with type 1 diabetes: impact of current medical treatment options on anthropometry and metabolic control

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Introduction: Treatment for juvenile idiopathic arthritis (JIA) has evolved, with less steroid use and increased reliance on biologic drugs. We hypothesize that these advances have reduced the impact on anthropometry and metabolic control in children with type 1 diabetes (T1D) and JIA.
Objectives: Our study examines the characteristics of children with JIA and T1D compared to a survey from 1995 to 2013 [1].
Methods: We evaluated data from patients with T1D, aged 0.5 to 16 years at diagnosis, and examinations documented between January 1995 and December 2023 at 417 DPV centers in Germany, Austria, Switzerland, and Luxembourg. JIA diagnoses were identified through documented diagnoses, ICD-10 codes and a list of trade names and active substances, including steroids and biologics. Statistical analyses compared JIA and non-JIA patients (χ^2-test, Wilcoxon-test) for demographic and treatment parameters. Treatment periods (1995–2013, 2014–2018, 2019–2023) were compared, and regression models evaluated outcome differences between JIA and non-JIA patients, adjusted for demographics and diabetes duration.

Results: Height was slightly lower in 212 children with JIA and T1D compared to 80899 children with T1D only, while body mass index (BMI) did not differ significantly. Weekly sports activities and the proportion of individuals with migration background were similar in both groups. Children with JIA and T1D more frequently used diabetes technologies, such as insulin pumps, glucose sensors and automated insulin dosing systems. They had a higher insulin requirement and a better metabolic control (see Table 1).
The prevalence of hypertension (29.7% vs. 31.7%; p = 1.0000) and dyslipidemia (34.2% vs. 33.9%; p = 1.0000) were comparable, but children with T1D and JIA were more frequently treated with antihypertensive medication (8.0% vs. 1.8%; p < 0.0001) and statins (2.8% vs. 0.7%; p < 0.01).
Compared to 1995–2013, the BMI of children with T1D and JIA was lower in 2014–2019 and 2020–2023 (BMI-SDS: 0.35 vs. 0.08 vs. 0.10), while height remained stable across periods (Height-SDS: −0.04 vs. −0.04 vs. −0.08). Weekly sports activities increased over time, particularly in children with T1D and JIA (1.2 to 2.7 h/wk vs. 1.8 to 2.7 h/wk in children with T1D alone).
Conclusion: Children with JIA more frequently use modern diabetes technologies and achieve better metabolic control than those with T1D alone. Their height was slightly lower, while BMI remained similar. These data confirm good diabetes outcome in children with JIA and T1D.

Patient Consent: Yes, informed consent for pseudonym zed documentation was received at the participating treatment centers.
Funding: The DPV registry is supported by the German Center for Diabetes Research (DZD) and as part of diabetes surveillance at the Robert Koch Institute (RKI). Both the DPV initiative and the analysis of anonymized data were approved by the ethics committee of the University of Ulm and the data protection officers of the participating centers.
Disclosure of Interest: ASP, CK, JR, JZ, KK, RWH, TH: no conflict of interest.

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Table 1 (Abstract A37). Comparison of patients with type 1 diabetes and juvenile idiopathic arthritis vs. patients with type 1 diabetes alone (percentages or mean values [standard deviation])

	Patients with T1D and JIA	Patients with T1D	*p*-value
n	212	80899	
Height-SDS	−0.06 [1.06]	0.13 [1.07]	0.4393
BMI-SDS	0.15 [0.99]	0.28 [0.93]	0.8741
Sports activities (h/wk)	2.3 [2.4]	2.7 [2.7]	1.0000
Migration background (%)	25.9	22.1	1.0000
Insulin pump (%)	64.5	47.6	< 0.0001
Glucose sensor (%)	68.9	51.2	< 0.0001
AID system (%)	26.6	15.1	0.0018
Insulin dose (IE/kg*d)	0.95 [0.4]	0.87 [0.4]	0.0061
HbA1c (%)	7.7 [1.5]	8.0 [1.7]	0.0388

A38

Efficacy of 1st, 2nd or following treatment courses with biologics/Janus kinase inhibitors for treatment in polyarticular juvenile idiopathic arthritis- an analysis from the BiKeR registry

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Introduction: The treatment of polyarticular juvenile idiopathic arthritis (pJIA) offers a growing range of biologics and janus kinase inhibitors (JAKI). However, some patients achieve sufficient response only after multiple therapies. This analysis aims to evaluate initial selection and sequential therapy in cases of inadequate response
Objectives: To analyze the choice and sequential order of a biologic/JAKI therapy in the treatment of pJIA.
Methods: In this ongoing non-interventional study, data from the Biologics in Pediatric Rheumatology (BiKeR)-registry are collected from pJIA patients (RF-negative/positive polyarthritis or extended oligoarthritis) treated with one or more biologics or JAKI. Baseline parameters, the choice of initial biologic/JAKI and the following order and choice in case of a sequenced biologic/JAKI therapy were analyzed. Therapeutic response was assessed after three months using the Juvenile arthritis disease activity score (JADAS)10. Minimial disease activity (MDA) and remission (REM) were defined regarding criteria by Trinciani C et al.* with a JADAS10 score ≤6 as MDA and a JADAS10 score ≤ 2.7 as remission.
Results: At data cut off (03/01/2023), 2581 patients with 3443 treatment courses with one and/ or multiple sequential biologic/JAKI therapy were analyzed. The following cohorts were formed based on their medication: abatacept (ABA), adalimumab (ADA), etanercept (ETA), golimumab (GOL), Infliximab (INF), tocilizumab (TOC), a group of other biologics (other biol.) and a group of JAKI. Parameters at therapy start with the first biologic/JAKI are described in Table 1.
The first, second, or third biologic/JAKI treatment attempt resulted in a favourable response in the vast majority of patients at three months of therapy. When subsequent biologics were needed, remission was achieved less frequently (Figure 1).
Etanercept was both, the most commonly used biologic overall and as a first-line treatment, followed by adalimumab and tocilizumab. As a second-line treatment, adalimumab was preferred, followed by tocilizumab, etanercept and golimumab. Abatacept and infliximab were almost only used as third- or fourth-line treatments. Among the fifth-line therapies, golimumab and tocilizumab were observed. JAKI have been used rarely overall (Figure 1).
Conclusion: Favourable targets for treatment have been achieved by 1st, 2nd or 3rd courses of biologics/JAKI while patients who need a 4th or 5th course responded less frequently and may define difficult to treat patients. Etanercept and adalimumab were the most frequently used biologics overall, as well as for first- and second-line therapy. In cases of non-response, other biologics such as tocilizumab, golimumab, and abatacept were used.

Patient Consent: Yes, I received consent of patients/ their legal guardians.
Funding: The BIKER registry is supported by unrestricted grants from Abbvie, Chugai, MSD, Novartis, Pfizer, Roche. Data accumulation, monitoring and statistical analysis is performed independently from the company sponsors.
Disclosure of Interest: Angela Zimmer: Travel grands: Novartis, Lilly; Speakers bureau: Lilly, Glaxo-Smith-Kline; Ariane Klein: Speakers fee: Novartis, Lilly, Normi Brueck: none; Jasmin Kuemmerle-Deschner: none; Frank Dressler: Advisory Boards by Novartis and Mylan, Speakers bureau: Abbvie, Novartis, Pfizer, Advisory Boards Novartis and Mylan; Anton Hospach: Consulting fees: Novartis, SOBI, Speakers bureau: Novartis and SOBI; Jens Klotsche: none; Kirsten Minden: received honoraria from Pfizer, Novartis and medac; Ralf Trauzeddel: none; Daniel Windschall: Grant/research support: Novartis, Roche, Pfizer, Abbvie, received honorary fees from Novartis, Pfizer, Abbvie, MEDAC, Roche, and Sobi; Gerd Horneff: Advisory Speaker: Pfizer, Novartis, Sobi; Consultant MSD, Lilly; Grants Novartis, MSD, Roche; Speakers bureau: Pfizer, Roche, MSD, Sobi, GSK, Sanofi, AbbVie, Chugai, Bayer, Novartis, Grant/research support from: Pfizer, Roche,MSD, AbbVie, Chugai, Novartis.

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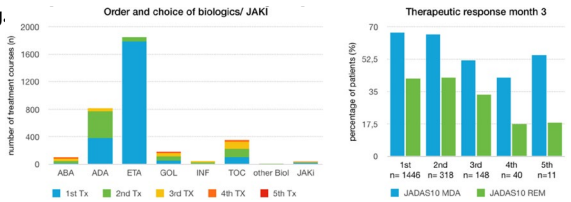
Table 1 (Abstract 38). Baseline parameters at therapy start 1st biologic/ JAKI

n	2581
Age at disease onset, years; mean (±SD)	6.7(±4.6)
Age at disease onset, years; median (IQR1-IQR3)	5.7(2.4–10.7)
Disease duration at baseline, years; mean (±SD)	4.7(±4.0)
Disease duration at baseline, years; median (IQR1-IQR3)	3.5(1.4–7.0)
Age at therapy start, years; mean (±SD)	11.4(±4.4)
Age at therapy start, years; median (IQR1-IQR3)	11.9(8.2–14.9)
ANA-positive n (%)	1557(60.3)
Uveitis n (%)	351(13.6%)
Disease activity	
Physician global assessment disease activity (scale 0–100); median (IQR1-IQR3)	49.8(±26.4)
Patient global assessment disease activity (scale 0–100); median (IQR1-IQR3)	39.8(±27.4)
Active uveits n (%)	182(7.1%)
Active joint count; mean (±SD)	6.9(±7.9)
Active joint count ;median (IQR1-IQR3)	4.0(2.0–9.0)
CHAQ; mean (±SD)	0.6(±0.6)
JADAS10; mean (±SD)	14.9(±7.5)
Therapy at baseline	
Steroids n (%)	737(28.6)
Methotrexate n (%)	1833(71.0)

Fig.



A39

Mucopolysaccharidosis Type IX mimicking juvenile idiopathic arthritis: the role of a newly identified HYAL1 variant

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Introduction: Juvenile Idiopathic Arthritis (JIA) is the most common type of arthritis in children under 16, presenting with symptoms such as joint effusions, restricted motion, and synovial inflammation. Diagnosing JIA can be challenging due to overlapping clinical features with other conditions, including rare genetic disorders. Among these, Mucopolysaccharidosis Type IX (MPS9) is particularly noteworthy. This lysosomal storage disorder, caused by a deficiency of hyaluronoglucosaminidase 1 (HYAL1), may mimic JIA with joint effusions, restricted mobility, and synovial irritation [1-3]. Its rarity, with only four reported cases to date [1, 2], contributes to misdiagnoses and delays in recognizing the underlying genetic cause.
Objectives: This study aims to emphasize MPS9 as a differential diagnosis in refractory JIA cases, highlighting clinical overlap to raise awareness and promote early diagnosis. Additionally, it seeks to expand understanding of MPS9 pathogenesis and support the development of improved diagnostic and therapeutic approaches.
Methods: Clinical characteristics of two affected siblings were thoroughly evaluated. Whole exome sequencing (WES) using next-generation sequencing (NGS) was performed to identify the underlying genetic cause. Additionally, a comprehensive review of the existing literature on MPS9 was conducted to contextualize the findings.
Results: The two siblings presented with widespread involvement of multiple large joints, characterized by joint effusions, restricted range of motion, and signs of synovial irritation. Both were initially misdiagnosed with JIA and treated with various immunosuppressive agents, none of which led to clinical improvement. WES revealed a novel homozygous deletion, c.676del, in the HYAL1 gene, in both siblings. This mutation results in a frameshift variant in exon 1, producing a premature termination codon (p.Arg226ValfsTer7). The variant is predicted to cause nonsense-mediated decay, leading to a complete loss of HYAL1 function and absent plasma hyaluronidase activity, consistent with previous reports. While clinical features overlapped with earlier MPS9 cases, including joint effusions and restricted mobility, our patients showed no proliferative synovial changes, popliteal cysts, chondral defects, dysmorphic features, or other significant skeletal abnormalities.
Conclusion: These two cases underscore the importance of considering MPS9 as a differential diagnosis in refractory JIA. Genetic testing is invaluable for identifying rare underlying causes, avoiding prolonged ineffective immunosuppressive treatments, and enabling timely, targeted management. Heightened awareness of MPS9 among clinicians can improve diagnostic accuracy and patient outcomes, demonstrating the critical role of genetic investigations in unresolved joint diseases.

Patient Consent: Yes, I received consent.
Funding: The authors declare no financial support.
Disclosure of Interest: The authors declare no disclosures.

