Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.857

POS1300 PAIN IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED TO TARGET: 24 MONTH RESULTS FROM A RANDOMISED TRIAL

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Background: Juvenile Idiopathic Arthritis (JIA) is the most common auto-immune disease in children and pain is a common symptom. Despite treatment advances in recent years, pain often persists when the disease is inactive. Treating JIA to target has been widely recommended¹, but effectiveness in pain reduction has not been proven yet².

Objectives: To compare pain scores over two years in three treatment arms in JIA patients that were treated to target and to identify baseline characteristics predicting unfavorable pain outcomes.

Methods: DMARD naïve children who participated in the BeSt for kids study³ with oligoarticular JIA, RF negative polyarticular JIA and juvenile psoriatic arthritis were included. Patient were treated to target aimed at inactive disease according to 1 of 3 different treatment groups; 1) initial sequential DMARD monotherapy 2) initial methotrexate (MTX) with prednisolone bridging or 3) initial MTX with etanercept. Pain intensity was measured using a 100mm Visual Analogue Scale during 24 months of follow up with 3-monthly intervals. Potential differences in VAS pain scores over time between treatment arms were compared using linear mixed models with random intercept and random slope for visits clustered within patients. A similar multivariable mixed model was used to assess the ability of several baseline characteristics to predict the chance of high pain levels during follow-up.

Results: 92 patients were randomized into the three treatment groups. Overall, pain scores over time reduced from mean 55.3 (SD 21.7) at baseline to 19.5 (SD 25.3) after 24 months. When comparing pain over time per arm, pain scores decreased significantly over time β -1.37 (95% CI -1.726; -1.022). No significant difference was found in pain over time between treatment groups (interaction term treatment arm*time (months) β (95% CI) arm 1 0.13 (-0.36; 0.62) and arm 2 0.37 (-0.12; 0.86) compared to arm 3), Figure 1. Correction for sex and symptom duration as possible confounders yielded similar results. Multiple baseline characteristics demonstrated a significant predictive value for pain over time: VAS pain (scale 0-100) with β 0.44 (95% CI 0.25; 0.65), VAS physician (scale 0-100) with β -0.34 (-0.55; -0.06), number of active joints with β 0.77 (0.19; 1.34), Child Health Questionnaire Physical summary Score with β -0.42 (-0.72; -0.11) and Psychosocial summary Score β -0.42 (-0.77; -0.06). Symptom duration, VAS patient/parent and NSAID use were no significant predictors, Table 1.

Conclusion: Treatment to target seems effective in pain reduction in non-systemic JIA patients irrespective of initial treatment strategy. Several baseline predictors for pain over time were identified, which could serve as an initial indication for non-systemic JIA-patients with a high risk of pain despite a strict treat-to-target strategy.

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Figure 1 | VAS pain over time. Linear mixed models with random intercept and random slope for visits clustered within patients. VAS pain measured on a 100mm scale. Error bars indicate 95% confidence intervals.

Table 1. Baseline Characteristics

	β	p-value	95% Confidence Interval
VAS Pain	0.45	0.000	0.25 to 0.65
VAS Physician	-0.31	0.014	-0.55 to -0.06
VAS Patient/parent	-0.02	0.873	-0.21 to 0.18
No. of active joints	0.77	0.009	0.19 to 1.34
PhS*	-0.42	0.008	-0.72 to -0.11
PsS**	-0.42	0.022	-0.77 to -0.06
Symptom duration (mo.)	8.09	0.118	-2.08 to 18.26
NSAID use	-1.30	0.791	-10.91 to 8.31

VAS Pain, VAS physician and VAS patient/parent was measures on a 100mm scale.*PhS= Physical Summary Score of the Child Health Questionnaire Parent form 50 (scale 0-100).**PsS= Psychosocial Summary Score of the CHQ-PF50 (scale 0-100).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.988

POS1301 DRUG SURVIVAL OF BIOLOGICS WITH RESPECT TO COMBINATION WITH METHOTREXATE IN TREATMENT OF POLYARTICULAR JIA

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Background: In polyarticular juvenile idiopathic arthritis (pJIA) biologic therapies are often combined with methotrexate (MTX). This combination was shown to increase efficacy in adult rheumatoid arthritis patients. MTX may also have a protective effect on the formation of anti-drug antibodies and thus may prolong drug survival. In pJIA, there are few and sometimes controversial data available.

