who had attended the 1st Greek Rheumatology Transition Clinic for Pediatric Rheumatic Diseases, following its establishment in 2013.
**Methods:** Retrospective cohort analysis of Greek adults with established diagnosis of JIA. The disease activity state was assessed by 2 contemporary quantitative tools: the Juvenile Arthritis Disease Activity Score-10 (JADAS 10) (Clinical Remission, CR, Low, Moderate and High Disease Activity, LDA, MDA, HDA, respectively) and Wallace criteria (CR on/off ETN). Baseline was defined as the 1st ETN dose.
**Results:** 35 patients (female 25), aged (mean±SD) 23.5±4.6 years, were followed for a median (IQR) of 9 (3.6, 12.7) years. The median (IQR) patients' age at the 1st ETN dose was 16.4 (12.1, 17.8) years and the lag time from JIA onset to baseline was 6.5 (2.8, 12.5) years. The majority of the patients had a polyarticular course (27/35, 77.1%), regardless of the JIA subtype. ANA positivity was recorded in 16/35 (45.7%) and previous uveitis in 4/35 (11.4%). Nine patients (25.7%) had previously received other anti-TNFs (Adalimumab n=6, Infliximab n=3). The baseline median (IQR) patients' JADAS-10 was 14/40 (9.5, 20.5) and the ETN yr-administration was 3.5 (2, 5.5). 33/35 (94.3%) patients were compliant to ETN and the study drug was well-tolerated. Regarding safety, only 3 patients (8.6%) experienced 6 adverse events (0.04/patient-years), namely injection site reaction (n=1), uterine hemorrhage (n=1), transient ANA positivity (n=1) and uveitis (n=3, 2/3 as flares). Uveitis under ETN led to the drug discontinuation in 2 patients (1 with new, 1 with pre-existing). Four patients discontinued ETN due to efficacy loss and one due to latent TB infection. 7/35 (20%) achieved CR and discontinued ETN after 3.3 (2, 4.5) years (median, IQR). The remaining 21 patients were still on ETN at the last evaluation. The median (IQR) percent duration of CR remission on ETN, according to the Wallace criteria, was 86%. CR off ETN lasted 1.17 (0.8, 4.3) years (median, IQR). In respect to the disease activity state at the last assessment: A) among the ETN ongoing receivers, 66.7% were in a CR state, 19% in LDA, 14.3% in MDA (median JADAS: 1). B) CR achievers still remaining off ETN, sustained this state in 85.7% (median JADAS: 0).
**Conclusion:** ETN in the critical transition period proved to be safe as adverse events were rare. ETN had a long-term and sustained efficacy, allowing CR off anti-TNF in 20% of the patients. Our transition policy supported the patients' meticulous follow-up and compliance to ETN in adulthood.

**Disclosure of Interest**
None Declared

## P190
## INFECTIOUS ADVERSE EVENTS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM THE JIRCOHORTE

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**Introduction:** Over the last fifteen years, the development of biological agents improved dramatically the outcome of children suffering from Juvenile Idiopathic Arthritis (JIA). Adult studies indicate that treatment with biological agents lead to an increased risk of serious infections, but very little is known about this risk in children.
**Objectives:** The main objective of our study is to assess the infectious adverse events (IAEs) occurring in JIA children treated with biological agents.
**Methods:** Patients were selected from the retrospective module of the JIRcohorte, a multicenter registry for children with inflammatory and rheumatological diseases. Data concerned the period between January, 10th 2001 and August 2015. Besides demography, diagnosis and treatment options of the patients, infectious adverse event (IAE) were retrieved. For every infectious side effect, the date, the severity, the need for an hospitalization, the accountability of the treatment on the occurrence, and the consequence of the event on the biologic course were noted. The type of microorgansim and the affected organ were also analyzed. Incidence rates were expressed in number of events per 100 person-years (100p-y), and OR were calculated; for their comparison, we used the Fischer test with a significance threshold at 0.05.
**Results:** Six hundred eighty-six patients with JIA from thirteen French-speaking rheumatologic reference centers were included in the study. A total of 1095 treatments with biological agent, for 3075.4 person-years of exposure were analyzed. One hundred eighty-four IAE occurring under a treatment with biologics were described, that is to say an incidence rate of 6.0 events/100 p-y, 15.5/100 p-y with Tocilizumab, 9.6/100 p-y with Canakinumab, 7.4/100 p-y with Abatacept, 6.9/100 p-y with Golimumab, 6.7/100 p-y with Aankinra, 6.3/100 p-y with Infliximab, 4.8/100 p-y with Etanercept, and 3.7/100 p-y with Adalimumab. Risk of developing an infection was significantly higher with IL6 antagonists than with TNF-inhibitor (TNFi) (OR 3.67 IC95% [2.41 ; 5.49] p<0.001), or with IL1 antagonists (OR 2.34 IC95% [1.7 ; 4.4] p=0.004). Forty point eight percent of the IAE affected the upper respiratory tract or the ENT sytstem. A total of 12 IAE were described as severe or very severe, which represented an incidence rate of 0.4/100p-y, 43% occurring with TNFi. The risk of developing a severe or very severe infection was higher with IL6 antagonist or IL1 antagonist than with TNFi. Twenty-two herpes zoster infections, including twenty under biologics were reported (0.7/100 p-y), and there were more virus due to immunosuppression with IL6 antagonist than with TNFi. No case of tuberculosis, opportunistic infection, or death was reported.
**Conclusion:** Infectious complications with biologics occurring in children treated for JIA are rare, and in most of the cases have a mild or moderate severity, affecting mainly the upper respiratory tract or the ENT.