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A40

Tofacitinib treatment in juvenile idiopathic arthritis -data on safety and efficacy from the German BIKER registry

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Pediatric Rheumatology 2025, **23(1):**A40

Introduction: Tofacitinib is an oral Janus kinase inhibitor recently approved for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) and juvenile psoriatic arthritis (jPsA). Long-term data in JIA patients are scarce. The German biologics in JIA register BIKER also monitors long-term safety and effectiveness of JAKI in routine clinical practice.
Objectives: To assess long-term safety and tolerability of tofacitinib in a cohort of JIA patients as well as effectiveness and reasons for discontinuation.
Methods: Male and female JIA patients aged 2 to 18 years with documented tofacitinib treatment were selected. Patient assessment was performed at baseline, after three and six months, and every six months thereafter. Baseline demographics and disease activity parameters have been documented. Efficacy was determined using the JADAS10. Safety assessments were based on adverse events reports (AE).
Results: Altogether, 79 JIA patients with 1553 patient years (PY) of tofacitinib exposure were identified. Baseline parameters are shown in Table 1. Only 9% (n=7) were biologic-naïve, while over half of the patients had used 3 or more biologics before.
After 12 months of tofacitinib treatment patients experienced improvement of the mean number of active joints from 4.5 to 1.5, the physician global assessment of disease activity from 3.5 to 0.9 and the mean JADAS10 from 10.3 to 3.8. JADAS inactive disease [1] was reached by 61.8% of patients, a further 8.8% reached JADAS minimal disease activity. Of the 7 biologic naïve patients all reached at least JADAS10 minimal disease activity at last follow-up.
In total, 70 adverse events (AE) were reported in 45 patients in this cohort, none of them were serious. 17 infections were documented in 15 patients (localized bacterial infection n=7, COVID n=6, upper airway infection n=3, varicella n=1), 3 patients reported new onset/recurrence of uveitis, 2 patients suffered from depression or anxiety, no thrombotic events were reported. Nearly one third of patients discontinued tofacitinib treatment (n=25), 17 patients (21%) due to lack of efficacy, 7 patients because of intolerance, 10 patients for other reasons.
Conclusion: In this cohort of patients with highly active and mostly refractory JIA patients tofacitinib use was safe and well tolerated. No new safety signals were identified
Tofacitinib treatment was associated with improvement in disease activity parameters although the cohort of patients had been heavily pretreated. In biologic naïve patients high response rates were observed.
Tofacitinib treatment in JIA patients will be monitored in a long-term post-marketing surveillance study (PASS).

Patient Consent: Patient consent was retrieved before enrolment in BIKER, no individual patient data are shown in this abstract.
Funding: The BIKER registry has been supported by unrestricted grants from Abbvie, Chugai, MSD, Novartis, Pfizer, Roche. The data collection, analysis and publication is not influenced by the sponsors and lay in the full and only responsibility of the authors.
Disclosure of Interest: AK has received speakers bureau from Novartis and Lilly, AZ has received travel grants from Novartis, Lilly, speakers bureau: Lilly, Glaxo-Smith-Kline, IF has received travel grant from Abbvie, Add board on Mitsubishi, Boehringer, KM has received honoraria from Amgen, Biogen, medac, Novartis, CR received speaker honoraria from Novartis, ucb and Galapagos, advisory boards: Pfizer, sobi, DW speakers bureau: Pfizer, Novartis, Abbvie, MEDAC, Canon, Grant/research support from: Novartis, Pfizer, HG none. GH has received personal fees from Abbvie, Boehringer, Celgene, Chugai, GSK, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, Sobi.

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Table 1 (Abstract 40). Baseline patient characteristics

Age, years Mean (SD), Range	**13.3+/−3.5; 3.4–18**
Disease duration, years Mean (SD), Range	**7.9+/−4.1; 0.4–16**
JIA category, n;%	
RF+ polyarthritis	6; 8%
RF- polyarthritis	39; 49%
Ext. oligoarth.	21; 27%
ERA-JIA	5; 6%
Juv. psoriatic arthritis	5; 6%
Systemic onset JIA	3; 4%
Concomitant Tx	
Methotrexate	29; 37%
Sulfasalazine	1; 1%
Leflunomide	1; 1%
Corticosteroids	15; 19%
Pretreatment, n, %	
Methotrexate	79; 100%
Abatacept	8; 11%
Adalimumab	51; 65%
Anakinra	3; 4%
Canakinumab	2; 3%
Etanercept	45; 57%
Golimumab	34; 43%
Infliximab	1; 1%
Secukinumab	5; 6%
Tocilizumab	45; 57%

Age, years Mean (SD), Range	**13.3+/−3.5; 3.4–18**
Disease duration, years Mean (SD), Range	**7.9+/−4.1; 0.4–16**
bDMARD pretreatment, n, %	
None	7 (9%)
1	13 (16%)
2	18 (23%)
3	22(28%)
4	14 (18%)
5	4 (5%)
6	1 (1%)

A41

Development and validation of a Pediatric Internationally agreed UltraSound Hip synovitis protocol (PIUS-hip), by the PReS imaging working party

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Pediatric Rheumatology 2025, **23(1):**A41

Objectives: To validate a musculoskeletal ultrasound (MSUS) protocol for the detection of hip synovitis in patients with juvenile idiopathic arthritis (JIA).

Methods: Consecutive JIA patients with hip arthritis on clinical examination underwent MSUS which included the longitudinal view of the anterior recess for the measurement of the bone to capsula distance as well as articular capsule thickness. Synovitis was graded using the pediatric OMERACT score for B-Mode (BM) and Power-Doppler Mode (PD). Femoral head cartilage thickness was recorded in the transverse plane. Anterior recess size was compared to measurements in the hips of the same patients without clinical arthritis. Additionally, previously published data of anterior recess size was included as a second control which included normal data measured in children without JIA (1). The MSUS-protocol was agreed by the Pediatric Rheumatology european Society (PReS) Imaging Working Party and interobserver reliability of BM and PD was tested first.

Results: The MSUS-protocol was performed in 76 hips with clinical arthritis and 32 hips without in 60 patients. Control data from 449 healthy children (both hips) was available for comparison (1). Interobserver reliability of BM and PD positivity showed 85 % agreement, with kappa 0.74. In hips with clinical arthritis, BM positivity (grading $\geq$1) in the longitudinal view was detected in a frequency of 71 (93 %), sensitivity 0.97 (0.93–1.0) and specificity 0.85 (0.74–0.97) versus a frequency of 2 (6 %, sensitivity and specificity not calculable) in hips without arthritis. PD positivity (grading $\geq$1) had a frequency of 6 (8%) versus 0 (0%) in hips without arthritis. Anterior recess size (mean$\pm$SD) was wider in patients with versus without clinical arthritis (9.9$\pm$2.5 vs 5.5$\pm$1.3, p-value 0.001). Anterior recess size in healthy hips was not statistically significantly different to size in hips of clinically unaffected hips of the JIA patients. Articular capsule and femoral head cartilage thickness did not differ between the groups.

Conclusion: BM positivity was sensitive and specific for hip synovitis, unlike PD. The evaluation of capsule thickness and femoral head cartilage did not differentiate between hips with and without clinical arthritis. However anterior recess size was significantly increased compared to controls in all age groups. Therefore the Pediatric Internationally agreed UltraSound Hip synovitis protocol (PIUS-hip)
Includes BM grading and measurement of anterior recess size in the longitudinal view.

Patient Consent: Yes, I received consent.

Funding: This study received partial funding support from Novartis. The funding body played no role in the design of the study or in the collection, analysis and interpretation of data or in writing the manuscript.

Disclosure of Interest: None to declare.

Reference

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A42

PI4KA-related disorder: a potential genetic explanation for a complex clinical picture of type I-interferonopathy, autoinflammation and autoimmunity – a case report

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Pediatric Rheumatology 2025, **23(1):**A42

Background: *PI4KA*-related disorder is a clinically variable condition with neurological dysfunction (limb spasticity, developmental and intellectual delay, seizures), gastrointestinal manifestations (inflammatory bowel disease and intestinal atresia) and immunodeficiency. A 17-year-old male with a history of spastic paraplegia, developmental delay, and recurrent fever presented with systemic inflammation, polyarthritis, and autoimmune symptoms. Genetic testing identified biallelic variants in the *PI4KA* gene.

Case report: The patient presented with progressive spastic paraplegia, epilepsy and intellectual disability from the first year of life. At the age of 17, he was hospitalized with fever and pleuropneumonia, polyarthritis, chilblain-lesions of the fingers and systemic inflammation (CRP 120 mg/l, ferritin 500 µg/l, calprotectin 95 mg/l). Immunological investigations showed lymphopenia, complement deficiency, elevated antibody profile (ANA 1:10.240, dsDNA and anti-Sm highly positive) and a strong interferon signature. Gastrointestinal disease was not observed.
Exome sequencing and segregation of identified variants in the parents was performed.We detected two biallelic variants of uncertain significance (VUS) in *PI4KA* encoding phosphatidylinositol 4-kinase. PI4KA synthesizes phosphatidylinositol 4-phosphate, an integral lipid of Golgi membranes required for membrane trafficking and signal transduction. A dysregulation of these processes may therefore cause the patient's inflammatory condition [1,2]. Of the *PI4KA* VUS identified in the patient, one was found 12x heterozygously in gnomAD and predicted to be deleterious, while the other has not been described in gnomAD with unclear functional prediction. Although antibiotic and immunosuppressive therapy (prednisolone, methotrexate, anakinra) resulted in partial symptom improvement, the patient's inflammatory markers (CRP, Ferritin) remained elevated, and the clinical picture fluctuated, especially during steroid tapering. A therapeutic trial with JAK inhibition (baricitinib) was initiated due to clinical similarities

with type I interferonopathies and systemic lupus erythematosus without success [3,4]. Tapering of steroids became possible after switch to canakinumab combined with methotrexate. Our patient differs from the typical immunologically manifestations described in *PI4KA*-related disorders (hypogammaglobulinemia, B-cell deficiency) - he rather presents with features of autoinflammation and autoimmunity.
Conclusion: This case highlights the importance of genetic testing in diagnosing rare complex disorders like *PI4KA* -related conditions. The identification of biallelic *PI4KA* variants provides a potential genetic explanation for the patient's multi-systemic disease. Further functional analysis is necessary to determine the causality *PI4KA* VUS in disease pathogenesis and to derive improved treatment strategies.

Patient Consent: Yes, I received consent.
Funding: None.
Conflict of interest: AS, MS, CW, KH, MLK and NB have no financial conflicts of interest.

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A43

A retrospective evaluation of therapy use in patients with chronic recurrent multifocal osteomyelitis with and without sacroilitis

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Pediatric Rheumatology 2025, **23(1):**A43

Objectives: To examine the demographic, clinical and therapeutic characteristics of patients with chronic recurrent multifocal osteomyelitis (CRMO) with and without sacroiliitis.
Methods: Patients with a new diagnosis of CRMO between 2019 and 2024 in a single tertiary pediatric rheumatology center were included. Demographics, disease and therapy characteristics were retrospectively analyzed with subgroup analysis in patients with CRMO and without radiologically diagnosed sacroiliitis.
Results: 45 patients (71 % female) aged median 11.1 years (IQR: 9.1–13.4) at first diagnosis were included. All patients initially received nonsteroidal anti-inflammatory drugs (NSAIDs). 24 patients (56%) required therapy escalation: 14 (31%) received prednisolone (4/15 intravenous, 10/15 oral), 18 (40%) were treated with disease-modifying antirheumatic drugs (DMARDs; 11 methotrexate, 8 sulfasalazine), 13 (29%) received TNF-α inhibitors (10 etanercept, 3 adalimumab), and 14 pamidronate (31%). One patient was treated with tofacitinib and another had multiple therapy changes due to therapy-resistant iridocyclitis associated with juvenile idiopathic arthritis. 42/45 patients had a whole-Body-MRI or targeted imaging of the pelvis with sacroiliitis diagnosed in nine (100% female). HLA-B27-positivity was 1/7 (14%) in the presence of sacroiliitis and 5/36 (14 %) without. 26/45 (58%) patients had elevated erythrocyte sedimentation rate (ESR) or c-reactive protein (CRP) at baseline: ESR in CRMO without sacroiliitis; 19/36 (53%), median 11,5, IQR 5–21 and with sacroiliitis 7/9 (78%), median 19 mm/h, IQR 11–27. Patients with sacroiliitis had higher use of etanercept compared to those without (67% vs. 22%). In 8/9 patients with sacroiliitis (1/9 lost to follow-up, FU) required therapies beyond NSAIDs. Use of other therapies varied as follows for patients with and without sacroiliitis: prednisolone 6/8 (75%) vs 8/33 (24%); DMARDs 7/8 (88%) vs 11/33 (33%); bisphosphonates 4/8 (50%) vs 10/33 (30%). At last observation, 19/45 (42 %) were in clinical remission, 52 % after NSAIDS alone, 16 % after bisphosphonates and 32 % after a combination of treatments. In patients with sacroiliitis, remission was reached in 3/8 (38%, median FU 1,8 years, range 0,5-4 years) vs 16/33 (48%, median FU 1,5 years, range 0,3 – 4,5 years) without.
Conclusion: Patients with CRMO and sacroiliitis required more intensive and diverse treatments, particularly TNF-α inhibitors and DMARDs, compared to the broader CRMO cohort. The presence of sacroiliitis therefore appears to represent a subgroup of patients with higher subclinical inflammation at baseline with a requirement for more intensive therapy. These results should be validated in other cohorts.

Patient Consent: Not applicable (there are no patient data).
Funding: None to declare.
Disclosure of Interest: No conflicts of interest to declare.

