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.

Methods: DMARD naïve children who participated in the BeSt for kids study4 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 0.27 (-0.12; 0.68) 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 with 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.

REFERENCES:

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Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>p-value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS Pain</td>
<td>0.45</td>
<td>0.000</td>
<td>0.25 to 0.65</td>
</tr>
<tr>
<td>VAS Physician</td>
<td>-0.31</td>
<td>0.014</td>
<td>-0.55 to -0.06</td>
</tr>
<tr>
<td>VAS Patient/parent</td>
<td>-0.02</td>
<td>0.873</td>
<td>-0.21 to 0.18</td>
</tr>
<tr>
<td>No. of active joints</td>
<td>0.77</td>
<td>0.009</td>
<td>0.19 to 1.34</td>
</tr>
<tr>
<td>PsS**</td>
<td>-0.42</td>
<td>0.008</td>
<td>-0.72 to -0.11</td>
</tr>
<tr>
<td>PhS**</td>
<td>-0.42</td>
<td>0.022</td>
<td>-0.77 to 0.06</td>
</tr>
<tr>
<td>Symptom duration (mo.)</td>
<td>0.09</td>
<td>0.118</td>
<td>-2.08 to 18.26</td>
</tr>
<tr>
<td>NSAID use</td>
<td>-1.50</td>
<td>0.791</td>
<td>-10.91 to 8.31</td>
</tr>
</tbody>
</table>

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).

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enrolled. The patients were grouped according to the “Mediterranean Fever” (MEVF) 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 = 1:1.13). 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 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 protruded febrile myalgia in 1% (n: 7) of the patients. It was observed that the musculoskeletal manifestations were significantly higher in patients with homozgyous 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, homozgous and compound heterozygous MEVF 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 MEVF gene can help reveal the underlying cause.

REFERENCES:

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

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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 to the originator for 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 were switched 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 at 1 patient from the originator to a biosimilar. Further 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 slightly comparable. The JIA category rheumatoid factor (RF) negative polyarthritis was less frequent in the biosimilar first cohort while RF positive polyarthritids 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 polyarthritids, persistent oligoarthritis but less had psoriatic arthritis and no had RF positive polyarthritids.