SERUM LEVELS OF CXCL13 ARE ASSOCIATED WITH ULTRASONOGRAPHIC SYNOVITIS AND PREDICT POWER DOPPLER PERSISTENCE IN EARLY RHEUMATOID ARTHRITIS TREATED WITH NON-BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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**Background**  The chemokine CXCL13 is involved in the cooperation and activation of B and T cells within lymphoid and extra-lymphoid sites. CXCL13 blockade reduces arthritis severity in the murine system, while its serum concentration associates with radiographic progression in patients. Systemic expression of CXCL13 protein has been shown to co-vary with the level of synovial cell infiltration in RA and has thus been proposed as a surrogate marker of synovitis. Whether CXCL13 may provide accurate prediction of the burden of the inflammatory process over time it is currently unclear.

**Objectives**  To investigate whether baseline serum levels of the chemokine CXCL13 might predict clinical and ultrasonographic (US) outcomes in patients with recent-onset RA within a structured treat-to-target protocol.

**Methods**  The study included 161 early rheumatoid arthritis (RA) patients (disease duration <12 months) treated according to a disease activity score (DAS) driven step-up protocol aiming at DAS<2.4. Clinical disease activity measures were collected at baseline, 2, 4, 6, 9 and 12 months, and US examination of the hands was performed at baseline, 6 and 12 months. Grey-scale (GS) and Power Doppler (PD) synovitis were scored (0–5), with overall scores as the sum of each joint score. CXCL13 levels were measured at baseline by ELISA and evaluated in relation to the achievement of low disease activity (LDA, DAS<2.4) and US residual inflammation (PD≤1) at 12 months.

**Results**  Baseline levels of CXCL13 were significantly higher in RA compared to healthy controls (n.19) (p=0.03) and correlated with measures of synovitis, such as the swollen joint count (R 0.28, p<0.001), the US-GS (R 0.27, p=0.003) and US-PD (R 0.26, p=0.005) score. Although CXCL13 did not predict the likelihood of achieving clinical LDA at 12 months within a structured treat-to-target protocol, elevated levels of CXCL13 were associated with more frequent increases of methotrexate dosage (p<0.001). Using adjusted analyses, the highest levels of CXCL13 (>100 pg/ml) were the only independent predictor of residual imaging inflammation (p=0.005), irrespective of initial US-PD scores, disease activity status, acute phase reactants and autoantibodies. Among the patients in clinical LDA at 12 months, US-PD scores ≤1 were less frequently achieved in the high baseline CXCL13 (>100 pg/ml) group, with an adjusted OR=0.06 (95% CI 0.01–0.55, p=0.01).

**Conclusions**  CXCL13 emerges as a new biological marker in early RA, accurate in assessing the severity of synovitis and the persistence of US-PD activity over time in response to conventional treatments.