Background: Juvenile dermatomyositis (JDM) is a systemic, autoimmune inflammatory muscle disorder and vasculopathy that affects children younger than 18 years. Although the cause of JDM remains unknown it is clear that genetic and environmental influences play a role in the aetiology. New treatments are becoming available and being tested through international multicentre trials. Increasing evidence suggests a role for types I and II IFN in juvenile and adult dermatomyositis, including elevated IFN-response gene signatures in the muscle, skin and blood. It has been reported that patients with refractory JDM responded well to treatment with tofacitinib, a JAK inhibitor, with corresponding downregulation in selected IFN-response genes.

Objectives: In this study, we evaluated our cases with resistant JDM who received tofacitinib treatment.

Methods: Six patients who received tofacitinib because of severe skin involvement of JDM were included in the study. The data were obtained retrospectively from the hospital records.

Results: The age ranges of the cases were between 7-17 years and the ratio of girls and boys was 1 (3/3). The age of diagnosis was between 2-13 years, and the follow-up period was between 3-8 years. Calcinosis cutis in 5 cases, decreased muscle strength in 3 cases, joint involvement in 4 cases were detected. Systemic steroids, methotrexate, and non-steroid anti-inflammatory drugs were given in all cases before tofacitinib treatment. Pademexone was used in 4 cases because of severe skin calcinosis, high dose intravenous immunoglobulin in 4 cases, mycophenolate mofetil in 3 cases, rituximab in 3 cases and cyclophosphamide in 1 case previously. Tofacitinib treatment (10mg/kg) was started in 6 cases with treatment-resistant JDM. Five cases had been treated with tofacitinib for 6-24 month intervals. The treatment was discontinued in one case because of severe allergic reaction. Variable level of improvement were detected in the skin findings of all cases during the therapy period. The treatment was interrupted for 1 month in only one case due to neutropenia.

Conclusion: Tofacitinib seems to be an effective and safe treatment option in patients with JDM who are resistant to conventional treatments. More studies are needed on this subject.

Disclosure of Interests: None declared

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FRI0461 SAFETY OF BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS: A META-ANALYSIS OF OBSERVATIONAL STUDIES


1. University Lyon 1, Laboratoire de Biométrie et Biologie Évolutive, Lyon, France; 2. Universidad Nacional de Asunción, Department of Research, San Lorenzo, Paraguay; 3. Hospital Woman Mère Enfant - HCL, Department of Paediatric Rheumatology, Bron, France; 4. Lyon Sud Hospital Center, Department of Rheumatology, Pierre-Bénite, France; 5. Universidad Nacional de Asunción, San Lorenzo, Paraguay; 6. University Lyon 1, Department of Pharmaco-Toxicology, Lyon, France; 7. Lyon Sud Hospital Center, Department of Internal and Vascular Medicine, Pierre-Bénite, France

Background: Follow-up cohorts (observational studies) were initiated consecutively or simultaneously to the development of randomised controlled trials (RCTs) in JIA patients 1-3. They help to identify many complications observed only in clinical practice related to off label use, coadministration of treatments, drug misuse, and occurrence of rare or unexpected event. In addition, observational studies include a higher number of patients with a longer duration of follow-up compared to randomised trials. Hence, they have a higher power to capture the occurrence of serious adverse events (SAE) in daily clinical practice 4.

Objectives: To estimate the incidence of serious adverse events (SAEs) including serious infections, malignancies, and death in patients with juvenile idiopathic arthritis (JIA) treated with biological agents (BAs) in daily clinical practice using meta-analysis techniques.

Methods: We systematically searched, up to May 2019, Medline and Embase databases for observational studies performed in JIA disease under BAs treatment. Outcomes were SAEs, serious infections, malignancies and all-cause mortality. Complementary, the incidence of SAEs in randomised controlled trials (RCTs) with withdrawal and parallel designs was performed by meta-analysis.

Results: A total of 31 observational studies were included (6811 patients totalizing 17530 patients-years [PY] of follow-up). The incidence rate of SAEs was similar in observational cohorts and withdrawal RCTs (4.46 events per 100 PY, 95% CI 2.85-6.38; I² = 95%) and 3.71 events per 100 PY (95% CI 0.0.0-13.34, I² = 56%), respectively. The incidence of SAE was lower in parallel RCT. The incidence rate of serious infections, malignancies and death in observational cohorts was estimated at 0.74 events per 100 PY (95% CI 0.32-1.30, I²=83%) 0.10 events per 100 PY (95% CI 0.06-0.16, I²=0%) and 0.09 events per 100 PY (95% CI 0.05-0.14, I²=0%), respectively. Infections were the known cause of death in 8 of the 14 deaths. In meta-regression and subgroup analysis, variation of serious infections rates were partially explained by follow-up time (R² = 30.3%, p = 0.0008). JIA categories (all JIA versus polyarticular versus systemic JIA categories, p = 0.001) and cohort quality (Newcastle-Ottawa score ≥ 6 versus ≤ 5 stars, p = 0.0025).

