FRI0560

EFFICACY AND SAFETY OF ANAKINRA IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS – DATA OF THE BIKER REGISTRY

Ariane Klein, Veronika Ntam Atemnkeng, Frank Dressler, Ivan Foeldvari, Rolf Michael Küster, Toni Hospach, Gerd Ganser, Kirsten Minden, Dirk Foell, Frank Weller-Heinemann, Jasmin Kuemmerle-Deschner, Boris Huegle, Christoph Rietschel, Eggert Lilienthal, Gerd Horneff, BIKER-Registry, BIKER-Registry, Sankt Augustin, Germany

Background: Anakinra (ANA) is recommended for treatment of systemic juvenile idiopathic arthritis (sJIA) and has recently received EMA approval. **Objectives:** To describe safety and effectiveness of ANA in clinical practice in sJIA patients documented in the German Biologics registry (BiKeR).

Methods: Demographic and clinical parameters of the patients were recorded at BiKeR enrollment, ANA effectiveness was evaluated by half-yearly evaluation of disease activity using JADAS-10. Safety assessments were based on MedDRA-coded adverse events (AE) reports.

Results: Until December 1 2018, 50 sJIA patients treated with ANA were registered, representing 113.4 patient-years (PY) of observation, with 10 patients (20%) receiving ANA for at least 4 years. The cohort treated with ANA had experienced a prior disease duration of 3.5+/-3.8 years (mean+/-SD).

Most sJIA patients treated with ANA received pretreatment: 35 patients (70%) were pretreated with at least one other biologic, mostly etanercept (n=28), followed by tocilizumab (6) and canakinumab (1). Further pretreatments included methotrexate (MTX, n= 35), ciclosporine A (n=13), azathioprine (n=8) and other DMARDs at lower frequency. 39 patients had received corticosteroids. Concomitant treatment consisted of NSAIDs (n=20), systemic steroids (n=35), MTX (n=29) and other DMARDs (n=8). At month 3, JADAS minimal disease activity (MDA)/JADAS remission and inactive disease according to Wallace [1] were observed in 42%/37% and 47%, respectively. After one year of treatment, the rates were 62%/45% and 56%, respectively (Figure 1).

Conclusion: The current analysis adds to the established safety profile of Anakinra and demonstrates that in ANA treated patients with sJIA the rate of SAEs was comparable and consistent with the overall AE profile of ANA in pediatric patients. Hospitalisation was the usual reason for classification as serious AE. No new safety signals specific to the paediatric population were identified in this large cohort of JIA patients.

Figure 1: Efficacy parameter over time (months) in JIA patients treated with Anakinra

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FRI0561

COMPARISON OF INITIAL PRESENTATIONS BETWEEN JUVENILE IDIOPATHIC ARTHRITIS CHILDREN WITH SYSTEMIC ONSET WITH NON-BIOLOGIC MONOCYCLIC AND PERSISTENT COURSES

Mikhail Kostik, Maria Romyantseva, Eugenia Isupova, Irina Chikova, Margarita Dubko, Vera Masalova, Ludmila Snegireva, Tatiana Kornishina, Tatiana Likhacheva, Ekaterina Gaidar, Andrey Santimov, Olga Kalashnikova, Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, Russian Federation

Background: Juvenile idiopathic arthritis with systemic onset (soJIA) may have monocycling, polycycling or relapsed course [1]. There were not known soJIA course predictors.

Objectives: The aim of our study was to evaluate initial clinical or laboratory features of the patients with soJIA who had monocyclic course without biologics.

Methods: In the present study were included data about 130 soJIA patients. After selection we identified a subgroup of the soJIA patients (n=22) who successfully achieved remission without any biologic medication and were stable in the remission off-medication at least two years. The second group consisted of the patients with chronic persistent course (n=83). The remained 25 patients were excluded due to missing data or who did not meet the selection criteria. We evaluated routine clinical (fever, rash, hepatosplenomegaly, serositis, lymphadenopathy, MAS, joint involvement) and laboratorial (WBC, PLT, Hb, ferritin, ALS, AST, LDH, GGTP, ALP, albumin, Na, triglycerids, ESR, CRP, prothrombin, fibrinogen) soJIA features in the onset of the disease.

Results: Patient with monocycling course have no any differences except the ferritin level: 275 (133; 698) ng/ml vs 950 (150; 3240) ng/ml, (p=0.04), time to achievement remission 17.7 (8.2; 38.0) months vs 60.2 (36.0; 99.0) months (p=0.00002) and rare elbow involvement 4.6% vs 30.9% (p=0.01). The parameters, associated with possible monocycling course are in the table.

Table. The parameters, associated with possible monocyclic course in soJIA patients.

