AN EVALUATION OF THE EFFICACY OF METHOTREXATE IN THE TREATMENT OF JUVENILE ENTHESIS RELATED ARTHRITIS

Keywords: Disease-modifying drugs (DMARDs), Spondyloarthritis, Enthesitis

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Background: Methotrexate (MTX) is quiet commonly used to treat all subtypes of juvenile idiopathic arthritis (JIA). Despite that, there are no studies on the efficiency of MTX treatment in juvenile enthesis related arthritis (ERA).

Objectives: This study aims to evaluate the efficacy of MTX treatment in children with juvenile arthritis of the ERA subtype.

Methods: We conducted a retrospective chart review from January 2017 to December 2021 of all patients who received MTX for at least 3 months. The clinical manifestation of the ERA was determined by using JADAS and the JSpADA. Good therapeutic response was defined by a reduction of the JSpADA by 0.6 points or more. A JADAS under 2 was considered minimal disease activity, whereas a JADAS <1 was interpreted as inactive disease.

Results: We found 188 patients in whom MTX was initiated, 117 (62.23%) of these patients were treated with MTX for at least three months and therefore fulfilled the criteria for this analysis. At all follow-ups, the patients showed a significant reduction in both scores compared to the start (see Table 1). After three months 49.57% of the participating patients were considered good responders, after twelve months it was 70%. Half of the followed patients achieved the state of remission after twelve months, another 12.82% showed only minimal disease activity at this point.

Conclusion: This study shows the efficacy of MTX as a first-line therapy for the treatment of children with ERA. A comparative study with Sulfasalazine would be interesting.

REFERENCES:

Table 1. BL Z-score by pt characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Median height</th>
<th>Mean Z-score (IQR)</th>
<th>Median height Z-score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JIA category</td>
<td>21</td>
<td>0.3 (-0.4–0.9)</td>
<td>0.2 (0.9)</td>
<td>0.17</td>
</tr>
<tr>
<td>Juvenile polyarticular</td>
<td>20</td>
<td>-0.1 (0.8–0.7)</td>
<td>0.0 (1.1)</td>
<td></td>
</tr>
<tr>
<td>RF+ polyarthritis</td>
<td>39</td>
<td>-0.1 (1.1–0.6)</td>
<td>0.1 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Age 2–&lt;6 years</td>
<td>104</td>
<td>-0.3 (1.1–0.6)</td>
<td>0.4 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Age 6–&lt;12 years</td>
<td>39</td>
<td>-0.1 (1.1–0.6)</td>
<td>0.1 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Sex Female</td>
<td>134</td>
<td>-0.3 (1.0–0.5)</td>
<td>0.1 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Race Asian</td>
<td>150</td>
<td>0.0 (0.9–1.5)</td>
<td>0.0 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity Hispanic/Latino</td>
<td>60</td>
<td>0.3 (1.0–0.5)</td>
<td>0.0 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Previous bDMARD naive</td>
<td>195</td>
<td>0.3 (1.0–0.5)</td>
<td>0.0 (1.1)</td>
<td></td>
</tr>
</tbody>
</table>

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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IMPACT OF TOFACITINIB TREATMENT ON HEIGHT IN JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Inflammatory arthritides, Targeted synthetic drugs, Randomized control trial

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Background: Diminished growth can be a consequence of juvenile idiopathic arthritis (JIA).1] Growth hormone signals through a Janus kinase (JAK2) tyrosine kinase-coupled receptor.2] Tofacitinib, an oral JAK inhibitor approved for JIA, preferentially inhibits signalling by heterodimeric receptors associated with JAK1 and/or JAK3 and has less functional selectivity for JAK2.

Objectives: To evaluate the growth of patients (pts) with JIA treated with tofacitinib.