A44

Wrist orthotic use in patients with juvenile idiopathic arthritis: a single-center retrospective evaluation

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Pediatric Rheumatology 2025, **23(1):**A44

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Objectives: Patients with juvenile idiopathic arthritis (JIA) have a high prevalence of wrist joint impairment, (1) however, data regarding the use of splints or orthoses is limited. The objective was therefore to evaluate the indication and effectiveness of resting wrist joint orthotics in a single specialist paediatric rheumatology center.
Methods: All patients with a JIA diagnosis according to ILAR criteria who received their initial wrist orthotic for day use between 01.01.−31.12.2020 were identified. Demographic and clinical data for analysis of indication, duration and effectiveness of treatment (change in wrist range of movement (ROM) and axis) was collected from case records. For analysis, normal values for ROM were defined as: extension=90°, flexion=90°, radial=25°, ulnar=45°.
Results: 16 patients (11 female, 69%), all rheumatoid factor negative, were identified. Median age at diagnosis was 45 months (IQR: 69). Orthoses were prescribed a median 3 (IQR: 8) months after diagnosis and after an acute flare of the same joint requiring intraarticular cortisone application in 16/16 patients. Patients had rheumatoid factor-negative Polyarthritis, n= 11; oligoarthritis, n=3; undifferentiated, n=1 and enthesitis-related arthritis, n=1. 24 individual hand orthoses were prescribed: eight patients (50%) received bilateral orthotics, four (25%) unilateral left-sided and four (25%) right-sided. In 23/24 of orthoses prescribed, acute arthritis of the same joint was present at the time, whilst 1/24 orthoses prescribed was for chronic arthritis of that joint. Wrist joint orthotics were first prescribed a median 3 months (IQR 6) after JIA diagnosis for correction of contractures (n=3, 16%), axial deviation (n=5, 31%), stabilization (n=1, 6%) or growth redirection (n=12, 75%). Duration of therapy was a median 7.5 months (range 1–15, IQR 3.3) and 12/16 (75%) were recommended outpatient occupational therapy. At start of orthotic treatment, passive extension deficit was median 10° (IQR 15, n=21/24) and flexion deficit 10° (IQR 10, n=22/24). At first follow-up (3–6 months), the equivalent values were 5° (5, n=24/24) and 0° (5, n=24/24), respectively. In the five patients (8 wrists) with orthotics prescribed for axial deviation, passive radial ROM was median 20° (IQR 20, n=5/8) and passive ulnar ROM 30° (1, n=4/8) at baseline and at first follow-up, 30 (8, n=7/8) and 40 (8, n=6/8) for radial and ulnar ROM, respectively.

Conclusion: 24 wrist orthoses were prescribed in one year, most commonly to correct axial deviation and growth. Combined with occupational therapy, improvement could be shown in all patients. Further studies are required to determine changes in functional outcome.

Patient Consent: No, not required.
Funding: None to declare.
Disclosure of Interest: No conflicts of interest to declare.

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A45

Hyperuricemia and Juvenile gout: linking *LDHD* mutations to purine metabolism disorders

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Pediatric Rheumatology 2025, **23(1):**A45

Background: Juvenile-onset gout, characterized by arthritis urica and hyperuricemia, is an exceptionally rare condition with limited documented cases. Typically associated with monosodium urate crystal deposition in joints, gout in adults often stems from secondary causes like high purine intake, obesity, or renal dysfunction. However, in pediatric cases, genetic etiologies, such as mutations in the *LDHD* gene encoding d-lactate dehydrogenase, are emerging as significant contributors[1,2]. LDHD is pivotal in purine metabolism, catalyzing the reduction of pyruvate to d-lactate. Loss-of-function mutations impair lactate metabolism, potentially elevating d-lactate levels, increasing renal urate reabsorption, and subsequently causing hyperuricemia. This highlights *LDHD* deficiency as a novel metabolic disruptor, linking intermediary and purine metabolism.
Case Report: We present the case of an otherwise healthy 17-year-old male (BMI 15.4) who initially presented with acute pain in his right great toe while waking up. Two days later, severe morning pain rendered him unable to bear weight, with increasing notable redness and swelling at the base of the toe. MRI confirmed active arthritis in the metatarsophalangeal joint without erosive changes. Another episode shortly after involved the lower right thumb. Persistent hyperuricemia (serum uric acid >600 µmol/L) and an absence of typical gout risk factors such as high BMI or excessive purine intake raised suspicion of an underlying metabolic etiology. Genetic analysis revealed two compound-heterozygous *LDHD* variants: c.561_562del (p.(Leu188Glnfs*56)) and c.1319C>T (p.(Thr440Met)), confirming the diagnosis of LDHD-associated hyperuricemia and juvenile gout.
Treatment included NSAIDs and short-term glucocorticoids for acute symptom control, followed by long-term urate-lowering therapy with allopurinol (initially 100mg/day, increased to 300 mg/day after another transient flare in the left index finger) and colchicine prophylaxis for 3 months (0.5 mg/day). This regime effectively reduced serum urate levels to around 470 µmol/l five months after disease onset without any residual signs of joint inflammation, enabling the patient to resume normal physical activity.
Conclusion: This case underscores the need for heightened awareness of genetic causes in pediatric gout presentations. *LDHD* mutations disrupt lactate metabolism, leading to hyperuricemia through compensatory increased renal lactate and decreased urate excretion. Early molecular diagnosis facilitates targeted interventions like urate-lowering therapies, preventing chronic joint damage. Moreover, this report highlights the broader metabolic implications of LDHD deficiency, advocating for further research to elucidate its role in intermediary and purine metabolism.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: None.

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A46

Still burning: multi-biologic therapy in refractory systemic JIA – alternative to HSCT?

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Pediatric Rheumatology 2025, **23(1):**A46

Introduction: Refractory systemic juvenile idiopathic arthritis (sJIA), resistant or relapsing despite established standard treatments with steroids and anti-IL-1 or -IL6, remains a clinical challenge. We conducted a chart review of an 8-year-old girl with refractory sJIA, documenting treatment escalation and monitoring.
Case report: We present the case of an 8-year-old girl with severe systemic inflammation and refractory arthritis, unresponsive to high-dose steroids and multiple standard therapies including Anakinra, Canakinumab, MTX, Tocilizumab or Tofacitinib. Disease course started at the age of six, developing progressive inflammation over the following two years. Whole exome sequencing ruled out underlying primary immunodeficiency or autoinflammatory conditions. Side effects of steroids were severe, and attempts to reach disease control by adding Ciclosporin (trough level ~150µg/l) and MTX had no impact on disease severity. S100A8/A9 was > 100.000 pg/ml and Juvenile arthritis disease activity score (JADAS10) was 27/40. Given the severity and steroid-refractory course of her disease, autologous stem cell transplantation was considered as an option for disease control. However, the parents declined this intervention, leading us to explore an alternative and somewhat brave multi-targeted biologic approach: In addition to steroids, high-dose, dual IL-1 inhibition (Anakinra, Canakinumab), TNF inhibition (first Etanercept, later switched to Adalimumab), and JAK inhibition (Baricitinib) at the same time. This regimen was implemented in a stepwise manner, especially to address uncontrolled systemic inflammation and severe arthritis, including cervical spine involvement, which influenced the decision for such extensive escalation. Therapy adjustments were guided by joint involvement and Serum-Calprotectin (S100A8/A9). Prophylactic antimicrobial coverage was administered to reduce infection risk, therefore no relevant adverse events were noticed. Over six months, the patient exhibited marked improvement enabling complete withdrawal of steroids and subsequently also Anakinra. Her systemic symptoms, joint involvement, and inflammatory markers stabilized, with nearly normalization

of S100A8/A9 and soluble interleukin-2 receptor (sIL2R) levels. Her JADAS10 decreased significantly to 1/40, reflecting disease control. Currently the patient is well with no noticeable disease activity under Canakinumab, Adalimumab and Baricitinib treatment.
Conclusion: This case highlights the potential of multi-biologic therapy in achieving remission for pediatric patients with refractory sJIA where traditional treatments have failed, especially when stem cell transplantation is not an option. Further studies are needed to confirm the safety, efficacy, and long-term outcomes of such strategies in similar cases.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: No COI.
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A47

Heterozygous PLCG2 gene deletion in a child with arthritis and recurrent infections: a variant of uncertain significance with potential pathogenicity

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Pediatric Rheumatology 2025, **23(1):**A47

Background: Pathogenic variants in the phospholipase C gamma 2 (PLCG2) gene are associated with autosomal-dominant immune dysregulation (ID), manifesting in a broad clinical spectrum. The two primary syndromes linked to PLCG2 variants are PLCγ2-associated antibody deficiency and immune dysregulation (PLAID) and autoinflammatory PLAID (APLAID). These conditions involve overlapping phenotypes of immunodeficiency, autoinflammation, and immune dysregulation. Gain- and loss-of-function (LoF) mutations have been implicated in diverse immunological abnormalities, including recurrent infections, autoimmunity, and susceptibility to herpesvirus infections (1).
Case report: A 4-year-old girl presented with a four-month history of limping gait and swelling in the right knee and upper ankle. Her medical history included recurrent respiratory and cutaneous infections, including multiple episodes of obstructive bronchitis, four instances of community-acquired pneumonia (not radiologically confirmed), recurrent skin infections such as impetigo contagiosa and a herpes simplex virus infection of the outer ear. Additionally, she experienced three episodes of purulent conjunctivitis. None of these infections were severe or required hospitalization. The patient was born to non-consanguineous Russian parents and has two healthy siblings. She was fully vaccinated according to German guidelines. Previous treatments included long-term inhalation therapy for persistent pulmonary symptoms and a six-week course of antibiotic prophylaxis for chronic productive cough. Laboratory evaluations revealed severe neutropenia without evidence of granulocyte-specific antibodies. Immunological testing detected specific antibody deficiency with absent vaccine responses to pneumococcus, tetanus, measles, mumps, rubella, hepatitis B, and varicella while total antibody analysis showed low IgM levels with normal IgA and IgG levels. B cell analysis indicated slight reductions in IgM memory B cells and total memory B cells. T-cell counts and function were normal. Bone marrow biopsy revealed intact hematopoiesis with evidence suggestive of peripheral granulocyte degradation, likely driven by an immune-mediated mechanism. Genetic testing identified a heterozygous 19.7 kB deletion in the PLCG2 gene (NC000016.10:g.81768661_81788375del), classified as a variant of uncertain significance (VUS). The deletion encompasses the 5′-untranslated region, including the promoter and first two exons, which may disrupt translation initiation. The findings suggest a possible contribution of this genetic variant to the patient's clinical presentation.
Conclusion: This case highlights the potential role of a PLCG2 gene deletion in immune dysregulation, with features of humoral immunodeficiency and recurrent infections. While the genetic variant is classified as a VUS, its overlap with known PLCG2-associated conditions suggests a likely pathogenic role. Ongoing parental testing and functional RNA studies are critical to elucidating the impact of this deletion.

Patient Consent: Yes, we received consent.
Funding: None.
Disclosure of Interest: AR: Novartis speaker's fee.

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A48

Recurrent sepsis-like episodes with fever, pain, vomiting and diarrhea

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Pediatric Rheumatology 2025, **23(1):**A48

Introduction: We report a case of an 18-month-old girl with recurrent episodes of sepsis-like presentation with fever, vomiting, pain crises and diarrhea.
During her first episode she also had an urticarial rash, an extensive sinus venous thrombosis (SVT), effusion in hip and temporomandibular joint - as well as myositis of legs and pelvis. Sudden painful swelling (sternal, legs) by suggested subcutaneous bleeding on ultrasound. Extensive infectious work up as well as bone marrow aspiration, lumbar puncture, CT Thorax were unremarkable.
During episodes CRP was elevated only once (up to 10mg/dl), as well as a remarkable leukocytosis up to 70 thousand/µl and intermittent thrombopenia. Interferone signature was strongly elevated (score 281, reference <12,49). Protein C deficiency was detected.
Whole exome sequencing (WES) showed a heterozygous mutation in the PLCG2 gene, c2180G>A, p.(Arg727Gln), a variant of unclear significance (VUS). The mutation is in a strongly preserved region, most probably relevant for function. Therefore the diagnosis of APLAID (autoinflammation and phospholipase C gamma 2-associated antibody deficiency and immundysregulation) was made. Moreover a heterozygous mutation in the RYR1 gene, c13582C>T, p(Pro4528Ser) was found, another VUS. However the patient reacted with prompt fever and elevated CRP to sevofluran. We therefore assume that this variant is responsible for symptoms of malignant hyperthermia in our patient.
Antibiotics and intravenous immunglobulines were not effective in our patient. Prednisolone (1mg/kg) lead to complete remission of symptoms. No effect of Anakinra (up to 7,5mg/kg) was seen. The girl is so far steroid dependent, weaning steroids resulted in relapses. Tofacitinib was started due to high interferone signature, effects will be evaluated. Plasma rich fibrin was injected into temporomandibular joint resulting in reduction of effusion. Therapeutical anticoagulation was given until complete remission of SVT.
Discussion: WES revealed variants of unclear significance in the genes PLCG2 and RYR1. Both of them seem to be causative for our patient´s symptoms. APLAID can present with systemic autoinflammation, interstitial lung disease, enterocolitis, recurrent infections, antibody deficiency and B cell/ NK cell defects (1). In our patient vomiting and enterocolitis are leading symptoms, so far no abnormalities in immune cells were found. If- besides Anakinra -Tofacitinib won´t be effective

either, therapy with calcineurin or TNF alpha inhibitors or even hematopoetic stem cell transplantation might be considered.
Conclusion: Especially in young patients who present with severe, unclear autoinflammatory symptoms, WES should be performed as soon as possible. Sepsis-like presentation with fever, pain, vomiting and enterocolitis can be leading symptoms of APLAID. IL-1-, TNF alpha-, JAK- and Calcineurin- inhibitors are treatment options for steroid dependent cases.