Objectives: To compare the effect of combination treatment with MTX on discontinuation due to inefficacy and on drug survival discontinuation of biologics approved for first line treatment of pJIA.

Methods: Patients from the German BIKER registry with their first treatment course with Adalimumab, Etanercept, Golimumab or Tocilizumab were selected. Rates of ineffectiveness-related withdrawal were analysed and compared using χ^2 -test, Wald-test and Kaplan-Meier analysis of patients receiving biologic monotherapy or concomitant methotrexate. Cases were censored if MTX was discontinued before the biologic.

Results: 2173 pJIA patients were identified who for the first time received a biologic. Etanercept (ETA) was by far the most frequently used biologic for first line biologic treatment in pJIA (77%) followed by Adalimumab (ADA, 16%). Patients on Golimumab (GOL) received most frequently a combination with MTX (86.5%), while patients on Tocilizumab (TOC) had the lowest rate of combination treatment (53%).

ETA/ADA/GOL/TOC was given as monotherapy in 500(30%)/89(26%)/5(13.5%)/46(47%) and combined with MTX in 1179 (70%)/259(74%)/32(86.5%)/51(53%)

%) cases. More patients with rheumatoid-factor negative (54 vs 50%; $p=0.04$) and rheumatoid-factor positive pJIA (13 vs 10%, $p=0.04$) received combination with MTX, while more patients in the monotherapy cohort had extended oligoarthritis (40 vs 32%, $p<0.001$). Patients with MTX had a shorter disease duration (4 vs 5.5 years, $p<0.001$) and received concomitant steroid more often (34 vs 24%), $p<0.001$). There was no statistical difference regarding disease activity parameters (active joint count, patient assessment and physician assessment of disease activity, ESR, CRP, CHAQ-DI, JADAS10). Discontinuation due to ineffectiveness was reported for ETA/ADA/GOL/TOC in 20%/18%/14%/28% of patients, respectively in 3.7/4.9/6/10.5 patients/100 treatment years. Thus discontinuation due to inefficacy was reported less frequently with ETA compared to ADA ($p=0.046$) and TOC ($p<0.001$) and with ADA compared to TOC ($p<0.001$).

Patients on ETA and ADA had a slightly, but not statistically significant lower rate of withdrawal for ineffectiveness if on methotrexate (Figure 1). There was no difference regarding baseline disease activity parameters in patients with ETA/ADA monotherapy compared with combination with MTX, apart from patients with ETA+MTX receiving more often systemic steroids at baseline (36 vs 24%, $p<0.001$). For both GOL and TOC treatment, no baseline differences in disease activity between cohorts with monotherapy and MTX combination could be shown. The combination with MTX led to significantly lower rates of discontinuation due to inefficacy ($p<0.05$) with GOL and TOC (Figure 1).

Conclusion: Patients with pJIA mostly were treated with a combination of the biologic and MTX rather than with biologic monotherapy. Treatment was discontinued due to lack of efficacy in 14% to 28%. No statistically significant effect of combination treatment with MTX versus monotherapy could be observed regarding the rate of treatment failures in patients treated with ETA or ADA. However, combination treatment with MTX significantly prolonged the survival of GOL and TOC in patients with polyarticular JIA. The results are limited by low patient numbers in the GOL cohort and possible bias by JIA category.

Figure 1. Kaplan Meier plot of drug survival in patients with monotherapy or with combination with MTX of the indicated biologic

Disclosure of Interests: Gerd Horneff Speakers bureau: MSD, Grant/research support from: Pfizer, Roche, Chugai, MSD, Daniel Windschall: None declared, Kirsten Minden Speakers bureau: Pfizer, Abbvie, Grant/research support from: Pfizer, Toni Hospach: None declared, Frank Dressler: None declared, Frank Weller-Heinemann: None declared, Boris Huegle: None declared, Ivan Foeldvari Speakers bureau: Pfizer, Ariane Klein: None declared

DOI: 10.1136/annrheumdis-2021-eular.995

POS1302 THE MUSCULOSKELETAL SYSTEM MANIFESTATIONS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is a monogenic inherited periodic fever syndrome presenting with episodes of self-limiting fever and inflammation of serosal membranes. The attacks emerge with arthritis were defined as one of the major diagnostic criteria besides involvement of serosal membranes. Non-specific musculoskeletal findings such as myalgia, arthralgia, transient synovitis, and more rare manifestations like protracted febrile myalgia can also be seen in FMF patients attacks

Objectives: We aim to reveal the frequency and genotype association of musculoskeletal manifestations in children with FMF.

