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RECOMBINANT INTERLEUKIN-1 RECEPTOR ANTAGONIST IS AN EFFECTIVE FIRST-LINE TREATMENT STRATEGY IN NEW-ONSET SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS, IRRESPECTIVE OF HLA-DRB1 BACKGROUND AND IL1RN VARIANTS

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Introduction: HLA-DRB1*15:01 has been recently associated with interstitial lung disease (LD), eosinophilia, and adverse drug reactions to biological therpay in systemic juvenile idiopathic arthritis (sJIA). Additionally, genetic variants in *IL1RN* have been linked to poor response to anakinra. These findings have spurred a debate among pediatric rheumatologists about the utility of pre-prescription HLA-typing to guide medication decisions for new-onset sJIA patients. Such decisions may include postponing and even forgoing highly effective biological therapy in new-onset sJIA patients who carry the commonly occurring HLA-DRB1*15 haplotypes.

Objectives: Here, we present HLA-DRB1 and *IL1RN* variant genotyping data from our prospective cohort of new-onset sJIA patients treated in a standardized manner with the recombinant IL-1 Receptor antagonist anakinra as first-line therapy. The objectives of the study were to describe the HLA-DRB1 background of our sJIA cohort in relation to disease course and to determine clinical inactive disease rates in the first 2 years of disease based on HLA-DRB1 background and *IL1RN* genetic variants.

Methods: HLA and *IL1RN* risk alleles were identified via whole genome sequencing. Treatment responses and complications were compared between carriers versus non-carriers.

Results: Seventeen of 65 patients (26%) carried HLA-DRB1*15:01, comparable to the general Dutch and European population. Furthermore we found enrichment for HLA-DRB1*11:01 (28%), a known risk locus for sJIA. The rates of clinical inactive disease (CID) at 6 months, 1 and 2 years were high (>80%), irrespective of HLA-DRB1 or *IL1RN* variants. One patient, an HLA-DRB1*15:01 carrier, developed sJIA-LD. Of the three patients with severe drug reactions to biologics, one carried HLA-DRB1*15:01. The prevalence of eosinophilia is common and did not significantly differ between HLA-DRB1*15:01 carriers and non-carriers at disease-onset (6.2% vs 14.9%, p=0.67) nor after the start of anakinra (35.3% versus 37.5% in the first 2 years of disease).

Conclusion: We observed high rates of CID using anakinra as first-line treatment irrespective of HLA-DRB1 or *IL1RN* variants. Only one of the 17 HLA-DRB1*15:01 carriers developed sJIA-LD, and of the 3 patients with drug reactions to biologics, only one carried HLA-DRB1*15:01. Although thorough monitoring for sJIA-LD and drug hypersensitivity in sJIA remains important, withholding effective biological therapy in new patients based solely on HLA-DRB1 or genetic *IL1RN* variants is not warranted.

Patient Consent: Yes, I received consent

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