

THU0485 A COMPARISON OF SERUM AND URINE BIOMARKERS FOR PREDICTING RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: The ability to predict progressive joint damage has the potential to improve disease management decisions and outcomes for patients with rheumatoid arthritis (RA). Advanced imaging techniques including ultrasound (US) can evaluate accumulated joint damage and provide information about erosive activity. Soluble biomarkers have the potential to be objective and quantitative measures of joint damage progression rate and provide mechanistic information that could help inform therapy decisions. Both serum and urine biomarkers have been associated with radiographic progression, but the relative predictive power of these 2 sample types in RA is undefined.

Objectives: Assess the relative utility of serum and urine joint damage biomarkers for predicting joint damage progression.

Methods: We examined samples and data from 24 patients followed in a 2-year blinded study comparing methotrexate+infliximab with methotrexate alone in aggressive early RA. Patients were evaluated with US at 0, 18, 54 and 110 weeks and scored for synovial thickening (ST) and for vascularity by power Doppler area (PDA). Radiographic examination with van der Heijde modified Sharp scores was carried out at 0, 30, 54 and 110 weeks. 93 serum proteins associated with biological processes underlying joint damage were measured in serum samples from 0, 6, 18, 54 and 110 weeks. 8 urine analytes were also measured (C1,2C, C2C, CTXI, CTXII, hyaluronan, IL8, NTXI, PYD) and adjusted by urine creatinine. Urine analytes were also analyzed in 22 non-RA patients. Associations were examined by Spearman correlation. Multivariate analysis used longitudinal hierarchical linear models, evaluated using leave-one-out cross validation.

Results: Patients all had erosions at baseline and experienced a wide range of changes in total Sharp scores over the 2 year study period (TSS; median change 6.25, inter-quartile range 4-14.5). 13 serum and 3 urine biomarkers were correlated with change in TSS when any individual biomarker time point was considered (FDR<0.2). Serum biomarkers had the higher correlations and represented diverse biological processes including inflammatory regulation, ECM degradation and collagen metabolism. Urine PYD, hyaluronan and CTXII were correlated with DAS28CRP4 and synovial thickening measured by ultrasound (P<0.05). However, stronger correlations were observed for serum biomarkers than for any urine analyte. NTXI, hyaluronan and PYD were elevated in RA urine relative to non-RA controls (P<0.01). Both US Power Doppler Area and multivariate models based on serum biomarkers performed well at predicting rate of change in TSS (correlation 0.58-0.87 between predicted and observed).

Conclusion: A large-scale quantitative assessment of serum biomarkers identified proteins correlated to joint damage progression. Correlations were highest 6 weeks after therapy initiation, suggesting effects of therapy on long-term outcome can be evaluated early in the treatment course. The highest correlations were observed for serum rather than urine biomarkers. Both ultrasonographic imaging and quantitative serum protein biomarkers can be used to estimate rates of progression and predict joint damage in RA.

Disclosure of Interest: G. Cavet Employee of: Crescendo Bioscience, Y. Shen Employee of: Crescendo Bioscience, S. Abraham: None Declared, D. Chernoff Consultant for: Crescendo Bioscience, L. Hesterberg Employee of: Crescendo Bioscience, M. Centola Consultant for: Crescendo Bioscience, P. Taylor Grant / Research Support from: GlaxoSmithKline, Astra-Zeneca, Roche, Celgene, Nuon, Merck, Consultant for: Abbott, Bristol-Myers Squibb, Centocor, Roche, Schering-Plough, Wyeth, UCB