**Disclosure of Interest**
None Declared

## P191
## ASSESSING THE CLINICAL RELEVANCE AND RISK MINIMIZATION OF ANTIBODIES TO BIOLOGICS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) (ABIRISK) - PRELIMINARY RESULTS

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**Introduction:** ABIRISK is a project funded by Innovative Medicine Initiative, with the aim to investigate anti-drug antibody (ADA) formation in the treatment of JIA with biologics (BPs). A major limitation to the use of biologics is the development of ADA that may decrease the efficacy of BPs.
**Objectives:** The aim of this project is to improve the capability to predict biologic immunogenicity in JIA patients.
**Methods:** JIA Patients (by ILAR criteria) followed by 24 PRINTO centres in 12 countries were prospectively enrolled and treated with Etanercept, Adalimumab or Tocilizumab. Patient's data were obtained from Pharmachild, a pharmacovigilance data registry of JIA patients. For each patient detailed demographic and clinical information were reported; biologic samples were collected for PK and ADA detection before therapy start as well as at periodic visits up to month 18 of follow-up. Disease activity was assessed with Juvenile Arthritis Disease Activity Score-10 (JADAS10) and JIA American College of Rheumatology (JIA ACR) criteria.
**Results:** 148 patients were included in the analysis. Five patients were considered twice because treated with 2 different sequential biologics. Demographic and clinical data by therapy are represented in the table. 54% of the patients were treated with Adalimumab. Disease duration was higher in the group receiving Tocilizumab. Disease activity showed a pattern of improvement over time both globally and for each treatment group (Table 1). Anti-adalimumab and anti-tocilizumab antibodies were detected respectively in 14 and 3 patients, while no patient developed antibodies anti-etanercept.

**Conclusion:** Preliminary data show a global improvement of disease activity during follow-up period. Analysis of the correlation between drug concentration/ADA development and clinical information will help to determine which patients will respond best to which biologic.

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**Table 1 (abstract P191).** Demographic and clinical characteristics of the JIA patients by therapy. Data are medians (1st –3rd quartiles) or frequencies (%).

| | Adalimumab n=80 (54%) | Etanercept n=36 (24%) | Tocilizumab n=32 (22%) | Total n=148 |
|---|---|---|---|---|
| Age at onset, years | 6.1 (3.1-10.4) | 4.9 (1.9-9.7) | 6.1 (3.8-9.1) | 5.8 (2.7-10.1) |
| Age at JIA diagnosis, years | 6.8 (3.3-11.9) | 5.5 (2.1-10.6) | 6.4 (4.1-9.2) | 6.4 (3.2-11.0) |
| Disease duration, years | 2.4 (0.9-4.8) | `2.2 (1.1-5.5) | 4.1 (1.4-6.5) | 2.6 (1.1-5.8) |
| Female | 60 (75.0) | 26 (72.2) | 23 (71.9) | 109 (73.6) |
| ILAR JIA category | | | | |
| Systemic | 2 (2.5) | 0 | 7 (21.9) | 9 (6.1) |
| Oligoarthritis | 30 (37.5) | 7 (19.4) | 9 (28.1) | 46 (31.1) |
| Polyarthritis | 27 (33.8) | 23 (63.9) | 13 (40.6) | 63 (42.6) |
| Psoriatic arthritis | 1 (1.2) | 0 | 0 | 1 (0.7) |
| Enthesitis related arthritis | 16 (20.0) | 3 (8.3) | 0 | 19 (12.8) |
| Undifferentiated arthritis | 4 (5.0) | 3 (8.3) | 3 (9.4) | 10 (6.7) |
| Anti-Drug Antibodies* | 14 (18%) | - | 3 (9%) | 17 (11%) |
| Anti-Drug Antibodies** | 5 (6%) | - | 2 (6%) | 7 (5%) |
| JADAS 10 | | | | |
| M0 | 12.6 (7–17) | 15.6 (10–18.5) | 15.6 (11.6–23.2) | 13.5 (8.5–18.3) |
| M1 | 4 (1.5–6.5) | 5.7 (3.4–12.7) | 5.5 (3–11.4) | 4.5 (2–8) |
| M3 | 2.7 (1–5.9) | 2.2 (0–7.7) | 2.5 (0.7–6) | 2.5 (0.5–5.9) |
| M6 | 1.5 (0–5) | 1 (0–8) | 2 (0.5–7.5) | 1.7 (0–5.8) |
| M12 | 0.5 (0–5) | 0.5 (0–4.2) | 2 (0.5–4.5) | 0.5 (0–4.7) |
| ACR 70 | | | | |
| M1 | 30 (46.2) | 8 (33.3) | 5 (31.3) | 43 (41.0) |
| M3 | 40 (62.5) | 17 (63.0) | 10 (62.5) | 67 (62.6) |
| M6 | 41 (67.2) | 18 (62.1) | 13 (76.5) | 72 (67.3) |
| M12 | 42 (71.2) | 19 (76.0) | 13 (76.5) | 74 (73.3) |

