Methods: Sera were obtained from 101 patients satisfying the ILAR classification criteria for JIA and in 25 patients with two other dysimmune disorders (type 1 diabetes and juvenile inflammatory bowel disease). Level of IgG antibodies against *P. gingivalis* and Prevotella intermedia were obtained by commercially available ELISA already used previously (5).

Results: The students were educated in children with JIA, Down’s Syndrome (trisomy 21 [T21]), and in healthy controls were assessed. The function of primary synovial fibroblasts (FS) was assessed in response to stimulation with pro-inflammatory mediators alone and in combination (TNF-α, IL-17α, IFN-γ, GM-CSF). The two major pathway genes (cytokines (ECAR) and oxidative phosphorylation (OCR)) were quantified by the Seahorse XFe96 Analyser. Migration, adhesion, invasion and cytokine/chemokine secretion were quantified by wound repair scratch assays, Transwell collagen invasion chambers, adhesion binding assays, and ELISAs.

Results: T cell frequencies were higher in DA compared to JIA and T21 in contrast to B cell frequencies which were decreased. T cell responses in DA were characterized by increased frequencies of CD4+ and CD8+ T cells and GM-CSF alone and in combination on DA FLs function. TNF-α, IL-17α and IFN-γ induced IL-6, RANTES and MCP-1 secretion, with no effect observed for GM-CSF. Furthermore, TNF-α and IL-17α induced DA FLs migration and PBMC adhesion to DA FLs. Finally IL17A and IFN-γ potentiated the effect of TNF-α on IL-6 and MCP-1 secretion compared to stimulations alone.

Conclusion: DA is a more common and aggressive form of arthritis compared to JIA. It is characterized by increased T cell responses and a more invasive FLs phenotype compared to that of JIA, with T cell derived cytokine alone and in combination further inducing DA FLs pathogenic mechanisms. These effects may mirror the increased erosive disease observed clinically.

REFERENCES:

Disclosure of Interests: None declared.

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**POS0069**

INCREASED T CELL RESPONSES, METABOLIC ACTIVITY AND FIBROBLAST INVASIVE CAPACITY IN CHILDREN WITH DOWN’S SYNDROME-ASSOCIATED ARTHRITIS COMPARED TO JUVENILE IDIOPTIACH ARTHRITIS

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**Background**: Juvenile idiopathic arthritis (JIA) was thought to be the most common inflammatory arthritis in children (Shih et al., 2019). However an aggressive, erosive arthritis of little-known immunologic mechanism occurs 20 times more frequently in children with Down’s syndrome (Foley et al., 2019).

**Objectives**: This study was undertaken to characterize immune cell responses and fibroblast pathogenic mechanisms in children with Down’s syndrome-associated arthritis (DA).

**Methods**: Multiparametric flow cytometric analysis was used to examine peripheral blood T, B, and monocyte populations. In addition, T cell cytokine responses and their metabolic profile in children with DA, JIA, Down’s Syndrome (trisomy 21 [T21]), and in healthy controls were assessed. The function of primary synovial fibroblasts (FS) was assessed in response to stimulation with pro-inflammatory mediators alone and in combination (TNF-α, IL-17α, IFN-γ, GM-CSF). The two major pathway genes (cytokines (ECAR) and oxidative phosphorylation (OCR)) were quantified by the Seahorse XFe96 Analyser. Migration, adhesion, invasion and cytokine/chemokine secretion were quantified by wound repair scratch assays, Transwell collagen invasion chambers, adhesion binding assays, and ELISAs.

**Results**: T cell frequencies were higher in DA compared to JIA and T21 in contrast to B cell frequencies which were decreased. T cell responses in DA were characterized by increased frequencies of CD4+ and CD8+ T cells and GM-CSF alone and in combination on DA FLs function. TNF-α, IL-17α and IFN-γ induced IL-6, RANTES and MCP-1 secretion, with no effect observed for GM-CSF. Furthermore, TNF-α and IL-17α induced DA FLs migration and PBMC adhesion to DA FLs. Finally IL17A and IFN-γ potentiated the effect of TNF-α on IL-6 and MCP-1 secretion compared to stimulations alone.

**Conclusion**: DA is a more common and aggressive form of arthritis compared to JIA. It is characterized by increased T cell responses and a more invasive FLs phenotype compared to that of JIA, with T cell derived cytokine alone and in combination further inducing DA FLs pathogenic mechanisms. These effects mirror the increased erosive disease observed clinically.

REFERENCES:

Disclosure of Interests: None declared.

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**POS0070**

POPULATION PHARMACOKINETICS OF INFliximAB IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Background**: Higher dosage regimes for Infliximab (IFX) have been described to be effective in partial- or non-responding adults and children with rheumatic disease and appear to be safe (1,2). To optimize IFX treatment in juvenile idiopathic arthritis (JIA) patients, therapeutic drug monitoring (TDM) might be beneficial. To support routine TDM of IFX and dose regimen optimization in JIA patients, more in-depth knowledge of the pharmacokinetic (PK) variability of IFX is needed. Ultimately, as soon as the optimal therapeutic drug ranges will be known, PK model-based simulation can be used to individualize drug dosing recommendations. Individual dosages may be adjusted by taking specific patient characteristics into account that explain inter-patient variability in pharmacokinetics (PK). Inter-patient variability can be quantified and investigated by the population approach.