Patient Consent: Yes, parental consent was received.
Funding: No.
Disclosure of Interest: No conflicts.

Reference
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A49

Survey via the GKJR from March 1st to April 15th, 2024, regarding off-label treatment, applications for reimbursement by the payers, and cost-effectiveness audits

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Pediatric Rheumatology 2025, **23(1):**A49

Introduction: The doctor must make his treatment decision based on scientific standards rather than on the approval status. This means a regular confrontation with a deviation from the approval status, an off-label situation.
Objectives: How do German pediatric and adolescent rheumatologists deal with this situation?
Methods: From March 1st to April 15th, 2024, an email survey regarding off-label treatment, applications for reimbursement by the payers, and cost-effectiveness audits was conducted via the *Gesellschaft für Kinder- und Jugendrheumatologie (GKJR)* for the German health system. The survey was sent to 170 GKJR members registered in Germany without differentiating whether they are directly or indirectly involved in outpatient statutory health care.
Results: Responses were received from 54 members. The survey found that in off-label situations, 57% of the responding physicians submit a direct application for reimbursement to the health insurance companies to support their patients; none took the alternative route of a private prescription, for which the patient has to handle reimbursement themselves. It was shown that 54 applications were submitted in the last 12 months. Guidelines. The drugs that were most frequently requested included Adalimumab, Etanercept, and others. The most common reason for the application for off-label use of a medication was a different indication than the one approved. The most common single reason for an application was treatment with Adalimumab for extended oligoarthritis.
It was found that the biggest obstacle for the use of off-label applications was the average time required by the physician, which was 52 minutes per application. The positive and approving response rate for the first request was 92%.
Two members stated that they had been affected by a cost-effectiveness audit.
Conclusion: A lot of german pediatric rheumatologist submit the application for the payment of the off-label-therapy themselves. The greatest help and wish for the GKJR members is a common database for off-label therapy applications. This database can be build using already filed applications, which can be submitted to the GKJR Pharmacotherapy and Guidelines Commission by german pediatric rheumatologists. To build this database the input of the members is required. This means that anyone who submits an off-label application to the health insurance companies should also please send an anonymized copy to pharmakotherapie@gkjr.de to help build the data.

Patient Consent: Not applicable (there are no patient data).
Funding: No.
Disclosure of Interest: No disclosures of interest.

A50

Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS): a conflict between bleeding and thrombosis in lupus erythematosus

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Pediatric Rheumatology 2025, **23(1):**A50

Introduction: Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS) is a rare condition that can occur in the context of systemic lupus erythematosus (SLE). This report presents a case of a 16-year-old female patient relapse of SLE accompanied by LAHPS.
Case Report: The 16-year-old patient initially presented with pseudotumor cerebri, fatigue and muscle pain in 2021. Laboratory findings revealed a tricytopenia, strongly positive ANA (1:3200), and dsDNA antibodies
(>800 IU/ml). She received treatment with methotrexate until 06/23 and hydroxychloroquine until 12/23, both of which could be discontinued upon remission.In 09/24, the patient developed a tendency to bleed, severe hypermenorrhea and fatigue with muscle pain. Laboratory tests again revealed tricytopenia, an ANA titer of 1:1000, and anti-dsDNA antibodies at 650 IU/ml. A significant new finding was proteinuria (3.1 g/g creatinine), leading to a diagnosis of lupus-associated nephritis. Due to the newly developed bleeding tendency, extended coagulation diagnostics were performed. These revealed elevated anticardiolipin and anti-β2-glycoprotein I antibodies, as well as the presence of lupus anticoagulant, consistent with antiphospholipid syndrome (APS). The coagulation was deranged with a INR value of 2.4 and aPTT of 66 seconds. Factor II activity was <5%, confirming the diagnosis of LAHPS. Further testing revealed highly elevated prothrombin antibodies with a titer >100 U/ml.
Due to the severe bleeding tendency, a kidney biopsy was contraindicated, and immunosuppressive therapy was initiated immediately. The patient received an initial methylprednisolone pulse followed by prednisone therapy, furthermore a therapy with mycophenolate and hydroxychloroquine was initiated. Under immunosuppressive therapy, coagulation normalized, and symptoms improved.
Once coagulation normalized, a kidney biopsy was performed without bleeding complications, revealing class II lupus nephritis. In the subsequent course, the patient reported headaches, nausea, and vomiting. A cranial MRI detected a small, recent infarction in the left middle frontal gyrus, likely due to her known APS. Bleeds were not found. An anticoagulant therapy with enoxaparin was initiated.
Conclusion: LAHPS is a rare condition, with approximately 100 cases reported in the literature, and can occur in the context of SLE [1]. Due to its rarity, no standardized treatment protocols exist. Early diagnosis is crucial in patients with severe bleeding tendencies to prevent bleeding complications, and coagulation diagnostics should be promptly performed when new bleeding symptoms arise. The added thrombotic risk from APS significantly complicates therapy and management.

Patient Consent: Yes, I received consent.
Funding: The authors did not receive support from any organization for the submitted work.
Disclosure of Interest: The authors have no conflicts of interest to declare.

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A51

Anifrolumab treatment in monogenic pediatric lupus: a case report

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Pediatric Rheumatology 2025, **23(1):**A51

Background: Variants in UNC93B1 lead to selective hyperactivation of the toll-like receptor TLR7, resulting in the incorrect recognition of the body's own RNA. This triggers uncontrolled production of type I interferons and inflammatory processes, ultimately causing a form of monogenic systemic lupus erythematosus (SLE).
Case Report: We have recently reported the case of a 15-year-old boy with SLE caused by a homozygous variant in UNC93B1 (c.275A>G, p.E92G), presenting with severe hematologic, immunologic, neurologic, and nephrological manifestations1. Multiple treatments (corticosteroids, hydroxychloroquine, mycophenolate mofetil (MMF), cyclosporine, rituximab, ruxolitinib) failed to achieve remission. In October 2023, treatment with anifrolumab, a monoclonal antibody that inhibits the type I interferon receptor (IFNAR), was initiated. Remarkably, renal function stabilized, B cell levels increased, complement factors normalized, C-reactive protein (CRP) levels decreased, and the SLE Disease Activity Index (SLEDAI) significantly reduced. The interferon signature improved but remained elevated. Serious Adverse Event (SAEs), (temporary headaches) were reported, but no significant severe adverse effects were observed.
Conclusion: In this case of monogenic SLE, Anifrolumab appeared to present a personalized targeted therapeutical approach. Further studies of patients with monogenic SLE, are necessary to definitively confirm the long-term safety and efficacy of Anifrolumab in this setting.

Patient Consent: Yes, I received consent.

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A52

From "Atopic Eczema" to polymyositis-systemic sclerosis overlap syndrome requiring mechanical ventilation: a diagnostic odyssey

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Background: Polymyositis-Systemic Sclerosis (PM-SSc) overlap syndrome is a rare autoimmune disease with multisystem involvement. Early recognition is essential for timely and effective treatment. This report details the clinical course of a pediatric patient initially misdiagnosed, emphasizing key diagnostic milestones.
Case Report: A 14-year-old female presented to the University Hospital Leipzig (UKL) with respiratory failure of unknown cause, requiring mechanical ventilation. Her symptoms began six months earlier with skin lesions, initially diagnosed as atopic eczema. Despite treatment with topical corticosteroids and even dupilumab her condition worsened. Additionally, she gradually developed muscle weakness, joint pain, fatigue and unintentional weight loss of 5 kg over four weeks. Difficulty with daily activities such as climbing stairs and opening bottles emerged. One week before admission to UKL the patient experienced severe dyspnea and proximal muscle weakness, requiring hospitalization for hypoxemia and respiratory distress. Initial investigations in the local hospital excluded pulmonary embolism but revealed elevated Troponin T and creatine kinase, suggestive of cardiac involvement. She was intubated, transferred to Leipzig Heart Center and after exclusion of a myocardial pump function disorder subsequently transferred to Pediatric Intensive Care Unit of UKL for further evaluation. Hallmark dermatological findings included (very mild) heliotrope rash, minor Gottron's papules and hyperpigmented mechanic hands (Figure 1). [1]
Neurological assessment confirmed proximal muscle weakness and diminished reflexes. Laboratory tests revealed elevated ANA titers (1:7100) and markedly increased CK (max. 33µkat/l, nv <2,05). Upon this, immunosuppressive treatment was immediately initiated. Histopathological findings of a muscle biopsy in combination with elevated Anti-PM/Scl antibodies later confirmed the diagnosis of PM-SSc overlap syndrome. [2] Treatment included high-dose methylprednisolone pulses, oral prednisolone, methotrexate, mycophenolate mofetil and intravenous immunoglobulin. With this, gradual weaning from invasive ventilation to CPAP via tracheostomy was achieved over several weeks. Intensive rehabilitation, including physiotherapy led to significant improvement in strength and function. The Childhood Myositis Assessment Scale CMAS-Score increased from 11 to 27 within one month and to 44/52 six months later.
Conclusion: This case highlights the diagnostic challenges of PM-SSc overlap syndrome particularly when initial presentations resemble common conditions like atopic eczema. The progression of muscle weakness, refractory skin findings and systemic symptoms underlines the importance of early referral and detailed investigation. Accurate diagnosis and timely intervention are crucial for preventing severe complications such as the necessity of mechanical ventilation or other long-term sequalae to optimize outcomes in such rare pediatric autoimmune diseases.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: None.

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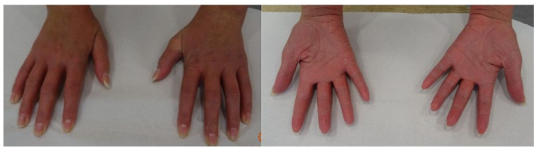

Fig. 1 (Abstract A52). "Mechanics hands" one month prior to rapid detoriation of muscle strenght: Dry, erythematous, rough skin and noticeable hyperkeratosis as well as scaling

A53

Cerebral calcifications and progressive autoimmune features in Spondyloenchondrodysplasia with Immune Dysregulation (SPENCDI): a longitudinal case study

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Introduction: Spondyloenchondrodysplasia with immune dysregulation (SPENCDI) is a rare autosomal recessive disorder caused by biallelic mutations in *ACP5*, encoding tartrate-resistant acid phosphatase type 5 (TRAP). Beyond its established role in bone metabolism, TRAP critically regulates type I interferon signaling. SPENCDI is increasingly recognized as a primary interferonopathy [1, 2, 3], characterized by skeletal dysplasia, progressive immune dysregulation, and autoimmunity, posing significant diagnostic and therapeutic challenges.

Case report: The patient, a 7-year-old child of consanguineous Syrian parents, initially presented with progressive skeletal deformities and growth retardation. Genetic testing prompted the diagnosis of SPENCD. During follow-up over the next two years (until recently), she developed unilateral foot drop, severe fatigue, autoimmune manifestations, including systemic lupus erythematosus (SLE)-like features, proteinuria, hepatopathy, livedo reticularis, vitiligo, acrocyanosis, intermittent headaches, and cerebral calcifications consistent with chronic interferon-mediated inflammation. This emerging phenotype of severe immune dysregulation led us to classify this Spondyloenchondrodysplasia with immune dysregulation (SPENDI). Laboratory findings included markedly elevated interferon scores (maximum 2199, normal <12, [4]), CD169 antigen/cell levels (~20,000–30,000, normal <1400 [5]), elevated erythrocyte sedimentation rate, hypergammaglobulinemia (IgG: 20 g/L), and reduced T-cell counts (CD3: 490 × 10^6/L; CD4: 260 × 10^6/L; CD8: 170 × 10^6/L) without significant functional compromise. Imaging revealed progressive hepatopathy with structural remodeling, and chronic inflammation exacerbated bone pain and muscle fatigue, significantly impairing quality of life.

Given the severe interferon hyperactivation and clinical deterioration, off-label treatment with JAK inhibition is being implemented to mitigate chronic immune dysregulation, based on established protocols for related interferonopathies [2, 3, 6, 7, 8].

Conclusion: This case highlights the intricate interplay between skeletal dysplasia and immune dysregulation in SPENCDI, reinforcing its classification as a type I interferonopathy. JAK inhibitors show promise in addressing immune-mediated complications, underscoring the need for personalized, multimodal therapeutic approaches. Further research into targeted treatments is essential to improve outcomes in SPENCDI and related disorders.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: No COI.