*in at least 1 determination ** in at least 2 determination

## P192

### METHOTREXAT TREATMENT IN 2 PATIENTS WITH ARTHRITIS AFTER LIVER TRANSPLANTATION ON PERSISTENT TACROLIMUS TREATMENT.

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**Introduction:** We are presenting 2 patients after liver transplantation who developed juvenile idiopathic arthtiris. Patients received combined therapy of tacrolimus and methotrexat.
**Objectives:** Case 1: Boy, born 18.08.2013, underwent liver transplantation in 2014, from mother, due to cirrhosis in the course of atresia of the bile ducts, on the chronic tacrolimus, heviran treatment.
In 08.2015 patient developed symptoms: pains and swelling of knees, wrists, elbows. In laboratory tests:ESR-95mm/h, Rheumatoid factor (RF) negative, antinuclear antibodies (ANA) negative; the number of EBV virus copies 3870, after correction of dose of tacrolimus 2050, other infections were excluded: CMV ( DNA CMV negative), Borelia brg, Yersinia sp, Tuberculosis, Campylobacter, Mycoplasma pn , Clostridium dif.. In USG active inflammation was found with effusion , swelling of synowial membrane. The Juvenile idiopathic arthritis polyarticular onset was diagnosed. Patient received encorton , metotrexat , tacrolimus. The remission was achieved.
**Methods:** Case 2 : Boy with autism, born 2003, in the neonatal period surgery due to obstruction of the duodenum secondary to the annular pancreas and imperfect turn of the intestine ( bowel restitution ); in the first year of life operational correction of ASD, VSD.
In 2012 patient underwent liver transplantation due to congenital extrahepatic portosystemic shunts with hyperamonaemia and hepatopulmonary syndrome and focal changes in the liver, tacrolimus treatment was conducted. Since 11.2015 there have been: pain, big edema and limitation of joint mobility in right wrist , rigth foot ( MTP joins). CRP-24 mg/l, ESR-54mm/h, WBC- 13 G/L, present HLA B27 antigen , negative RF, ANA, infection were excluded: Borelia brg, Yersinia sp, Tuberculosis HCV . In Xray of hand (04.2016)- generalized osteoporosis and periarticular osteoporosis bones of wrist and bones of IV ,V MCP joints of right hand. In feet Xray-hypetrophy of further physis of metatarsal bones of right foot. In USG thickened synovium with intensive increased vascularity in the joints of right wrist and MCP; also in right MTP 3-4, PIP 3-4 joints, thickened synovium in the MTP 1-2 joints and the toe IP. USG of liver – no abnormalities. Enthesitis related arthritis was diagnosed. Methotrexat was used to treat 15mg/ week , then 20mg/week ( 15mg.m2 bs), a gradual resolution of inflammatory changes in the joints was achieved. In 2017 in USG of right foot was in norm, in right wrist was thickening, moderately increased vascularity of synovium , intrarticular glikokortykosteroid was injected to the wrist. Within 2 years of treatment liver enzymes were correct. In January 2018, was noticed temporarily increase of GGTP-154 U/L , ALAT-34 n 26 U / L, AST-23 U / L, CMV DNA - not detected, EBV DNA - not detected. Ultrasound showed transplanted liver unimpaired, non-biliary oblong vein, portal vein width 6mm, PV vmax 48cm / sec, HAV max 69cm / sec, hepatic flow three-phase normal. In Liver biopsy 01.2018: The organ structure preserved, without features of acute cell rejection. The stipend of fibrous connective tissue with the creation of port-port bridges within the port space (S3 according to Ishak). Discrete inflammatory infiltrates of a chronic nature in the area of the gantry-biliary and focaly intralobulary, no cholestasis, no steatosis, no ductopenia.
The hepatologist decided to add to treatment encorton, continue tacrolimus and methotrexat.
**Results:** The use of methotrexate due to JIA in patients after liver transplantation on tacrolimus treatment allowed for rapid improvement in joints.
**Conclusion:** During 2 years of obserwation frequent laboratory control and liver assessment in USG and liver biopsy showed a stable function of the transplanted organ. Informed consent to publish had been obtained.

**Disclosure of Interest**
None Declared