Conclusion: Our results suggest that the incidence rate of SAEs related to BAs in JIA disease is similar to those observed in randomised withdrawal trials. The overall incidence remained low. However, unsatisfactory description of SAEs prevents analysis of hospitalisation causes. Infection and, to a lesser extent, cancer and death, explain only part of burden of BAs.

References:
Table 2 shows the disease characteristics at MTX initiation and discontinuation. Relapse who have reached JADAS27 inactive disease (≤1 and no active extra-articular manifestations) and discontinued MTX before the age of 18 years-old. Relapse, while both rheumatoid factor (RF) positive polyarthritis and extended extra-articular disease before MTX withdrawal is associated with lower likelihood of relapse. There is some evidence that a longer period of inactive disease before MTX withdrawal is associated with two times the likelihood of relapse. Like in other studies we also showed that the time in remission before MTX discontinuation was associated with two times the likelihood of relapse. Like in other studies we also showed that the time in remission before MTX discontinuation is the main predictor of relapse. We found no association between the JIA category and the risk of relapse.

Conclusion: MTX, biologics and JIA durations are factors influenced on anti-vaccine antibody levels. It is necessary to regularly check the levels of anti-vaccine antibodies, especially anti-measles and anti-diphtheria for creation of the individual vaccination plan for JIA patients, treated with MTX and biologics.

Disclosure of Interests: None declared

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FR10462 PREDICTIVE FACTORS OF RELAPSE AFTER METHOTREXATE DISCONTINUATION IN JIA PATIENTS WITH INACTIVE DISEASE

S. Azevedo, J. Tavares-Costa, A. T. Meto, R. Freitas, M. Cabral, M. Conde, F. Aguiar, A. F. Mourão, F. Oliveira-Ramos, M. J. Santos, D. Peixoto, 1Unidade Local de Saúde do Alto Minho, Rheumatology Department, Ponte de Lima, Portugal; 2Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Pediatric Rheumatology Unit, Lisboa, Portugal; 3Hospital Garcia de Orta, Rheumatology Department, Almada, Portugal; 4Hospital Prof. Doutor Fernando Fonseca, Pediatric Department, Amadora, Portugal; 5Hospital Dona Estefânia, Centro Hospitalar Lisboa Central, Pediatric Department, Lisboa, Portugal; 6Centro Hospitalar Universitário São João, Pediatric Rheumatology Unit, Porto, Portugal; 7Hospital de Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Rheumatology Department, Lisboa, Portugal

Background: Methotrexate (MTX) is the most widely used conventional synthetic-disease-modifying antirheumatic drug (csDMARD) in the treatment of juvenile idiopathic arthritis (JIA). When remission is achieved, questions remain about discontinuing MTX. There is some evidence that a longer period of inactive disease before MTX withdrawal is associated with lower likelihood of relapse, while both rheumatoid factor (RF) positive polyarthritis and extended extra-articular disease categories are associated with higher probability of disease relapse.

Objectives: To identify predictive factors of relapse after discontinuation of MTX in JIA patients with inactive disease.

Methods: Prospective multicentre cohort study in patients diagnosed with JIA, according to the ILAR classification, using real world data from the Portuguese national register database, Reuma.pt (Fig 1). We evaluated patients who have reached JADAS27 inactive disease (≤1 and no active extra-articular manifestations) and discontinued MTX before the age of 18 years-old. Relapse was defined as recurrence (>1 or extra-articular manifestations) or restarting a DMARD. To identify differences of relapse risk, univariate analyses were performed. Persistence in remission was estimated using the Kaplan-Meier method. Subsequently, Cox regression analyses were performed to identify predictors of relapse.

Results: 119 JIA patients discontinued MTX due to inactive disease (Fig 1). 69.7% were females and 60.6% had oligoarticular JIA. Sociodemographic and clinical characteristics are shown in Table 1. Relapse has occurred in 32.8%. Table 2 shows the disease characteristics at MTX initiation and discontinuation and at relapse or last visit.

In univariate analysis, relapse was associated with the use of NSAIDs at the time of MTX discontinuation (p=0.027) and with a period of less than two years in inactive disease before MTX suspension (p=0.040). We found no association with gender, race, immunology (RF, antinuclear and cyclic citrullinated peptide antibodies), MTX dose, discontinuation modality (tapering and spacing the doses or just tapering the dose), extra-articular manifestations, previous corticotherapy, family history, body mass index, JADAS, CHAQ index, inflammatory parameters, tender and swollen joint counts at MTX initiation or discontinuation nor with age at remission or at MTX suspension. Median persistence in inactive disease was significantly higher in patients with more than two years in remission before MTX discontinuation (p=0.034) and in those who did not use NSAIDs at time of MTX discontinuation (p=0.026) (Fig 2). After adjustment for age at diagnosis, MTX tapering and JIA category, use of NSAIDs at the time of MTX discontinuation (HR, 1.98 95%CI 1.03-3.82) and less than two years in remission (HR, 3.12 95%CI 1.35-7.13) remained associated with relapse.

Conclusion: In this large cohort we found that the use of NSAIDs at the time of MTX discontinuation was associated with two times the likelihood of relapse. Like in other studies we also showed that the time in remission before MTX discontinuation is the main predictor of relapse. We found no association between the JIA category and the risk of relapse.

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