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A54

Association between enjoyment, self-concept, and movement behaviour in adolescents with juvenile idiopathic arthritis

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Introduction: Enjoyment of physical activity (PA), defined as positively valenced emotion directed towards PA, is an attribute of intrinsic motivation. It may increase long-term PA participation by minimizing negative PA experiences and counteracting the development of avoidance. Physical self-concept has been suggested as one factor influencing its perception [1].
Objectives: This study aimed to investigate associations between movement behaviour, PA enjoyment, and self-concept of motor abilities in patients with JIA.
Methods: Data from 10- to 20-year-old patients with JIA recruited in the German multicentre ActiMON study were used. Movements were recorded for eight consecutive days using an ActiGraph accelerometer (model wGT3X-BT) before being classified into sedentary behaviour (SB), light PA (LPA) and moderate to vigorous PA (MVPA). The WHO recommended minimum level of MVPA was considered to be met from an average of ≥60 minutes per day. PA enjoyment was measured using the 16-item Physical Activity Enjoyment Scale (PACES) [2], while physical self-concept of motor abilities (endurance, coordination, strength, flexibility, speed) was assessed with items from the Physical Self-Description Questionnaire (PSDQ) [3]. Statistical analyses were performed using multiple linear regression analyses, taking into account compositional data analysis (CoDA) approaches [4].
Results: 126 patients (mean age 15.0 ± 2.1 years, female 67%, mean disease duration 8 ± 4 years, oligoarthritis 46%, cJADAS-10 2 ± 3, mean PACES score 45 ± 5) fulfilled inclusion criteria of wear time (≥ five days incl. ≥ one weekend day with ≥ 8 hours each). On average, 86% of wear time was spent in SB, followed by 8% in LPA and 6% in MVPA. Time-use composition of movement behaviours was associated with PACES total score. Specifically, a higher total PACES score was significantly associated with less time in SB (relative to LPA and MVPA) (p=0.008) and a higher likelihood of meeting current WHO guidelines (p=0.001). These associations remained statistically significant for both SB (p=0.005) and guideline meeting (p=0.003) after adjusting for age, gender, socioeconomic deprivation, disease activity (cJADAS-10), and season of data collection. Physical self-concept of motor ability (PSDQ, 5 item score) explained a significant amount of variance of PA enjoyment even after controlling for age, gender, socioeconomic deprivation, functional ability (CHAQ), and severity of depressive symptoms (PHQ-9) (p=0.004).
Conclusion: Results of this study suggest a positive association between movement behaviour and PA enjoyment in adolescents with JIA. Fostering a positive motor self-concept may contribute to the development of PA-promoting emotions in JIA, which should be further investigated in longitudinal studies.

Patient Consent: Not applicable (there are no patient data).
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Disclosure of Interest: None declared.

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A55

Unveiling immune heterogeneity in JIA: a multiplex cytokine and principal component approach

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Pediatric Rheumatology 2025, **23(1):**A55

#both authors contributed equally

Background: Juvenile idiopathic arthritis (JIA) comprises heterogeneous subtypes characterized by varying immunopathological mechanisms. A deeper understanding of cytokine profiles among JIA subtypes can aid detecting critical courses earlier in order to refine therapeutic approaches. This study utilized multiplex cytokine analysis to explore cytokine biomarkers in four distinct JIA subtypes and applied principal component analysis (PCA) for data reduction and pattern identification.
Methods: We analyzed serum samples from 289 patients of four JIA subtypes: persistent oligoarthritis (n=65), extended oligoarthritis (n=115), seronegative polyarthritis (n=67), and seropositive polyarthritis (n=42). Forty-five biomarkers were measured simultaneously using ProcartaPlex™ Multiplex Immunoassays (Affymetrix, eBioscience). Variables with over 25% missing data were excluded, and probabilistic PCA was applied to address incomplete datasets. Cytokines were standardized (z-scores) before PCA, which identified principal components (PCs) explaining key variance patterns. Subgroup-specific analyses were conducted to evaluate clinical relevance.
Results: PCA identified seven PCs, explaining 65% of variance. Key findings included: PC1 (Inflammatory cytokines and growth factors) (Fig. 1): Positively loaded with pro-inflammatory markers (e.g., TNF-α, IL-1α, CCL2/MCP-1) and anti-inflammatory markers (e.g., IL-4, IL-13), indicating a mixed cytokine milieu (Fig. 2). Growth factors (e.g., β-NGF, HGF) were also prominent. PC2 (Clinical disease activity): Correlated with clinical parameters such as JADAS27 scores, physician global assessment, and patient-reported outcomes. PC3 (Inflammatory markers): Highlighted systemic inflammation with ESR and CRP as dominant variables.
Other PCs reflected chemokine-mediated immune responses, angiogenesis, and interferon-associated pathways. Notably, PC6 was linked to antiviral immunity, while PC7 related to patient age and disease duration. Distinct cytokine profiles were observed across subtypes (Fig. 2). Extended oligoarthritis exhibited lower systemic inflammation, while persistent oligoarthritis demonstrated elevated pro-inflammatory cytokines as compared to both polyarthritis groups (Fig 1). Subgroup-specific differences in growth factors and chemokines suggested differential tissue involvement and immune regulation.
Conclusion: Multiplex cytokine analysis combined with PCA provides a robust framework to discern immunological patterns in JIA. The heterogeneity in cytokine profiles across JIA subtypes underscores the complexity of its immunopathology. PC1 and PC2 highlight the interplay between inflammation and clinical activity, offering potential biomarkers for subtype-specific stratification. Future research is needed focusing on integrating cytokine profiles with clinical data to enhance diagnostics and personalized therapeutic strategies.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: No conflicts.

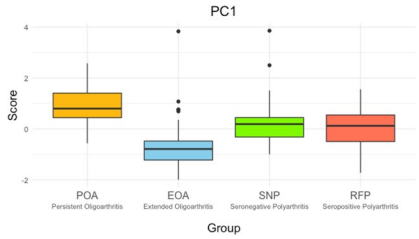

Fig. 1 (Abstract A55). Boxplot of Principal Component 1 (PC1) scores across JIA Subtypes. This figure illustrates the distribution of PC1 scores among four juvenile idiopathic arthritis (JIA) subtypes: Persistent Oligoarthritis (POA), Extended Oligoarthritis (EOA), Seronegative Polyarthritis (SNP), and Seropositive Polyarthritis (RFP). PC1 represents the component primarily associated with inflammatory cytokines. Boxplots display the median, interquartile range (IQR), and outliers for each group, highlighting differences in inflammatory profiles between subtypes

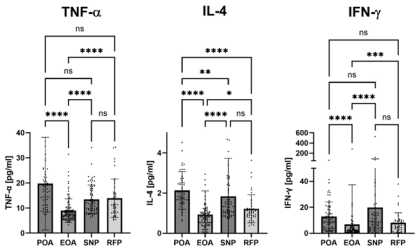

Fig. 2 (Abstract A55). Comparison of key cytokine levels among JIA subtypes. Serum concentrations of selected cytokines (TNF-α, IL-4, and IFN-γ) across four JIA subtypes: Data are shown as boxplots, with whiskers representing the range and dots indicating individual data points. Statistical significance indicated as follows: ns = not significant, *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001

A56

Exploring soluble CD206 as a marker for macrophage-driven inflammation in juvenile idiopathic arthritis subtypes

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Pediatric Rheumatology 2025, **23(1):**A56

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Introduction: In patients with Juvenile Idiopathic Arthritis (JIA) early diagnosis and introduction of appropriate therapy are crucial for improving patient outcomes. Especially in the oligoarticular subtype accurate subtype classification is often delayed. Soluble mannose receptor (sCD206), a macrophage activation marker, has shown promise as a biomarker in inflammatory diseases. In rheumatoid arthritis, sCD206 levels correlate with disease activity, reflect macrophage-driven inflammation, and decrease with effective treatment. Synovial macrophages expressing CD206 are implicated in sustaining joint inflammation. This study explores the potential of sCD206 as a biomarker for differentiating JIA subtypes and monitoring disease activity.
Objectives: To evaluate serum sCD206 levels across JIA subtypes, investigate their relationship with disease activity, and assess their utility in early subtype classification and therapeutic monitoring.
Methods: This cross-sectional study included 283 children (ages 1–18) diagnosed with four JIA subtypes: persistent oligoarthritis (n=65), extended oligoarthritis (n=115), seronegative polyarthritis (n=67), and seropositive polyarthritis (n=42). Serum sCD206 levels were measured using enzyme-linked immunosorbent assay (ELISA). Statistical analysis included mean rank comparisons across subtypes.
Results: Significant differences in serum sCD206 levels were observed between most JIA subtypes ($p<0.05$). Mean serum sCD206 levels were highest in the seropositive polyarthritis subtype and lowest in extended oligoarthritis. Specifically, extended oligoarthritis showed significantly lower levels compared to persistent oligoarthritis, seronegative polyarthritis, and seropositive polyarthritis ($p<0.0001$). No significant differences were noted between seronegative and seropositive polyarthritis subtypes. These findings suggest that sCD206 levels vary among JIA subtypes, particularly between oligoarthritis and polyarthritis groups.
Conclusion: Serum sCD206 levels demonstrate significant variation across JIA subtypes, with the highest levels observed in seropositive polyarthritis, consistent with a macrophage-driven inflammatory phenotype. While sCD206 shows promise in distinguishing certain JIA subtypes, its utility as a standalone biomarker is limited by overlap between subtypes such as seronegative and seropositive polyarthritis. Further studies are warranted to evaluate its integration with other biomarkers and its role in therapeutic monitoring.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: No conflicts.

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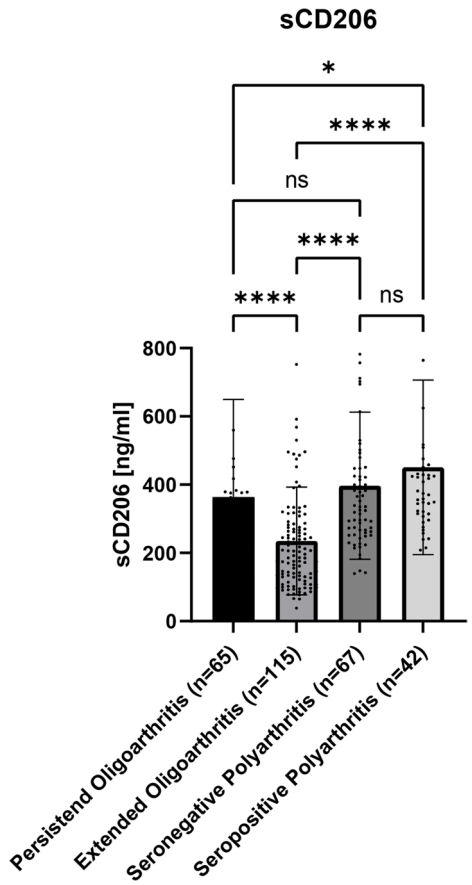

Fig. 1 (Abstract A56). See text for description

A57

Long-term methotrexate treatment does not impair pulmonary function in children and adolescents with juvenile idiopathic arthritis

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Pediatric Rheumatology 2025, **23(1):**A57

Objectives: Methotrexate (MTX) is the standard treatment for children with juvenile idiopathic arthritis (JIA). However, concerns about tolerability are frequently raised due to the sometimes serious side effects of MTX observed in adults. Therefore, we examined longitudinally the effects of MTX on pulmonary function and transaminases in the hitherto largest reported cohort of JIA patients treated with MTX.
Methods: In a single center over a 28-year period, 274 patients with JIA were treated with MTX, and annual pulmonary function tests (PFTs) were performed. The development of transaminases was retrospectively analyzed by chart review. Values were compared by paired t-test.
Results: Eighty-five of 274 patients were male (31%), and 189 were female (69 %). The median age of disease onset was 7.0 (range: 0.8–17.4). The median duration of MTX therapy was 37.5 months (range: 1–168).
Longitudinal assessment of PFT revealed no significant change of FEV1, FVC, TLC, MMEF, RV, and DLCO, even under long-term treatment with MTX. None of our patients developed any MTX-associated lung disease. Hepatic side effects manifested as transient elevations in liver enzymes, with alanine aminotransferase (ALT) levels exceeding twice the upper limit of normal in 63 patients (31%), and in 57 of these cases, the elevation surpassed threefold. In 24/63 (38%) patients, this required a temporary pause of 2–4 weeks, and in 13/63 children (21%) the MTX dose was reduced. In 9/63 patients (14%) medication was switched, and also 9/63 patients were observed in terms of a watchful waiting strategy. In five patients (8%), MTX-therapy was stopped, and no other systemic therapy needed to be started.
Conclusion: In children with JIA, long-term treatment with MTX appears to be safe regarding the pulmonary outcome. However, liver affection frequently requires interventions, including discontinuation of the drug.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: No conflicts.

A58

Clinical presentation of Systemic Lupus Erythematosus (SLE) in a two year old boy with pathogenic variant in nras. what's the final diagnosis?

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Pediatric Rheumatology 2025, **23(1):**A58

Introduction: Initial presentation with macrohematuria, elevated temperature (38°C), and symptoms of an upper respiratory tract infection. Laboratory findings showed anemia, thrombocytopenia, and leukocytosis. Sonographically, an enlarged left kidney was visible. Eight months later, admission with recurrent (every 2 weeks) painful swelling of the hands and legs for the past 6 months. Temporary refusal to walk. Continued anemia, thrombocytopenia, and leukocytosis. Recurrent purpura-like skin lesions. ANA 1:160.
Admission findings: good general condition. Abdomen: distended, no masses. Lymph node status: smaller cervical and inguinal lymph nodes palpable. Gait with possibly slight protective limping. Joint status unremarkable. Skin: no rash. Temperature: 36.7°C.
Objectives: To race awareness on monogenic causes of SLE.
Methods: Case report, discussion of mutations.
Results: Hemoglobin: 9.6 mg/dl, platelets 66,000/µl, leukocytes: 21,180/µl. ANA 1:640, anti-ds-DNA antibodies positive (in Blot/IFT/Farr assay), C3 0.77 g/l (0.8–1.5), C4 0.04 g/l (0.12–0.42), IgG 22.95 g/l (5–13), positive Coombs test, without signs of hemolysis (haptoglobin, LDH, and uric acid normal). Slightly elevated double-negative T cells. Vitamin B12 slightly elevated (1128 pg/ml). Increased B cells. sFasL 334 pg/ml (normal range <250 pg/ml. High probability of Fas mutation if sFasL >800 pg/ml. Sonography: hepatosplenomegaly, enlarged intra-abdominal lymph nodes. Bone marrow puncture: unremarkable findings. No evidence of leukemia. Kidney biopsy: changes consistent with lupus nephritis class III and V. Type 1 interferon signature moderately elevated. WGS: pathogenetic Variant in NRAS (c.38G>A), VUS in TNFAIP3.
The clinical and laboratory findings are consistent with SLE. Due to the atypical age and male gender, genetic testing was initiated on suspicion of monogenic lupus erythematosus. Genetic testing revealed a pathogenic variant in NRAS and VUS in the TNFAIP3 gene. Germline variants primarily associated with Noonan syndrome or RASopathy. Somatic variants described as a cause of ALPS IV. Missense variant in the TNFAIP3 gene (c.1630A>G), VUS associations with SLE described.