Parameter	AUC (95%CI)	Se	Sp	OR (95% CI)	p
CRP≤3.1 mg/dl	0.59 (0.48; 0.69)	0.53	0.77	3.6 (1.3; 10.3)	0.014
ESR≤ 53 mm/h	0.62 (0.51; 0.71)	0.9	0.43	6.8 (1.5; 31.3)	0.006
Ferritin ≤1340 ng/ml	0.69 (0.58; 0.79)	1.0	0.46	-	0.003
Active joints < 8	0.5 (0.4; 0.6)	0.82	0.39	4.6 (1.3; 16.8)	0.013
Onset age <7 years	0.57 (0.47; 0.66)	0.86	0.4	4.2 (1.5; 15.3)	0.022
No elbow involvement, n (%)	-	0.96	0.31	9.4 (1.2; 73.6)	0.012

Conclusion: Patients with soJIA initially have quit similar clinical presentations independently the further clinical course. The prediction of possible course of soJIA is a difficult problem. Patients with soJIA with monocycling course were younger and had less impressive laboratory activity. Further investigations required.

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FRI0562

CONCENTRATION OF SURVIVIN IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) – DIAGNOSTIC AND PROGNOSTIC VALUE

Joanna Lipinska¹, Joanna Swidrowska-Jaros¹, Krystyna Wyka², Elzbieta Smolewska¹. ¹Medical University of Lodz, Department of Pediatric Cardiology and Rheumatology, Łódź, Poland; ²Medical University of Lodz, Department of Pediatrics, Oncology, Hematology and Diabetology, Lodz, Poland

Background: Survivin is an anti-apoptotic protein that has been suggested as a predictive marker of severe course of adult rheumatoid arthritis and could be used for preclinical recognition of rheumatoid process.

Objectives: The goal of the study was to evaluate the diagnostic and prognostic value of survivin in Juvenile Idiopathic Arthritis (JIA).

Methods: Sixty three children with newly diagnosed JIA (46 girls and 17 boys) aged 1.5-17 years and 32 healthy children as a control group appropriately matched in terms of sex and age, hospitalized in the Department of Pediatric Cardiology and Rheumatology, Medical University of Lodz due to functional disorders of the cardiovascular system were included into the study. Concentration of survivin was assessed by an ELISA test in blood and 18 matched synovial fluid samples collected from JIA patients and in sera of children from control group.

Results: Children with JIA were divided according to the subtype of the JIA. In 68.2% of patients oligoarthritis was diagnosed. The disease activity was established on the basis of JADAS-27 criteria, distinguishing three levels of rheumatoid process activity: low, medium and high. The largest group comprised children of low activity (56%). The concentration of survivin was significantly higher in JIA compared to the controls ($p=0.00041$). Higher concentration of survivin correlated positively with the presence of anti-CCP antibodies ($p=0.004$) and with higher disease activity ($p=0.0014$). The higher survivin concentration was found more often in polyarticular and systemic JIA onset. In all synovial fluid samples the concentration of survivin was higher than in matched blood ($p=0.0002$).

Conclusion: On the basis of the conducted study, it could be concluded that the higher concentration of survivin is being associated to more severe course of the JIA. Determination of survivin may be helpful in the diagnosis of JIA and may be used to identify a group of children with early arthritis and JIA with bad prognosis who should be treated more aggressively early from the disease onset.

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FRI0563

A NATIONAL SURVEY ACROSS GENERAL PAEDIATRICIANS REGARDING IMMUNIZATION PRACTICES IN CHILDREN WITH RHEUMATIC DISEASES

Despoina Maritsi^{1,2}, Irene Eleftheriou², Katerina Markante², Olga Vougiouka², Maria Tsolia². ¹Athens Medical School, National and Kapodistrian University of Athens, Rheumatology Unit, Second Department of Paediatrics, Athens, Greece; ²Athens Medical School, National and Kapodistrian University of Athens, Rheumatology Unit, Second Department of Paediatrics, Athens, Greece

Background: Robust scientific evidence on the safety and efficacy of certain vaccines in patients with rheumatic diseases is available; therefore guidelines regarding immunizations in this vulnerable group of children are published via a variety of official health organizations/societies including the Greek Rheumatology Society. Nonetheless, the uptake of specific immunizations is suboptimal. In Greece, vaccinations are mainly delivered by primary care Paediatricians.

Objectives: The purpose of this study was to describe the knowledge, attitude and current practice of General Paediatricians working in primary care regarding vaccination in children with rheumatic diseases on immunosuppressive medication across Greece and to identify barriers and facilitators that could be used to promote uptake.

