

A44: High Levels of DEK Autoantibodies May Predict Early Flare Following Cessation of Anti-TNF Therapy

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Background/Purpose: The nuclear oncoprotein DEK is a biochemically distinct protein, modulating heterochromatin integrity, chemoattractant of neutrophils and T-cells and vital for the formation of neutrophil extracellular traps (NETs). NETs are important for resolution of inflammation suggesting that DEK contributes to the development of autoimmune diseases. High levels of DEK autoantibodies have been found in several autoimmune diseases including juvenile idiopathic arthritis (JIA) but their role in disease pathogenesis is not clear. Since DEK and DEK autoantibodies can contribute to the development of immune complexes and NET formation we suggest that DEK antibody levels can predict flare with the discontinuation of anti-TNF therapy.

Methods: In 16 pediatric rheumatology centers, sera samples were collected from 137 children with polyarticular JIA with clinically inactive disease (CID) on anti-TNF therapy. The therapy was stopped and disease activity was monitored for at least 8 months or until disease flare. DEK antibody levels were measured

in sera collected at time of enrollment and 6 months (when anti-TNF therapy was stopped) by ELISA. DEK antibody levels relative to healthy controls were calculated by area under the curve (AUC), expressed as unit-free ratios.

Results: 103 females and 34 males patients were enrolled. Mean age 11.3 years and disease duration 5.0 years. JIA included: 13% extended oligoarthritis, 74% polyarthritis rheumatoid factor (RF) negative and 12% polyarthritis RF positive and 46% positive ANA. 77% were taking etanercept, 18% adalimumab, 5% infliximab and 40% methotrexate. 31 patients (23%) discontinued the study prior stopping the therapy for various reasons, including loss of CID. Of 106 subjects who stopped the therapy, 39 (37%) flared within 8 months (mean of 104.8 days). 67 subjects (63%) had no flares within 8 months after stopping the therapy. 71 out of 106 patients samples were analyzed thus far for DEK antibody levels. DEK antibody level ratios compared to healthy controls was -0.36 (some patients had lower antibody levels than did healthy controls) to 1.41, median ratio of 0.11 (Q1–Q3 of 0.09–0.24) and 0.13 (SD, 0.3). High levels of DEK antibodies, mean and SD of 0.209 ± 0.36 were detected in the 21 patients that flared within 8 months compared to lower levels of DEK antibodies (0.09 ± 0.27) in 50 patients with CID for at least 8 months (ANOVA $P = 0.1832$). Negative correlation was observed between the days to flare and DEK antibody levels (spearman $\rho = -0.31$, $P = 0.07$), suggesting that when therapy stopped, patients with higher levels of DEK antibodies will flare sooner with estimated odds ratio of 3.3 (95% CI, 0.61, 18.0), suggesting that each unit increase in DEK antibodies is associated ($P = 0.17$) with more than a 2-fold increased risk of flare within 8 months.

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Conclusion: In children with JIA extended oligoarthritis and polyarthritis on anti-TNF therapy that maintain CID for at least 6 months while on therapy, high DEK antibody levels may be correlated with flare within the first 8 months after stopping the therapy. This study suggests that DEK antibody levels can predict the outcome of discontinuation of anti-TNF therapy, although more patient samples need to be analyzed from this study and future studies.

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