ALPS was ruled out. Currently, no evidence of lymphoma or JMML. Since pathogenic changes in the NRAS gene can be associated with various diseases and there are differences depending on whether they are somatic or germline variants, further investigations are currently underway (contact with Freiburg CCI - EWOG study center and human genetics in Dresden). Under treatment with prednisolone, hydroxychloroquine, mycophenolate mofetil 400 mg 1-0-1 (equivalent to 1,200 mg/m² BSA), good general condition.
Conclusion: In the unusual constellation of SLE (male gender and young age), genetic causes must be considered, and molecular diagnostic testing should be initiated.

Patient Consent: Yes, consent received.
Funding: None.
Disclosure of Interest: None.

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A59

Clinical presentation of *RELA*-associated Autoinflammatory Disease (RAID)

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Pediatric Rheumatology 2025, **23(1):**A59

Background: Variants in *RELA* lead to dysregulated NF-kB-mediated inflammation. Increased TNF-dependent apoptosis of mucosal cells and enhanced TLR7-driven secretion of type I/III interferons (IFNs) seem to be playing a leading role in disease pathophysiology [1,2]. Published cases are few, and strategies for diagnostic and therapeutic approach have yet to be implemented.
Case report: We compare three non-related cases of RAID. Case 1: 17-year-old girl of German-Turkish descent with a novel heterozygous variant of unknown significance c.1515_ 1516 del; p.(Ala507Profs*25) presenting with recurrent oral and genital ulcers and vaginal aphthae, facial rash, headaches and fatigue. Symptoms show little to no response to immunosuppressive therapy. Case 2: 2-year-old boy with a heterozygous, pathogenic *de novo* variant c.592C>G; p.(Arg198*) presenting with recurring fever episodes from four months of age. As of now, no immunosuppressive therapy has been administered. Case 3: 18-month-old boy with a heterozygous, likely pathogenic *RELA* variant c.506C>G; p.(Ser169*) presenting with early onset severe enteropathy with zinc deficiency, lymphadenopathy, hypothyroidism, severe eczema, and failure to thrive. Multimodal treatment strategy including dietary modification to amino acid-based formula and both local and systemic immunomodulatory medication, including dupilumab, resulted in marked clinical improvement across gastrointestinal and dermatological involvement as well as systemic parameters.
Conclusion: RAID should be considered a differential diagnosis in patients presenting with features of autoinflammatory disease. Management strategies must be carefully tailored to each patient's clinical manifestations. The potential role of patient-specific cytokine profiling or gene expression profiles in guiding therapy remains unclear and warrants further investigation. Collaborative efforts at both national and international levels are crucial for advancing the understanding and treatment of RAID, thereby ensuring better outcomes for those affected.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: None.

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A60

Effects of canakinumab dose adjustments on disease control of monogenic autoinflammatory diseases – interim results of the reliance registry

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Pediatric Rheumatology 2025, **23(1):**A60

Introduction: Treatment of autoinflammatory diseases (AID) with the interleukin-1β inhibitor canakinumab (CAN) has been shown to be safe and effective in controlled clinical trials and real-world setting.

Objectives: The RELIANCE registry investigates long-term safety and effectiveness of CAN in the treatment of patients with cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) or tumor necrosis factor receptor-associated periodic syndrome (TRAPS) in routine clinical practice. This interim analysis examines dose adjustments of CAN with regards to a treat-to-target strategy.

Methods: RELIANCE is a prospective, non-interventional study in Germany, which enrolled patients with confirmed diagnosis of AID, routinely receiving CAN. Efficacy and safety parameters were assessed at baseline and at 6-month intervals. The recommended starting dose (SD) of canakinumab was 150 mg (>40 kg body weight) or 2 mg per kg body weight (≤40 kg) administered subcutaneously every 8 weeks for CAPS patients and every 4 weeks for patients with FMF, TRAPS or HIDS/MKD. Less than SD (<SD) was defined as <87.5% of SD and higher than SD (>SD) was defined as >112.5% of SD.

Results: This interim analysis includes data from N=268 AID patients including 45.1% pediatric (2–18 years) patients enrolled between September 2017 and June 2023. The median duration of CAN treatment before enrollment was 2 years (0−15 years).

During the study, the proportion of patients receiving a dose higher than SD increased from 33.6% (baseline) to 54.8% (month 30) and 80.0% (month 60) (Table 1). Control of disease activity was comparable across all three dosing groups during this study: More than 90% of patients had no or mild/moderate disease activity across all dose categories and time points as assessed by investigators (PGA; data for month 60 not yet available) and patients (median VAS scores between 1.0 and 3.0) (Table 1).

Non-serious adverse drug reactions (nsADR) were more frequent in the >SD group (44.2% of patients) than in the <SD (24.6%) or SD group (20.5%). While no patients in the SD group experienced serious adverse drug reactions (SADR), 7.2% and 8.4% of patients in the <SD and >SD groups experienced SADR, (p=0.783; chi-square test: not statistically significant) (Table 1).

Conclusion: This interim analysis of the RELIANCE study confirms safety and efficacy of long-term treatment with canakinumab. An increasing proportion of patients received higher doses over the course of the study, reflecting the implementation of a treat-to-target strategy.

Patient Consent: Yes, I received consent.

Funding: This study was funded by Novartis Pharma AG.

Disclosure of Interest: Jasmin B. Kuemmerle-Deschner: has received grant/research support and speaker fees from Novartis and Sobi; and is a consultant of Novartis and Sobi. Joerg Henes has received grant/research support from Novartis, Roche, Sobi; is a consultant of Novartis; and has contributed to speakers bureaus with AbbVie, AstraZeneca, BMS, Boehringer-Ingelheim, Chugai, Janssen, Novartis, Pfizer, GSK, Sobi, Roche, UCB. Anne Pankow has received study support from Novartis. Tilmann Kallinich has received research support from Novartis.

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Ioana Andreica has contributed to speakers bureaus with AbbVie, Chugai, Novartis, UCB, MSD, Lilly, Sobi, AstraZeneca, Amgen, Pfizer and Gilead; received consultant fees from AstraZeneca and UCB; is a consultant for AbbVie, Chugai, Novartis, UCB, Galapagos, Takeda, AstraZeneca, Lilly, Boehringer Ingelheim, Amgen and Sobi. Michael Borte has received grant/research support from Pfizer, Shire, and Novartis. Martin Krusche has received study support from Novartis. Michael Fiene has received study support from Novartis. Norbert Blank has received grant/research support from Novartis and Sobi; and is a consultant of Novartis, Sobi, Lilly, Pfizer, AbbVie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim and Roche.

Table 1 (Abstract A60). Overview of CAN dosing, disease activity and safety in the RELIANCE study across all study indications (*N*=268 patients)

	Baseline (*n*=265)*			Month 30 (*n*=120)*			Month 60 (*n*=17)*		
CAN dose category[1]	< SD	SD	> SD	< SD	SD	> SD	< SD	SD	> SD
n (% of patients)	8 (3.3)	152 (63.1)	81 (33.6)	19 (18.3)	28 (26.9)	57 (54.8)	2 (13.3)	1 (6.7)	12 (80.0)
Investigator's assessment of disease activity (PGA), n (% of patients)									
Absent	29 (59.2)	9 (25.7)	28 (37.8)	13 (76.5)	4 (66.7)	22 (62.9)	n.a.	n.a.	n.a.
Mild/moderate	15 (30.6)	25 (71.4)	40 (54.1)	4 (23.5)	2 (33.3)	13 (37.1)			
Severe	3 (6.1)	0 (0.0)	4 (5.4)	0 (0.0)	0 (0.0)	0 (0.0)			
Not done	2 (4.1)	1 (2.9)	2 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)			
Missing	20	38	21	12	22	23			
Patient's assessment of disease activity									
(VAS score 0-10), median	2.0	2.0	3.0	1.0	2.0	1.0	2.0	n.a.	1.0
(min.; max.), n	(0.0;10.0, *n*=66	(0.0; 10.0), *n*=71	(0.0; 10.0), *n*=93	(0.0; 9.0), *n*=27	(0.0; 6.0), *n*=26	0.0; 8.0), *n*=49	(0.0; 5.0), *n*=3		(0.0; 4.0), *n*=12
	Safety (interim analysis cut-off date December 2023), all patients (*N*=268)								
	< SD (*n*=69)		SD (*n*=73)		> SD (*n*=95)		Dose missing (*n*=31)		
Patients with nsADR, n (%)	17 (24.6)		15 (20.5)		42 (44.2)		8 (25.8)		
Patients with SADR, n (%)	5 (7.2)[#]		0 (0.0)		8 (8.4)[#]		1 (3.2)		

*Patients with baseline, month 30 and 60 visits yet documented. [1]Body weight > 40kg: Standard dose is 150 mg per 8 weeks for CAPS and 150 mg per 4 weeks for FMF, TRAPS and HIDS/MKD. Body weight ≤40 kg: Standard dose is 2 mg per kg per 8 weeks (CAPS) or per 4 weeks (FMF, TRAPS and HIDS/MKD). Less than SD (<SD) defined as <87.5% of SD and greater than SD (>SD) defined as >112.5% of SD

[#] Comparison of SADR rates between <SD and >SD groups showed no statistically significant difference (p=0.783; chi-square test). n.a.: not annotated (data not yet available); nsADR: non-serious adverse drug reactions; PGA: physician global assessment; SADR: serious adverse drug reactions; SD: recommded starting dose; VAS: visual analogue scale (range 1-10)

A61

A rare case of panniculitis: Nemo-Deleted exon 5–autoinflammatory syndrome- (NEMO-NDAS)

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Pediatric Rheumatology 2025, **23(1):**A61

Background: NF-kB- essential- modulator (NEMO) plays an important role in the immune response of the adaptive and innate immune system as well as in inflammation. Mutations in *IKBKG*-gene typically lead to the NEMO- deficiency syndrome with anhidrotic ectodermal dysplasia und immunodeficiency. Splice- mutations with loss of exon 5 of the *IKBKG*-gene lead to activation of NF-kB and systemic inflammation with panniculitis: NEMO-Deleted exon 5 Autoinflammatory Syndrome (NEMO-NDAS). There are only few patients described in the literature. Here we describe the first case in Germany.
Case report: A 3- year old girl of African descent presented initially in our clinic at the age of 8 months with recurrent panniculitis. Episodes of recurrent subcutaneous nodules evolving the entire body except for the face occurred irregularly since the age of 2 months. Initial skin biopsy was consisting with lobular panniculitis. The CBC at presentation showed normal values for leukocytes, hemoglobulin and platelets. Due to recurrent panniculitis an autoinflammatory syndrome was suspected. Initial gene panel analysis for autoinflammatory syndromes did not reveal any causative gene mutation except for a variant of unknown significance in the *NLRP3*-gene. At the age of 16 months the patient developed high fevers, extensive panniculitis, lymphadenopathy, hepatosplenomegaly with elevated liver enzymes and pancytopenia. Biopsies of lymph node, liver and bone marrow did not show evidence for a malignancy and were suggestive for non-Langerhans cell histiocytosis. Due to the high clinical suspicion of systemic autoinflammation the patient was treated with a pulse corticosteroid therapy and continued on oral prednisolone afterward. Under this therapy the patient improved clinically with resolution of lymphadenopathy, panniculitis and pancytopenia and normalization of liver enzymes. Second genetic testing revealed a pathogenic variant in intron 4 of the *IKBKG*-genes, confirming the diagnosis of NEMO-NDAS.
Conclusion: NEMO-NDAS is a rare autoinflammatory syndrome, which should be considered in patients with recurrent panniculitis.

Patient Consent: Yes, I received consent.
Funding: No external funding.
Disclosure of interest: No disclosures.

A62

APDS masquerading as growth failure and oligoarthritis

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Introduction: Activated phosphokinase δ syndrome (APDS) is a rare inborn error of immunity with a heterogeneous clinical picture.
Objectives: To illustrate the spectrum of signs and symptoms and organ involvement of APDS type 1 in order to shorten diagnostic delay, and possibly offer targeted treatment to affected patients.
Methods: Patient report, presentation of study data, and review of the literature.
Results: A 3 year-old with growth retardation and lymphadenopathy was referred to the paediatric rheumatologist for evaluation. He presented with 4 inflamed joints compatible with oligoarthritis, and lymphadenopathy and marked hepatosplenomegaly. Evaluation of failure to thrive revealed inflammatory bowel disease. Laboratory results were also notable for bicytopenia and hypogammaglobulinaemia, as well as an elevated IgM. Retrospectively this child had suffered from recurrent upper respiratory infections not requiring hospital admission. In whole exome sequencing the most frequently reported pathogenic gain of function variant for APDS1 (E1021K in p110δ) was identified. Patient management includes immunoglobulin substitution, antibiotic prophylaxis, selective PI3Kδ inhibition. Definite treatment may be offered via hematopoietic stem cell transplant.
Conclusion: Awareness for APDS, although a rare immunological entity, should be known to the paediatric rheumatologist, haematooncologist and other specialities in charge of patients with signs of immune dysregulation and inflammation, especially when individuals also have an infection susceptibility.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: Universitaetsklinikum Carl Gustav Carus, TU Dresden is the German Site for the National Study Center for both the Phase III and OLE studies by Pharming between 2021–2024.