Methods: This was a cross-sectional survey, conducted with an anonymous questionnaire of 25 items distributed to Paediatricians via an online platform. Data collected included demographics, questions on knowledge, perceptions and opinions as well as advice given to families. Additionally, questions addressed three specific categories: live-vaccines, non-live vaccines and annual influenza vaccine. This study was approved by the "P. & A. Kyriakou" Children's Hospital Research and Ethics Committee.

Results: Out of 400 questionnaires sent out, 256 were returned. Mean age was 48 years age (± 8.2) mean duration of working as a Paediatrician was 15 years (± 6.7). 25% of the responders worked in rural areas and the remaining in urban areas. 67% worked in the private sector. The majority (78%) of doctors felt that vaccination in children with rheumatic diseases is of pivotal importance. 50% gave specific advice on immunisations at initial diagnosis and 25% checked vaccination status at regular intervals. Responders were using a variety of guidelines in order to reach a clinical decision; still 45% were unaware of the existing national guidelines. 50% were hesitant to adhere to the national

vaccination scheme without expert input. Reasons were: not convinced from current literature that the vaccine is safe (32%), afraid to cause disease flare (43%), unable to deal with parental concerns/refusal (54%). 12% of responders felt that the rheumatic disease may have been triggered by a vaccine. The majority (95%) were pro annual influenza vaccination, while a minority (15%) was against live vaccines administration even if the patient was not on immunosuppressive treatment. 75% of doctors were keener to administer booster doses rather than primary ones, while 75% of respondents would postpone vaccinations in all cases if disease was active.

Conclusion: Variation in opinion and clinical practice exists. Overall, although Greek Paediatricians are well informed regarding efficacy and side effects of immunizations, there are steps to be made form principle to practice. Further research will allow the development of clear guidelines to aid in the management of increasing numbers of children with rheumatic diseases.

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PSTPIP1- ASSOCIATED MYELOID-RELATED PROTEINEMIA INFLAMMATORY SYNDROME/PAMI SYNDROME: CASE REPORT AND REVIEW OF THE LITERATURE

Manel Mejri, Katerina Theodoropoulou, Michael Hofer. *Lausanne, Pediatric Rheumatology, Lausanne, Switzerland*

Background: PAMI syndrome is a recently described condition, previously known as Hyperzincemia/Hypercalprotectinemia (Hz/Hc) syndrome. It is a very rare auto-inflammatory disorder characterized by a chronic systemic inflammation, cutaneous and osteo-articular manifestations, hepatosplenomegaly, anemia and neutropenia. Increased blood levels of MRP 8/14 (S100A8/A9 or calprotectin) and zinc distinguish this condition. Specific pathogenic mutations in PSTPIP1 gene (p.E250K and p.E257K) were identified as the genetic cause of this condition.

Objectives: Case presentation and review of literature

Case Presentation: We report a case of 13 months age female referred to our unit for recurrent episodes of osteoarthritis. Physical examination showed hepatosplenomegaly. Blood work revealed a systemic inflammation, a microcytic anemia and neutropenia. A complete workup for metabolic disorders, oncologic processes and uncommon infections was negative. Because of history of recurrent osteoarthritis, a whole-body MRI was performed and confirmed a multifocal osteomyelitis. Whole exome sequencing identified the missense p.E250K in the PSTPIP1 gene.

Methods: A literature search on PAMI syndrome was performed until the 15 October 2018. Pubmed was screened using a combination of the following terms: Hyperzincemia, Hypercalprotectinemia, E250K mutation, PSTPIP1 mutation, PAPA with E250K mutation.

Results: We identified 20 cases of PAMI syndrome in the literature. PAMI syndrome is an early onset inflammatory disease with a median age of 2.4 years. Clinical manifestations include Osteo-articular manifestations (80%), skin lesions (71%), splenomegaly (89%), hepatomegaly (68%), lymphadenopathy (42%), growth failure (58%) and hemorrhagic diathesis with recurrent epistaxis and/or haematoma tendency in 5 patients. All cases had relevant abnormalities in hematologic parameters: mild to severe neutropenia and anemia (100%). Thrombocytopenia (42%). Systemic inflammation was confirmed in 94% using the monitoring of CRP, ESR or SAA. Zinc and MRP 8/14 blood concentrations were markedly elevated in all tested patients. Genetic analyses of PSTPIP1 gene revealed the two specific identified mutations (p.E250K and p.E257K) in all patients. Response to the treatment was variable with no consistently effective therapy. Most common therapeutic options were AINS, Corticosteroids (n=9), Anakinra (n=9), Anti-TNF (n=6) and Cyclosporine A (n=4).

Conclusion: PAMI syndrome is a rare auto inflammatory condition which should be considered in patients with undefined systemic inflammation and neutropenia, even without skin or osteo-articular manifestations. Zinc and serum MRP 14/8 measurement may be helpful tools for the diagnostic orientation in these cases.

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