Background: Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is one of the best-known monogenic auto-inflammatory disorders resulting from an autosomal dominant variation in the TNF superfamily receptor 1A (TNFRSF1A) gene (1).

Objectives: To define best treatment approach in patients with TRAPS and effect on long-term outcome.

Methods: We reviewed data on patients with TRAPS enrolled in the Eurofever international registry according the INSAID gene variant classification and the new Eurofever/PRINTO classification criteria (EPCC).

Results: Data on 226 patients were available. Patients not fulfilling the EPCC carrying likely benign/benign variants (40 patients, 18%), were not fulfilling the EPCC with VOUS/not classified variants (38 patients, 17%) or pathogenic/likely pathogenic variants (127 patients, 56%). In particular, in patients not fulfilling the EPCC, less frequent abdominal pain and skin rashes, higher efficacy rate likely pathogenic variants (127 patients, 56%). In particular, in patients not fulfilling the EPCC with VOUS/not classified variants (38 patients, 17%) or pathogenic/likely pathogenic variants (40 patients, 18%) displayed a milder disease than the patients fulfilling carrying likely benign/benign variants (21 patients, 9%) or VOUS/not classified variants (21 patients, 9%).

Conclusion: Anti-TNF drugs are the best maintenance treatment in TRAPS with potential to reverse the most serious disease complications of AA amyloidosis and infertility. The diagnosis of TRAPS should be considered very carefully in patients carrying VOUS/not classified variants not fulfilling the EPCC.

References:

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FRI0458

EFFICACY AND SAFETY OF PCV13 VACCINATION IN JIA PATIENTS WITH SYSTEMIC MANIFESTATIONS ON TOCILIZUMAB AND CANAKINUMAB TREATMENT


Background: The need for continuous use of immunosuppressive drugs leads to increased risk of developing infectious diseases in children with juvenile idiopathic arthritis with systemic manifestation (sJIA). Questions about choosing the optimal vaccination time and the effect of different classes of therapy on vaccination effectiveness are still open.

Objectives: To study clinical and laboratory effectiveness of PCV13-vaccination in children with sJIA on tocilizumab (TOC) and canakinumab (CAN) treatment depending on disease activity stage. Efficacy was evaluated by achieving of protection level of anti-pneumococcal antibodies after 4 weeks and by clinical indicators after 6 month follow-up: frequency of acute respiratory infections, frequency of antibiotics treatment courses, frequency of temporary withdrawal of biologics treatment due to severe infections. Frequency of events was counted per patients-years.

Methods: Prospective cohort study included 2 groups of sJIA patients: in stable remission (Remission group, n=53) receiving CAN (n=10) or TOC (n=43) treatment, and in acute stage of disease (Acute group, n=25) which started to receive CAN (n=7) or TOC (n=18) either before vaccination (Acute Treated Before subgroup, n=17) or after vaccination (Acute Treated After subgroup, n=8). 0.5 ml of the 13-valent PCV was administered once subcutaneously. Efficacy was evaluated by achieving of protection level of anti-pneumococcal antibodies after 4 weeks and by clinical indicators after 6 month follow-up: frequency of acute respiratory infections, frequency of antibiotics treatment courses, frequency of temporary withdrawal of biologics treatment due to severe infections. Frequency of events was counted per patients-years.

Results: Four weeks after vaccination, protection level of anti-pneumococcal antibodies was achieved for 36 (67.9%) patients in Remission group, 16 (64%) patients in Acute group (intergroup p=0.932), and in 8 (47.06%) patients in Acute Treated Before subgroup and in 8 (100%) patients in Acute Treated After subgroup (intersubgroup p=0.022). PCV13 have shown high clinical effectiveness in both Remission group and Acute group. Reducing of acute respiratory infections frequency was as follows: from 4.57 to 2.15 episodes per patient-year in Remission group (p=0.001) and from 4.32 to 1.28 per patient-year in Acute group (p=0.001).

Conclusion: Vaccination with the 13-valent PCV has demonstrated high clinical efficacy and safety in children with sJIA both in the acute stage of the disease and during remission. Vaccination of patients in acute stage of sJIA before treatment has advantages over vaccination during remission or after prolonged immunosuppressive therapy in terms of achieving an adequate vaccine response.

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FRI0459

TOFACITINIB TREATMENT IN RECALCITRANT JDM PATIENTS

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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 recently 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 3-9 years. Calcinosis cutis in 5 cases, decreased muscle strength in 3 cases, joint involvement in 4 cases were detected. Steroidal, methotrexate, and non-steroidal anti-inflammatory drugs were given in all cases before tofacitinib treatment. Pamidronate 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/qm) was started in six cases with treatment-resistant JDM. Five cases had been treated with tofacitinib for 6-24 months interval. 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.

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FRI0460 SAFETY OF BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS: A META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: Follow-up cohorts (observational studies) were initiated consecutively or simultaneously to the development of randomised controlled trials (RCTs) in JIA patients 1,2,3. They help to identify many complications observed only in clinicopathologic arthritis (JIA) treated with biological agents (BAs) in daily clinical practice, using meta-analysis techniques.

Objectives: To estimate the incidence of serious adverse events (SAEs) including serious infections, malignancies, and death in patients with juvenile idiopathic arthritis 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 published 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 totalising 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 0.0-13.34, 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= 0.0009, 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:

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FRI0461 THE ANTI-VACCINE ANTIBODY AGAINST MEASLES, PAROTITIS, RUBELLA, DIPHTHERIA AND HEPATITIS B IN 170 JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Patients with juvenile idiopathic arthritis (JIA) may have lower protective levels of anti-vaccine antibodies due to high immunological activity, interrupted or incomplete vaccination schedule, and due to using of immune-modulating drugs, e.g. systemic corticosteroids (CS), methotrexate (MTX) and biologics.

Objectives: The aim of our study was to find the predictors of low levels of anti-vaccine antibodies in patients with JIA.

Methods: In the present study were included data 170 JIA (55 boys and 115 girls) aged from 2 to 17 years, who received scheduled vaccination before the age of 2 years and before JIA onset against measles, parotitis, hepatitis B, diphtheria and rubella. In all patients the Ig G anti-vaccine antibodies levels were detected with ELISA. In each patient we evaluate the type of the disease (oligoarthrits - 73, polyarthritis - 61, systemic-16 and enthesis-related arthritis - 20), onset age, presence of uveitis, duration of JIA, treatment with corticosteroids (CS), methotrexate (MTX) and biologics. Data presented with median and 25%-75%.

Results: The main demographic characteristics: age of inclusion in the study 11.4 (76-14.8) years, disease onset – 6.0 (3.7-9.0) years, disease duration – 3.8 (1.9-6.5) years. Treatment with CS was in 43 (25.3%), MTX in 154 (90.6%) and biologics 82 (48.2%) patients, among them 53 had TNFa-inhibitors. More than 1 biologic consequently received 16/82 (19.5%) patients. Protective levels of anti-measles antibodies was in 98 (57.6%) of all JIA population, anti-parotitis – 136 (80.0%), anti-hepatitis B – 85 (50.0%), anti-diphtheria – 88 (51.7%), anti-rubella – 167 (98.8%). Data of vaccination status and anti-vaccine antibodies levels in the table. In univariate and multivariate regression analysis the main risk factors for anti-measles antibodies levels were MTX using (p=0.045), more than 1 biologics (p=0.0004); for anti-hepatitis B – MTX (p=0.03), for anti-diphtheria antibodies: onset age (p=0.0002), JIA duration (p=0.0007), number vaccine doses (p=0.02), more than 1 biologics (p=0.01); combined treatment with biologics and other drugs (MTX or CS).