Methods: The patients diagnosed with FMF between January 1, 2017 and June 1, 2019, and followed for at least 6 months in our pediatric rheumatology clinic were included in the study. Musculoskeletal manifestations of patients were

enrolled. The patients were grouped according to the "Mediterranean Fever" (MEFV) gene variants. Musculoskeletal manifestations of the patients were compared between the groups

Results: The study group included 634 children with FMF (336 female and 298 male, F/M: 1.13/1). The clinical manifestations of patients in attack period were as follows: 99% of the patients had fever, 87.3% had abdominal pain, 20.7% had chest pain, 11.3% had vomiting, 10.7% had erysipelas like erythema, and 9.3% had headache. The musculoskeletal symptoms were accompanied by 58.6% (n: 372) of the patients during the attack period. The most common musculoskeletal manifestation was found as arthralgia (32.6%, n: 206). Also, the other musculoskeletal manifestations were found as follows during attacks; arthritis in 23.7% (n: 150), myalgia in 20.5% (n: 130), exertional calf pain in 6.5% (n: 41), and protracted febrile myalgia in 1% (n: 7) of the patients. It was observed that the musculoskeletal manifestations were significantly higher in patients with homozygous M694V variant in exon-10 ($p=0.017$). Also, it was found that the musculoskeletal manifestations are more common in the attack periods of patients carrying the M694V variant in at least one allele ($p=0.019$).

Conclusion: It was determined that the musculoskeletal manifestations were seen as an attack symptom in more than half of FMF patients. Also, homozygous and compound heterozygous MEFV mutations including M694V variant found as a risk factor for emerge of musculoskeletal manifestations. In children with unexplained and recurrent musculoskeletal symptoms, especially in ethnicities with the high frequency of FMF, analysis of MEFV gene can help reveal the underlying cause.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1169

POS1303 EXPERIENCE WITH ADALIMUMAB BIOSIMILAR USE IN CLINICAL PRACTICE: DATA FROM THE GERMAN BIKER-REGISTRY

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Background: In 2017, Adalimumab Biosimilars became approved. Comparative studies to the originator have been performed in adult patients with rheumatoid arthritis, ankylosing spondylitis and psoriasis and extrapolation led to approval for juvenile idiopathic arthritis (JIA).

Objectives: So far there is limited experience with biosimilars in JIA: The large national data base of the BIKER-registry was used to describe experience with Adalimumab biosimilars in clinical practice

Methods: This retrospective analysis used data of the German BIKER-registry. The data basis was screened for patients exposed to Adalimumab. Subcohorts with initiation of treatment after 2017, use of the originator and of biosimilars were built. The course of JADAS10, Physician global assessment VAS 0-100-mm, Parent/patient global assessment VAS 0-100-cm, Active joint count 0-71, truncated at 10, ESR and CHAQ-DI was analyzed. Descriptive statistics was used for demographic, clinical data, drug exposure, adverse events (AEs) and events of special interest (ESI).

Results: Until 31.10.2020, 1173 JIA patients were reported to have received Adalimumab. 352 treatments have been started after January 1, 2017. A biosimilar was used first line in 44 patients. Further 55 patients switched for the originator to a biosimilar. 2 patient switched from a biosimilar to the originator. 3 patients switched to a second biosimilar while 5 patients who switched from the originator to a biosimilar reswitched back to the originator.

After 2017, 33 pediatric rheumatology centres reported initiation of Adalimumab treatment. 17 have used a biosimilar. 15 centres have switched at least 1 patient from the originator to a biosimilar and 14 have used first line a biosimilar in at least 1 patient. In a single centre, initiation of a biosimilar was used more frequently (8 versus 7).

The patients' characteristics and disease activity parameters were brightly comparable. The JIA category rheumatoid factor (RF) negative polyarthritis was less frequent in the biosimilar first cohort while RF positive polyarthritis and psoriatic arthritis was more frequent. In patients with idiopathic uveitis the originator was used more often. In the switching cohort, more patients had RF negative polyarthritis, persistent oligoarthritis but less had psoriatic arthritis and no had RF positive polyarthritis.