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Paediatric rheumatology

THU0549

ABSENCE OF ASSOCIATION BETWEEN DRUG EXPOSURE AND INFECTION IN PATIENTS WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGIC OR NON-BIOLOGIC DMARDS TREATED WITH SC AND IV ABACEPT

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Background: Infections are the most common expected AEs linked to biologic (b) DMARDs in paediatric patients (pts) with juvenile idiopathic arthritis (JIA). Blood concentrations achieved with bDMARDs vary greatly between individual pts. It is not known if higher abatacept (ABA) exposure is linked to higher infection risk in paediatric populations.

Objectives: To assess the relationship between the incidence of infection and SC (50–125 mg weekly) and IV (10 mg/kg monthly) ABA exposure in pts with polyarticular-course JIA (pJIA).

Methods: Data from the 4 month open-label periods of a Phase III SC ABA study (NCT01844518; weight-tiered ABA: 10–<25 kg [50 mg], 25–<50 kg [87.5 mg], ≥50 kg [125 mg]; 219 pts aged 2–17 years) and an IV ABA study (NCT00095173; ABA 10 mg/kg monthly; 184 pts aged 6–17 years) in pts with pJIA were analysed. The association between serum ABA exposure measures (steady-state trough [$C_{\min}$], maximum [$C_{\max}$] and time-averaged [C_{avg}] concentrations) estimated by population pharmacokinetic analysis and time to first infection (regardless of seriousness) was assessed. Kaplan–Meier (KM) plots of infection probability versus time to first infection by ABA exposure quartiles were created and log-rank test was performed to test the differences in distribution of time to first infection across exposure quartiles. Box plots of ABA exposure measures over time to Month 4 were generated, stratified by first infection occurrence (yes/no). Data for SC and IV ABA were assessed separately and pooled.

Results: Baseline demographic and clinical characteristics were comparable in the SC and IV studies.^{1,2} Overall, 135/403 pts (33.5%) had ≥1 infection over 4 months: 77/219 (35.2%) with SC ABA and 58/184 (31.5%) with IV ABA. KM plots for pooled SC and IV ABA showed no statistically significant difference in infection probability across four quartiles of ABA $C_{\min}$ (Fig A; $p=0.2317$; log-rank test), $C_{\max}$ ($p=0.5501$) or C_{avg} ($p=0.3808$). Consistent results were seen for individually studied SC and IV ABA $C_{\min}$ (Fig B, C), $C_{\max}$ and C_{avg} (not shown). In addition, there was no difference in median ABA exposure measures by infection occurrence (yes/no) in pooled and separate SC and IV analyses.

Abstract THU0549 – Figure 1. Kaplan–Meier Plots of Probability of First Infection, Regardless of Seriousness, Versus Days From First Dose to Infection by Abatacept $C_{\min}$ ss Quartiles and Route of Administration: Pooled SC and IV (A); SC (B); IV (C)

Conclusions: In pts with pJIA who received SC or IV abatacept, higher relative abatacept exposure was not associated with a higher risk of infections for 4 months.

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THU0550

NEW IL10 RECEPTOR GENE MUTATION ASSOCIATED TO A SPECTRUM OF INFLAMMATORY APHTHOSIS AND CROHN'S DISEASE

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Background: IL-10 is defined as an anti-inflammatory cytokine. Its activity is mediated by interaction with a cell surface receptor composed of 2 subunits: alpha (IL-10RA) and beta (IL-10RB). Homozygous mutations of IL-10RA gene have been linked to Very Early Onset Inflammatory Bowel Disease (VEO-IBD) in children with a total of 28 mutations identified till present.

Objectives: We report a Lebanese family presenting with a new exonic mutation in the IL-10RA gene variably associated to inflammatory aphthosis and adult onset IBD.

Methods: The proband is a boy born to consanguineous parents who presented to our attention at the age of 9. He suffered from persistent severe oral aphthosis, recurrent fever and intermittent diarrhoea since the age of 2 months, and anal aphthosis since the age of 7.

His Familial history is notable for moderate oral aphthosis in the father and adult onset Crohn's disease in a paternal uncle.

He was diagnosed with Behçet disease and received colchicine since the age of 8 with no efficiency.

His physical exam was normal except for severe oral and anal ulcers. No history of genital ulcers.

Laboratory tests revealed normal inflammatory markers. ANA titers, anti-DNA and anti-ENA were negative with normal complement level. Pathergy test and HLA B51 were negative as well as pANCA and cANCA. Iron, Zinc, vitamin and immune deficiencies were ruled out.

Yearly ophthalmologic screening revealed no signs of inflammation.

Repeated gastroscopy and colonoscopy and enteric MRI showed no pathologic findings.

Results: A genomic sequencing study for recurrent fever was performed. A novel heterozygous exonic mutation of the IL-10RA gene (c.G172A G>A, p.E58K) was identified. The child's father and his uncle were found to have the same mutation at homozygous state, however with different phenotypic presentations.

The child was started on Infliximab with favourable outcome after 3 months.