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A63

Osteitis Fibrosa Cystica ("Brown Tumor") due to primary hyperparathyroidism: a rare differential diagnosis for bone and joint pain in adolescents

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Pediatric Rheumatology 2025, **23(1):**A63

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Introduction: Bone and joint pain in children and adolescents is often attributed to inflammatory rheumatologic conditions. However, non-inflammatory etiologies, such as metabolic, neoplastic, or traumatic disorders, must also be considered. Primary hyperparathyroidism, though rare in pediatric populations, is a clinically significant metabolic cause. It is typically due to a parathyroid adenoma, which leads to excessive parathyroid hormone (PTH) secretion, resulting in increased osteoclast activity, bone resorption, and skeletal demineralization. Advanced cases may manifest as osteitis fibrosa cystica, or brown tumor, a localized bone lesion characterized by osteoclast proliferation, fibrosis, and hemosiderin deposition. These lesions can mimic neoplastic or cystic processes on imaging, complicating diagnosis.
Case Description: A 14-year-old female presented with chronic, bilateral, activity-related knee pain persisting for over a year. Symptoms lacked inflammatory features such as swelling, warmth or morning stiffness. Initial sonography was unremarkable and MRI findings indicated tibial and femoral bone marrow edema, consistent with a stress reaction. Despite extensive workup, no rheumatologic diagnosis was established.
Over time, the patient experienced pain and swelling in her hand after minor trauma. An external X-ray identified a cystic lesion, prompting re-evaluation by a pediatric radiologist. Imaging revealed severe osteopenia, subperiosteal bone resorption and acroosteolysis, hallmark findings of hyperparathyroidism. MRI findings confirmed the presence of a brown tumor. Laboratory tests supported the diagnosis, showing elevated calcium (3.6 mmol/L; normal 2.2–2.6), low phosphate (0.8 mmol/L; normal 1.0–1.5), markedly elevated PTH (111 pmol/L; normal 1.6–6.9), and elevated alkaline phosphatase (17 µkat/L; normal 1.1–6.5). Neck ultrasound identified a parathyroid adenoma, which was histologically confirmed after surgical excision. Postoperatively, serum calcium normalized and supplementation with calcium and vitamin D improved skeletal mineralization. Symptoms, including the brown tumor, resolved.
Conclusion: This case highlights the importance of considering metabolic disorders like primary hyperparathyroidism in the differential diagnosis of unexplained bone and joint pain. Early detection through basic laboratory tests such as serum calcium and alkaline phosphatase can significantly expedite diagnosis and treatment. Revisiting imaging studies with a focus on metabolic patterns is crucial for recognizing rare conditions. Incorporating routine metabolic assessments into the diagnostic workup for persistent bone pain is a simple yet effective strategy to prevent diagnostic delays and optimize outcomes in conditions such as osteitis fibrosa cystica.

Patient Consent: Yes, I received consent.

Funding: None.
Disclosure of Interest: No COI.

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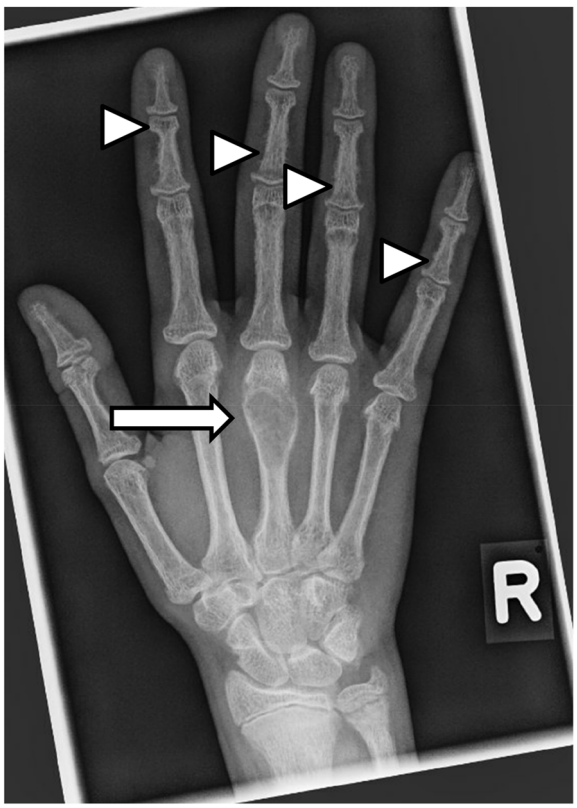

Fig. 1 (Abstract A63). X-Ray of the right Hand after the reportet minor trauma. Arrow: Cycstic lesion. Triangles: subperiosteal bone resorption and acroosteolysis

A64

Effects of a janus kinase (JAK)1/3-inhibition with tofacitinib on T cells, activated under differing inflammatory conditions

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Introduction: The JAK1/3-inhibitor tofacitinib is licensed for a variety of inflammatory diseases, including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis and ulcerative colitis. The anti-inflammatory effects of tofacitinib are mediated by inhibition of a broad spectrum of cytokine receptors. Secondary effects of the cytokine receptor inhibition on T cell activation and proliferation, however, are less well investigated.
Objectives: An explorative analysis was set up in ulcerative colitis patients and healthy controls to investigate the effects of

JAK1/3-inhibition on activated T cells in a Th1-, Th17-, or Treg-promoting cytokine milieu *in vitro*.
Methods: Peripheral blood mononuclear cells (PBMC) of ulcerative colitis patients (n=11) and healthy controls (n=12) were incubated with T cell receptor activating anti-CD3/CD28-antibodies in a Th1-promoting (Interleukin (IL)12, IL2, Interferon (IFN), anti-IL4-antibodies), Th17-promoting (IL1b, IL23, IL6, TGF, anti-IFN-antibodies, anti-IL-4-antibodies) or regulatory T cell (Treg)-promoting (IL2, TGF, IL10, anti-IL4-antibodies, anti-IFN-antibodies) cytokine milieu in the absence or presence of tofacitinib (40 ng/ml). CD4+ T lymphocytes were characterized by flow cytometry, cytokine concentrations in cell culture supernatants were assessed by a flow cytometry-based multiplex assay, and the suppressive capacity of isolated Treg was determined in co-culture experiments with autologous effector cells.
Results: The Th17- and Treg-promoting cytokine milieu induced an up-regulation of the CC motif chemokine receptor (CCR) 6 expression, which was further enhanced by JAK1/3-inhibition. Furthermore, tofacitinib induced a down-regulation of the IL-2-receptor (CD25) and the IL-7-receptor -chain (CD127), independent of the cytokine milieu, whereas the amount of proliferating, Ki67-expressing CD4 T cells was not altered. The secretion of IL5, IL9, IL10 and IL13 by the anti-CD3/CD28-antibody stimulated PBMC was significantly inhibited by tofacitinib, independent of the surrounding cytokine milieu. The secretion of IL2 was enhanced by tofacitinib upon T cell activation without further cytokine stimulation. This effect, however, was abrogated by a Th17-promoting cytokine milieu. Furthermore, tofacitinib reduced the secretion of TNF and IL22 in a Th17- or Treg-promoting cytokine milieu, but not under Th1-stimulating conditions. Whereas tofacitinib had no effect on the suppressive function of Treg in a Th17-promoting cytokine milieu, the effects of the Treg-promoting cytokine milieu were abrogated by JAK1/3-inhibition. No differences were found between ulcerative colitis patients and healthy controls.
Conclusion: Whereas JAK1/3-inhibition effectively suppresses inflammation in a variety of diseases, it also inhibits the secretion of the cytokines IL10 and IL22, playing roles in the regulation of inflammation and tissue regeneration. Furthermore, JAK1/3-inhibition with tofacitinib abrogates the effects of a Treg-promoting cytokine milieu.

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Disclosure of Interest: The authors declare that they have no competing interests.

A65

From recurrent erythema nodosum to psychogenic purpura: diagnostic challenges in gardner-diamond syndrome

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Introduction: Psychogenic purpura, also known as Gardner-Diamond syndrome, autoerythrocyte sensitization, or painful bruising syndrome, is a rare condition characterized by largely unexplained, painful bruises on the extremities or face, triggered by stress. It is frequently described in young women with a vulnerable psychological profile or psychiatric comorbidities. This report discusses the diagnostic complexity of a case initially presenting as recurrent erythema nodosum (EN), later recognized as Gardner-Diamond syndrome, emphasizing the interplay between somatic and psychosomatic factors.
Case Description: A 17-year-old female presented with recurrent EN localized to the left wrist, first documented in 2019 (Fig. 1). A biopsy performed upon reoccurrence showed relatively mild inflammation with dermal perivascular lymphocytic and neutrophilic dermatitis with septal panniculitis, which is overall consistent with EN. Over time, however, the recurrent lesions became chronic, and transitioned to persistent hematoma-like, painful ecchymoses of the entire arm (Fig 2). Extensive evaluations, including radiologic, autoimmune, infectious, and genetic workups, were inconclusive. Symptoms were resistant to topical or systemic corticosteroids, potassium iodide, and dapsone. Pain relief could not be achieved even with opioids or anticonvulsants. A discrepancy between reported severe pain and minimal functional impairment was noted in the course of disease. Repeated deep biopsies revealed rather discreet changes with focal hemorrhage and necrosis and only minor inflammatory changes, suggestive of Gardner-Diamond syndrome. During a prolonged inpatient evaluation, multidisciplinary management included psychosomatic assessment. This revealed a secondary gain related to stress from her apprenticeship in customer retail and recurrent absenteeism due to EN. Psychosomatic contributors and hormonal fluctuations were implicated in the evolution of her condition. No signs of intentional factitia were observed. Explanation of this psychogenic purpura to the patient and cessation of somatic diagnostic and treatment resulted in complete remission.
Conclusion: This case underscores the clinical and histopathological challenges of EN(-like) lesions as a first manifestation of psychogenic purpura, highlighting the diagnostic pitfalls posed by this condition. The overlap increases the complexity of diagnosis and treatment, as EN, with its potential serious underlying causes, required thorough exclusion, while Gardner-Diamond syndrome symptoms could be exacerbated by extensive diagnostic attention to somatic causes. The lack of obvious factitious behavior, failure of analgesics, and identification of secondary stressors reinforced the diagnosis of Gardner-Diamond syndrome. Multidisciplinary care, including psychosomatic support, was pivotal. Gardner-Diamond syndrome should be considered in patients with atypical chronic panniculitis and unexplained bruising, particularly in young women with psychosocial stressors or vulnerable psychological profiles. Effective management requires balancing thorough diagnostic evaluation with psychosomatic support to prevent symptom exacerbation.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: No COI.

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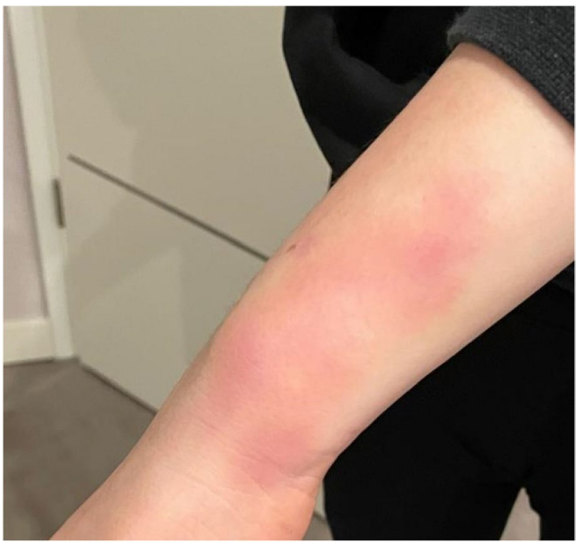

Fig. 1 (Abstract A65). Painful and tender, erythematous nodules with smooth surface suggestive of EN in 2023

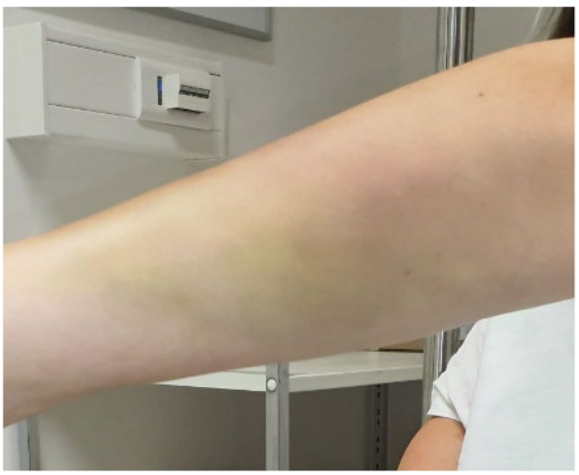

Fig. 2 (Abstract A65). Spontaneous, painful bruises and purpuric lesions suggestive of Gardner-Diamond-Syndrome in 2024A66

Type-I-interferonopathies: neurology meets rheumatology – phenotype description and treatment approach for rnaset2-deficient cystic leukoencephalopathy

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Pediatric Rheumatology 2025, **23(1):**A66

Introduction: Type-I-Interferon (IFN-I) is a critical antiviral cytokine that induces a broad range of antiviral effector genes, inhibits cellular transcription, translation, and proliferation, enhances cross-presentation, and drives T cell expansion. However, chronic or constitutive IFN-I release can lead to severe autoinflammation, particularly in the central nervous system (CNS). Type-I-interferonopathies, first described as a distinct disease group in 2011, now include over 40 monogenic disorders [1].

