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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 ABATACEPT

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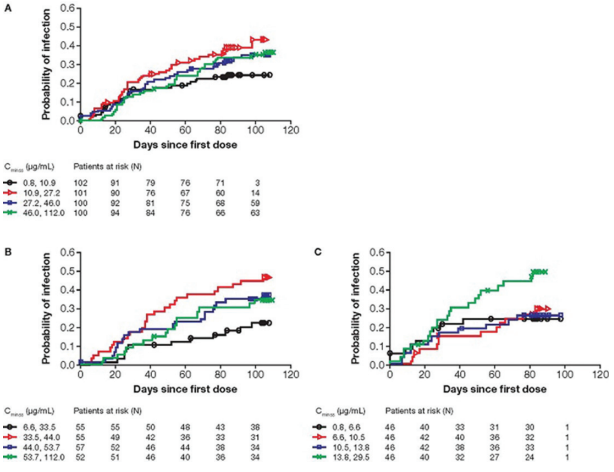
Background: Infections are the most common expected AEs linked to biologic (b) DMARDs in paediatric patients (pts) with juvenile idiopathic arthritis (JIA). Blood concentrations achieved with bDMARDs vary greatly between individual pts. It is not known if higher abatacept (ABA) exposure is linked to 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_{minss}], maximum [C_{maxss}] and time-averaged [C_{avgss}] 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_{minss} (Fig A; p=0.2317; log-rank test), C_{maxss} (p=0.5501) or C_{avgss} (p=0.3808). Consistent results were seen for individually studied SC and IV ABA C_{minss} (Fig B, C), C_{maxss} and C_{avgss} (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_{minss} 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.

REFERENCES:
[1] Ruperto N, et al. Lancet 2008;372:383–91.
[2] Lovell D, et al. Arthritis Rheumatol 2016;68(Suppl 10), abstract 948.

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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: alfa (IL-10RA) and beta (IL-10RB). Homozygozous 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