Conclusions: In this Lebanese family, the previously unreported IL-10RA gene mutation (c.G172A G>A, p.E58K) is associated to a variable spectrum from

benign oral aphthosis to IBD, both in homozygous and heterozygous forms. Our finding suggests that the presence of this mutation is a risk factor for inflammatory aphthosis. Whether this mutation will eventually lead to IBD is uncertain. Other unknown environmental and genetic factors might have a role in the final phenotype of the disease.

As bipolar aphthosis and recurrent fever can be misdiagnosed as Behçet disease, pro-inflammatory genetic mutations such as IL-10RA mutations should be considered in the setting of incomplete Behçet disease.

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THU0551 TREATMENT STRATEGY STUDY IN NEW ONSET DMARD NAIVE JUVENILE IDIOPATHIC ARTHRITIS FIRST RESULTS ON 24 MONTHS CLINICAL OUTCOME

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Background: In rheumatoid arthritis treatment, targeted treatment has shown to improve disease outcomes including the option of drug tapering and discontinuation. In non-systemic juvenile idiopathic arthritis (nsJIA) this has not been tried in a trial.

Objectives: To investigate which of three treatment strategies, targeting at drug-free inactive disease, is most effective and safe in recent onset DMARD-naïve nsJIA.

Methods: We conducted a randomised, multicenter, treatment strategy study with 24 months of follow up. Patients, 2–16 years old with symptom duration <18 months were randomised to 1) Sequential DMARD-monotherapy (sulfasalazine (SSZ) or methotrexate (MTX), 2) Combination therapy MTX +6 weeks prednisolone, 3) Combination therapy MTX +etanercept. Treatment to target entailed three-monthly treatment intensifications in case of persistent disease activity. DMARDs were tapered to nil in case of inactive disease for at least 3 (in oligoarticular) or 6 (in polyarticular) months. After 24 months, primary outcomes were time-to-inactive-disease and time-to-flare after DMARD discontinuation. Secondary outcomes were adapted ACRPedi30/50/70/90scores, functional ability and toxicity. Missing data were imputed.

Results: 94 children (67% girls) with a median (InterQuartile Range) age of 9.1 (4.6–12.9) years were enrolled: 32 in arms 1 and 2, 30 in arm 3. Eleven had oligoarticular JIA, n=73 polyarticular JIA and n=8 juvenile psoriatic arthritis, 37% were ANA positive. At baseline VAS physician was median (IQR) 50^{39–58} mm, VAS patient 54^{37–70} mm, ESR 6 (2–14) mm/hr, active joints 8, ^{5–12} limited joints 2.5 (1–5), and CHAQ score 0.9 (0.6–1.5).

After 24 months 61% (arm 1), 63% (arm 2) and 61% (arm 3) of patients had inactive disease and 45% (arm 1) 31% (arm 2) and 38% (arm 3) had stopped all DMARD(s). Time to inactive disease (median 9.0 (6.0–12.0) months) was not significantly different between arms, nor was time to flare (18.0 (15.0–21.0) months). Adapted ACRPedi-scores were comparably high between arms. Functional ability

improved and remained almost normal. Toxicity reports showed mild events in similar rates across all arms.

	Arm 1 n=31	Arm 2 n=32	Arm 3 n=29
ACRPedi50 (%) (CI)	85.5 (72.4–98.6)	83.8 (70.1–97.4)	93.1 (83.7–102.4)
ACRPedi70 (%) (CI)	69.0 (52.1–85.9)	68.8 (51.6–85.9)	82.8 (68.8–96.8)
ACRPedi90 (%) (CI)	58.4 (40.6–76.1)	55.3 (37.3–73.3)	69.0 (51.8–86.1)
Inactive disease (%)	61.0 (39.7–82.3)	63.1 (43.6–82.7)	61.0 (40.9–81.2)

Results after 24 months by GEE.

Conclusions: Treatment to target drug free inactive disease is feasible in recent onset non-systemic JIA, resulting, regardless of initial treatment, in over 60% of patients in inactive disease and 38% drug free.

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THU0552 ARTICULAR AND EXTRA-ARTICULAR DAMAGE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS – RESULTS FROM THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (ICON)

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Background: Juvenile idiopathic arthritis (JIA) may lead to disability and damage, preventing both is an important therapeutic goal. The frequency of damage in children and adolescents with JIA and the question of whether the damage increases with the duration of the disease also in the biologic treatment era have hardly been investigated.

Objectives: To assess the prevalence and accrual of damage in patients with JIA over six years and to analyse damage association with disease activity, quality of life and functional limitations.

Methods: We analysed data of patients with JIA who were enrolled in ICON. Clinical characteristics such as disease activity (e.g. JIA core set criteria) and details on current treatment as well as patient's quality of life (PedsQL) and functional limitations (CHAQ) were assessed quarterly during the first 12 months in ICON and half-yearly thereafter. The Juvenile Arthritis Damage Index (JADI, range 0–89, best=0) was reported by the physician at the 3 year, 4 year and 6-year-FU, respectively. The JADI is composed of two sub-scores, the JADI-A scores joint