Methods: This post hoc analysis of the Phase 3 trial of tofacitinib in pts with JIA (NCT02592434; a 44-week, 2-part, double-blind [DB], withdrawal study in 225 pts aged 2–<18 years) enrolled 212 pts (pts with systemic JIA were excluded). In part 1, pts received open-label tofacitinib 5mg twice daily (BID); in part 2, pts received either tofacitinib or placebo. Both parts were conducted over a 44-week follow-up period. In part 1, pts were randomized to tofacitinib or placebo until Week 18. In part 2, pts then received tofacitinib in a long-term extension study. Height Z-scores were calculated on baseline (BL), Weeks 18, 44, 68 and 92 using age- and sex-matched reference data from the World Health Organization. A repeated measures mixed-effects analysis of variance was performed on change in height Z-scores over time on all pts. The impact of JIA category, age, sex, race, ethnicity, biologic disease-modifying antirheumatic drug (bDMARD)/conventional synthetic DMARD (csDMARD) use, and C-reactive protein (CRP; normal/elevated) on BL height Z-score was also assessed. A separate analysis assessed the impact of treatment on change in height Z-scores during the DB phase. Growth velocity (cm/year) from BL to Week 44 was calculated.

Results: Ethnicity was the only characteristic associated with BL height Z-score (Table 1). For B3 pts who received continuous tofacitinib, mean (95% confidence intervals [CI]) BL height Z-score was -0.4 (-0.7–0.1), and was stable up to Week 18 (Figure 1). Mean (95% CI) change in height Z-score from BL of the DB phase (Week 18) to Week 44 was not different for pts receiving tofacitinib (N=56; -0.03 [-0.1, 0.04]) vs placebo (N=36; -0.04 [-0.1, 0.04]). Growth velocities in the 56 pts who received tofacitinib for 44 weeks was within normal range for age and sex with peak values at ages 9–10 years and 11–12 years for females and males, respectively (data not shown).

Table 1. BL Z-score by pt characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>Median height</th>
<th>Mean Z-score (IQR)</th>
<th>Median height Z-score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity Hispanic/Latino</td>
<td>60</td>
<td>-0.6 (1.5–0.1)</td>
<td>-0.5 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Previous csDMARDs</td>
<td>152</td>
<td>0.0 (1.7–0.7)</td>
<td>0.0 (1.1)</td>
<td></td>
</tr>
</tbody>
</table>

For pts at baseline (BL), Weeks 18, 44, 68, and 92 using age- and sex-matched reference data from the World Health Organization. A repeated measures mixed-effects analysis of variance was performed on change in height Z-scores over time. The impact of JIA category, age, sex, race, ethnicity, biologic disease-modifying antirheumatic drug (bDMARD)/conventional synthetic DMARD (csDMARD) use, and C-reactive protein (CRP; normal/elevated) on BL height Z-score was also assessed. A separate analysis assessed the impact of treatment on change in height Z-scores during the DB phase. Growth velocity (cm/year) from BL to Week 44 was calculated.

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Disclosure of Interests: None Declared.

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Conclusion: In this post hoc analysis, pts with JIA began with near normal height Z-scores and tofacitinib had no negative impact on height Z-scores after 92 weeks. Growth velocity was within the normal range for age up to Week 44. Catch-up growth was not observed, possibly due to the study duration being too short and the BL height Z-scores being near normal.

REFERENCES:

Acknowledgements: This study was sponsored by Pfizer. We thank the PRCSG and PRINTO investigators for the collection of serum samples and data used. Medical writing support, under the direction of the authors, was provided by Lauren Moghart, MSC, CMCC Connect, a division of IPG Health Medical Communications, and was funded by Pfizer, New York, NY, USA, in accordance with Good Publication Practice (GPP 2022) guidelines (Ann Intern Med 2022;175:1298-1304).


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POS0765

SERUM BASIC FIBROBLAST GROWTH FACTOR IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Biomarkers, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Patients with rheumatic diseases are at high risk for poor outcomes and gaps in care when severe fibrosis occurs, as a result of tissue damage caused by chronic phase of persistent inflammation. Only limited data also controversial results are available on the fibrosis predictors in patients with juvenile idiopathic arthritis (JIA) on long-term methotrexate (MTX) treatment [1,2].

Objectives: To evaluate serum levels of basic fibroblast growth factor (bFGF) in children with juvenile idiopathic arthritis treated with methotrexate.