**Objectives**: Our hypothesis is that optimizing dosage and frequency of IFX administration for individual patients will improve treatment outcome. In this current study, the population PK for IFX are described for JIA patients.

**Methods**: Data including IFX trough concentrations and anti-IFX antibodies of 27 JIA patients on IFX maintenance treatment were retrieved from electronic charts. Three population pharmacokinetic models from literature were validated for our dataset using nonlinear-mixed effects modeling program NONMEM (3,4,5). A novel population pharmacokinetic model was developed based on our study data.
Results: A total of 65 obtained blood samples after a median of 32 days after the last IFX infusion (IQR 28–42) were analyzed. The three published models under-predicted the observed trough concentrations. A newly developed one compartment model best described the IFX serum concentration over time data in JIA patients (see Figure 1).

Conclusion: Our study shows a novel and the first PK model for IFX in JIA patients. Our main finding was that a one-compartment model best described the IFX serum concentration over time data. Predictive performance of the known models from literature was insufficient for our patient data. Our data also show that different PK models are needed for different age categories (children or adults) and in different diseases.

REFERENCES:

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>N=27 patients</th>
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<td>BSA</td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Male, N (%)</td>
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<tr>
<td>CRP (mg/L)</td>
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<tr>
<td>WBC count</td>
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<tr>
<td>Antibodies-to-IFX</td>
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<tr>
<td>Dose (mg)</td>
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<td>Dose (mg/kg)</td>
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<td>Hemoglobin (mmol/L)</td>
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<td>ESR (mm/h)</td>
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Figure 1: Visual predictive check final model

Disclosure of Interests: None declared.
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POS0071
IS ANTI-NXP2 AUTOANTIBODY A RISK FACTOR FOR CALCINOSIS AND POOR OUTCOME IN JUVENILE DERMATOMYOSITIS PATIENTS?

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Background: It has been published that the presence of NXP2 autoantibodies presents a risk for calcinosis in patients with JDM.

Objectives: To investigate the incidence of calcinosis and response to the treatment in NXP2 positive JDM patients with calcinosis.

Methods: The study design is a retrospective, multinational, multicenter study. Data on gender, race, age at disease onset and age at disease diagnosis, age at inclusion in the study, clinical presentation, muscle function tests, laboratory results, imaging, data on treatment and outcome of disease were collected.

Results: We collected 26 patients (19 F, 7 M) with JDM and positive NXP2 antibodies. Fourteen patients were white, eight asian, three black and one Hispanic ethnicity. The mean age at disease presentation was 6.5 years (SD 3.7), the median diagnosis delay was 4 months (range 0.5-27 months). Patients were divided in two groups (A and B) based on the presence of calcinosis.

Eleven patients (42%) developed calcinosis (group A) in the course of the disease, 10 females and 1 male. Four patients already had calcinosis at presentation, 1 developed after 4 months, and 6 developed calcinosis later in disease course (median 2 years, range 0.8-7.8). Four patients developed lipoatrophy in group A (1 in group B), 2 patients had polyarthritis (1 in group B), 2 patients had gut involvement (1 in group B) and 1 patient had lung involvement (2 in group B).

The mean age at disease presentation (5.2 / 7.5 y) and mean CK level (1548.6 / 1811.6 U/L) were lower in group A. The platelet count (306.5 / 258 10^9/L), and mean values of AST (111.4 / 103.9 U/L), ALT (72.2 / 50.9 U/L), LDH (1048.3 / 808 U/L), and IgG (11.6 / 9.9 g/L) were higher in group A. However, the differences were not statistically significant. ANA antibodies were positive in 9/11 in group A and 12/15 in group B. One patient in group A was also positive for anti-MDA5 antibody. The data on muscle strength measurement (MMT/CMAS) were available only in a few patients.

Treatments used for patients with calcinosis includes, methotrexate and glucocorticosteroids (GCS) (all patients), hydroxychloroquine (9), IVIG (7), cyclosporine (4), biphosphonate (4), MMF (5), rituximab (4), cyclophosphamide (1), abatacept (1) and TNF alpha blocker (1).

Discussion: Disease outcome (by evaluation of the treating physician) was excellent in 4, good in 2, stable in 2 and poor in 3 patients. None of the patients from group B had a poor disease outcome. Patients with excellent disease outcomes from group A were treated with GCS and methotrexate (4), hydroxychloroquine (3), IVIG (1) and cyclosporine (1). One of two patients who had good outcomes, was additionally treated with MMF, biphosphonates and rituximab and the second was treated with cyclophosphamide and rituximab. One patient with calcinosis at the presentation (age 4 years) was treated also with anti-TNF alpha therapy and a subcutaneous calcinosis developed and the therapy was changed to MMF and rituximab, which stopped the progression of calcinosis.

Conclusion: Our preliminary results showed that calcinosis occurred in 42% of NXP2 positive JDM patients. Children with calcinosis were treated with several combinations of drugs. In four cases, rituximab and in one case, for limited time of 2 years, anti-TNF alpha agent, were used successfully.

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[1] Chung MP, Richardson C, Kirakossian D, Orandi AB, Saketko LA, et al. Calcino-

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