A specific subgroup with predominantly neurological phenotypes is Aicardi-Goutières-Syndrome (AGS), which typically causes significant neurological deterioration within the first year of life. RNASET2 deficiency, an ultra-rare disorder, shares similarities with AGS and closely resembles the neurological phenotype of congenital cytomegalovirus (CMV) infection [2, 3].

Objectives: To describe the phenotype of RNASET2 deficiency in detail and share the initial treatment outcomes with tofacitinib in an individual therapeutic trial.

Methods: The phenotypic characterization included 19 patients with genetically confirmed RNASET2 deficiency. Data were collected via a custom questionnaire, incorporating information from medical publications, collaboration partners, and the authors' medical records and follow-up examinations. Detailed analyses were performed on MRI and CT scans from 13 patients, with blood and cerebrospinal fluid (CSF) investigations conducted in 7 patients.

Results: RNASET2-deficient cystic leukoencephalopathy typically presents within the first year of life. Affected infants often exhibit muscular hypotonia and absent or severely delayed motor development. Approximately half of the patients experience epileptic seizures. During disease progression, a reduction in head circumference is observed, indicative of primary or secondary microcephaly. MRI findings commonly reveal calcifications, temporopolar cystic lesions and brain atrophy, predominantly affecting the thalamus and hippocampus.

Laboratory findings indicate that nearly all patients exhibit antinuclear antibodies, with some also testing positive for double-stranded DNA antibodies. The interferon score in blood is elevated in only a subset of patients. However, CSF analysis reveals pleocytosis in approximately half of the cases, and all tested patients demonstrate elevated neopterin levels.

A two-year-old patient was treated with tofacitinib as part of an individual therapeutic trial. After 12 months of follow-up, stabilization of neurological development was observed, along with a reduction in autoimmune phenomena in both blood and CSF.

Conclusion: RNASET2 deficiency, a rare type-I-interferonopathy resembling congenital CMV infection, typically presents in infancy with hypotonia, delayed motor development, seizures, and progressive microcephaly. MRI findings often show calcifications and atrophy in the thalamus and hippocampus, while laboratory tests reveal antinuclear antibodies and elevated neopterin in CSF. Treatment with tofacitinib in a two-year-old patient stabilized neurological development and reduced autoimmune markers after 12 months.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: We have nothing to declare.

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A67

Time is brain? The crucial role of early diagnosis and treatment initiation with JAK Inhibition for an infant with Type 1 interferonopathy Aicardi Goutières Syndrome 7

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Introduction: Aicardi Goutières Syndrome type 7 (AGS7) is a rare, early-onset encephalopathy caused by mutations in the *IFIH1* gene. It is characterized by chronic upregulation of type 1 interferon (IFN) and resultant tissue damage. Janus Kinase (JAK) plays a critical role in type 1 IFN signaling, making JAK inhibition (JAKi) with Ruxolitinib (RXL) a potential treatment strategy for AGS [1, 2, 3].
Case report: We document the case of a male neonate diagnosed with AGS7 presenting with hypotrophy, petechiae, elevated bilirubin, and severe multi-organ involvement shortly after birth. The diagnosis was confirmed through trio-exome sequencing. RXL treatment was initiated at 4 months, with dosage adjustments based on growth and subclinical interferon-stimulated gene (ISG [4]) score relapses.
Results: Over 24 months of RXL therapy, the patient showed marked improvement in developmental domains, liver function tests (LFTs), and soluble interleukin 2 receptor (sIL2R) levels. The ISG score decreased significantly, though two relapses were noted without clinical correlation. Magnetic resonance imaging (MRI) showed stable leukodystrophy without new hyperintensities, calcification, or generalized atrophy. The patient achieved milestones with only moderate motoric developmental impairment and good social interactions. Adverse events were mild and transient.
Conclusion: Early initiation of high-dose RXL was well tolerated and associated with clinically mitigated disease progression, rapid control of hepatitis, and achievement of developmental milestones without regression. Despite low cerebrospinal fluid (CSF) -RXL levels, sufficient inhibition of neurological deterioration was observed. However, ISG score relapses without clinical correlates occurred despite JAKi therapy. Future research should focus on identifying and validating biomarkers for treatment guidance and evaluating RXL's safety/benefit profile in AGS through larger, long-term studies. Additionally, the potential benefits of even earlier JAKi initiation warrant investigation.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: No COI.

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A68

New therapeutic approach for difficult to treat systemic-onset JIA: a case report

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Background: Systemic juvenile idiopathic arthritis (sJIA) is a complex, heterogeneous disease characterized by systemic inflammation and chronic arthritis and an unpredictable clinical course. Although Interleukin-1 (IL-1) and IL-6 blockers have significantly improved outcomes of sJIA, a substantial proportion of patients do not achieve optimal disease control. TNF-inhibitors can provide improvement in patients with predominant arthritis, but are less effective in controlling systemic manifestations. Consequently, patients with refractory course of sJIA require an individualized management using alternative approaches.
Herein we describe a patient with sJIA failing initial treatment with anti-IL-1 and -IL-6, who was successfully treated by combination of two biologicals and methotrexate. Furthermore, we illustrate the course of IL-18 levels in relation to disease activity.
Case presentation: A female patient of Turkish descent presented at age 16 months with antibiotic resistant fever, polyarthritis and a volatile maculopapular rash. Laboratory findings showed leucocytosis and significantly elevated inflammatory markers, including serum amyloid A, ferritin, serum calprotectin and IL-18. Besides hepatosplenomegaly, she did not show any signs of other organ involvement. After exclusion of infectious, neoplastic and autoimmune diseases, she was diagnosed with systemic juvenile idiopathic arthritis. Genetic testing remained without known pathogenic variants. Initial treatment with methylprednisolone pulses, followed by oral prednisolone was associated with rapid clinical improvement. After tapering steroids she flared with fever and painful polyarthritis. We started anti-IL-1 therapy with anakinra, up to 9 milligram per kilogram/day, but remission without steroids was not achieved. The patient then was switched to anti-IL-6 therapy with tocilizumab, which was followed by significant improvement of systemic inflammation and arthritis, as well. Unfortunately, the patient experienced a severe anaphylactic reaction after the third infusion in her home country, where she was switched back to anakinra along with colchicine and methotrexate, failing to reach steroid-free remission. Further treatment regimens included alternative anti-IL-1 (canakinumab), anti-IL-6 (sarilumab) and anti-TNFα agents (etanercept, golimumab) without improvement and persistently high levels of IL-18.
After failing all those therapeutic attempts and recognition of multiple side effects of long-term steroids, a multi-disciplinary approach with an off-label combination of Anakinra und Golimumab, in conjunction with methotrexate, was started, followed by steroid-free remission after eight years of treatment with an IL-18 level in normal range.
Conclusion: SJIA can be difficult to treat. Our case shows that a combined treatment of an anti-IL-1- and anti-TNF-inhibitor with concomitant MTX is a treatment option in sJIA patients failing anti-IL-1 or anti-IL-6 therapy. IL-18 shows to be a key role biomarker for sJIA disease activity.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: None.

A69

Anakinra-induced amyloidosis in a patient with NOMID

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Background: Neonatal onset multisystem inflammatory disease is the most severe form of cryopyrin-associated periodic syndromes, belonging to the spectrum of autoinflammatory diseases. It is caused by autosomal dominant gain-of-function mutations in the NLRP-3 gene, leading to excessive overproduction of interleukin-1 (IL-1). Disease-associated complications include decreased visual acuity and hearing loss, as well as AA amyloidosis, that should be prevented by early use of IL-1 inhibitors. Anakinra, an IL-1 receptor antagonist, is the preferred choice due to its better central nervous system (CNS) permeability.
In the last 2 years, two NOMID cases with iatrogenic amyloidosis at the application site were reported (1). A recently published first case of anakinra-associated systemic amyloidosis is alarming (2). We report a fourth case and describe the successful management of the patient.
Case presentation: A 16-year-old patient with mutation-confirmed NOMID was treated with anakinra from the age of 3 months. Dosages up to 10 mg/kg/day were necessary to control CNS inflammation. Due to increasing stress caused by the daily painful injections, a switch to canakinumab, an anti-IL-1 antibody, was attempted at the age of 4 years. Despite increasing dosages up to 8 mg/kg every 4 weeks, no adequate disease control could be achieved, and the patient was switched back to anakinra. The further course and psychomotor development were satisfactory until diagnosis of severe bilateral sensorineural hearing loss was made at the age of 10 years. After obtaining expert opinions, the dosage of anakinra was increased to 12 mg/kg/day, divided into 2 daily doses, leading to stabilization of hearing.
During a routine check in August 2022, fist-sized, firm, non-tender nodules were noticed at the anakinra injection sites. Nodule biopsy confirmed anakinra-associated amyloidosis.
To reduce anakinra, we decided on a combined anti-IL-1 therapy, although switching to canakinumab had failed previously. With canakinumab (450 mg; 9 mg/kg every four weeks), anakinra dosage could be reduced by 60% within 2 months and skin nodules regressed substantially over time. The patient showed no evidence of systemic amyloidosis. No side effects were observed under combined anti-IL-1 treatment.
Conclusion: Anakinra is used in NOMID patients to prevent AA amyloidosis. Our report supports observations that anakinra paradoxically has amyloidogenic potential. High doses and long-term use seem to be risk factors. Dose reductions or attempts to switch to canakinumab are often frustrating. Awareness and careful observation of the injection sites are essential in NOMID-patients under treatment with anakinra. Our case shows that combined anti-IL-1 therapy can be a therapeutic option to prevent systemic amyloidosis.

Patient Consent: Yes, I received consent.
Funding: None.
Disclosure of Interest: None.

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A70

Infection rates in children and adolescents with rheumatic diseases in 2022/23: initial findings from the National Pediatric Rheumatology Database

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Introduction: Infections might be more frequent in children and adolescents with rheumatic diseases compared to the general population due to disease-inherent immune dysregulation or required medication, but studies upon this topic are scarce and show conflicting results.
Objectives: To compare frequencies of selected infections among children and adolescents with inflammatory (IRD) and non-inflammatory rheumatic diseases (NIRD) and to investigate possible associations with anti-inflammatory treatment.
Methods: Demographic, clinical, and treatment data from children and adolescents with juvenile idiopathic arthritis (JIA), juvenile systemic lupus erythematosus (jSLE), juvenile dermatomyositis (jDM), chronic non-bacterial osteitis (CNBO), or pain disorders, registered in the National Pediatric Rheumatology Database (NPRD) in 2022 or 2023, were analyzed. Information on infections, hospitalizations due to infection, and antibiotic treatments in the past 12 months was collected through a special infection questionnaire completed by the parents.
Results: Data from 7,977 patients with IRD (JIA: 6,864; jSLE: 215; jDM: 143; CNBO: 755) and 1,805 patients with NIRD (arthralgia: 1,135; pain amplification syndrome: 557; hypermobility syndrome: 88; growing pains: 125) were analyzed. Among patients with IRD, treatments included csDMARDs (39.0%), bDMARDs (27.7%), tsDMARDs (1.3%), systemic glucocorticoids (7.7%), and intra-articular glucocorticoids (13.0%).
The most common infections in both the IRD and NIRD groups within the past 12 months were upper respiratory tract infections (73.8% vs. 82.4%), gastroenteritis (28.4% vs. 36.8%), warts (9.5% vs. 11.4%) and tonsillitis (7.8% vs. 12.4%). Overall, infection frequencies (85.1%, mean 3.1 vs. 92.0%, mean 3.7), hospitalizations for infection (3.6% vs. 4.5%), and antibiotic therapies (21.2% vs. 28.6%), were not higher in patients with IRD compared to those with NIRD.
Among inflammatory disease subgroups, jSLE patients had higher rates of herpes infections (14%) and pneumonias (3.7%) compared to those with JIA, jDM, or CNBO. Antibiotic use (27.9%) and hospitalizations (9.8%) were also more frequent in jSLE patients. Patients on specific anti-inflammatory therapies exhibited higher infection rates. Pneumonias were more common in those on high-dose ($\geq$0.2 mg/kg) glucocorticoids (5.2% vs. 0.9% for no glucocorticoids) and rituximab/cyclophosphamide/MMF (6.3% vs. 1.1%).

Conclusion: Children and adolescents with inflammatory rheumatic diseases do not have higher rates of infections, antibiotic use, or infection-related hospitalization compared to those with pain disorders. However, patients with jSLE and those receiving high-dose glucocorticoids or rituximab/cyclophosphamide/MMF appear to be more susceptible to infections. Further analyses and comparisons with data from the general population are planned.

Patient Consent: Yes, I received consent.
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