Methods: 104 patients with polyarthritis (50.96%), and oligoarthritis (40.38%), variants JIA (mean age 13.3 yrs, 59.62% female, mean age of JIA onset 7.2 yrs, mean disease duration 5.06 yrs) were included in this 4-years prospective study. In 104 children with JIA were treated with MTX 75.96% (vs. 24.04% not treated with MTX, 16.35% were prescribed MTX, but they didn’t receive any dose yet on investigation day). Among patients treated with MTX 4.81% had dose less than 10mg/m2/week, 32.69% 10-12.5mg/m2/week, 31.73% 12.5 - 15mg/m2/week, 6.73 % over 15mg/m2/week. bFGF levels were determined by bFGF ELISA kits (ELabscience, USA). Serum levels of bFGF were analyzed depending on patients’ gender, age, and age of JIA onset, its variant, duration, activity, and presence of MTX in treatment and its dose. Levels of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), circulating immune complex (CIC) and antistreptolysin-O (ASLO) were analyzed in this study.

Results: We evaluated bFGF level for children with JIA (min: 417.156 pg/ml; Me:7089.28 pg/ml; max: 180125 pg/ml). The average level of bFGF significantly increased in children with age of JIA onset from 15 to 18 years versus age of JIA onset up to 3 years (p = 0.009) and 11-14 years (p = 0.014). It was also found higher bFGF in patients with an average activity according JADAS-27 pattern versus a low one (p = 0.0005). Activity according JADAS-27 pattern, levels of ESR, CIC and ASL-O was associated with bFGF level. Mostly bFGF was correlated with ASLO (among: boys n=0.45, patients with oligoarthritis n=0.49, moderate disease activity according to JADAS-27 n=0.58, MTX treatment n= 0.38, dose of MTX, 12.5-15mg/m2/week n=0.50 p * 0.05), with CIC (among: patients with polyarthritis n=0.37, low activity disease according to JADAS-27 n=0.34, dose of MTX, less 10mg/m2/week n=0.96 p * 0.05), with ESR (among: girls n=0.37, patients with polyarthritis n=0.38, p * 0.05).

Conclusion: Children with JIA had a higher bFGF level in patients with JIA onset after 15 years old and moderate disease activity. CIC and ESR were corresponded with high bFGF level. Presence of additional streptococcal infection impact on fibrosis formation in children with JIA.

REFERENCES:

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Disclosure of Interests: None Declared.

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POS0766

CIRCULATING SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR (SUPAR) ASSOCIATES WITH JOINT DESTRUCTION IN JUVENILE IDIOPATHIC ARTHRITIS: A CASE-CONTROL STUDY WITH LONGITUDINAL FOLLOW-UP

Keywords: Inflammatory arthritides, Prognostic factors, Biomarkers

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Background: Reliable biomarkers in the early stages of juvenile idiopathic arthritis (JIA) are scarce. The disease heterogeneity makes it clinically challenging to predict the risk of future permanent joint damage. Some indicators of poor outcome have been identified, e.g. rheumatoid factor (RF) and antibodies against cyclic citrullinated peptides (anti-CCP), but additional biomarkers with predictive potential are warranted in order to start optimal treatment before tissue damage occurs. The soluble urokinase plasminogen activator receptor (suPAR) has been reported as an easily measurable biomarker for prognosis and severity in several disease, including adult rheumatoid arthritis, systemic lupus erythematosus and other inflammatory conditions [1]. However, to our knowledge, suPAR has never been studied in JIA.

Objectives: We asked whether suPAR could predict a more severe course with erosions in JIA.

Methods: 51 well-characterized patients with recent-onset or established JIA and 50 age- and sex-matched healthy control subjects were included. Blood sampling was performed at inclusion and sera were stored for later analysis of suPAR by suPARnostic ELISA (Virogates, Birkerød, Denmark). The patients were carefully followed over 3 years and erythrocyte sedimentation rate, C-reactive protein, RF, anti-CCP and antinuclear antibodies were analyzed as part of clinical routine. Signs of joint destruction were evaluated by radiographic investigation of affected joints. Data was evaluated using non-parametrical statistical methods.

Results: Overall, the levels of suPAR did not differ significantly between JIA and controls (Figure 1). Still, the subgroup of subjects with polyarticular disease showed higher suPAR than the controls (p<0.013). In addition, elevated suPAR levels were associatered with joint erosions (p<0.022). In 2 individuals with erosions, high levels of suPAR were found despite absence of RF and anti-CCP.

Conclusion: We present new data on the biomarker suPAR in JIA. The results indicate that, in addition to RF and anti-CCP, analysis of suPAR could be of additional value in predicting the risk of joint erosions. Early analysis of suPAR could potentially guide treatment decision-making in JIA, but our findings call for confirmation in larger cohorts.

REFERENCE: