

FRI0106 PERFORMANCE OF SERUM BIOMARKERS AND A PRE-SPECIFIED MULTIVARIATE BIOMARKER-BASED TEST TO MEASURE DISEASE ACTIVITY IN EARLY RHEUMATOID ARTHRITIS TREATED ACCORDING TO THE CAMERA PROTOCOL

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Background: The CAMERA study showed that intensive treatment with methotrexate (MTX), driven by regular disease activity assessment aiming at remission, could improve patient outcomes in early RA. Measurement of disease activity using serum biomarkers could enhance patient assessment and facilitate tight control.

Objectives: To evaluate a broad set of serum biomarkers of RA disease activity and confirm the performance of a pre-defined biomarker-based test for RA disease activity that was developed in independent samples.

Methods: The concentrations of 23 serum protein biomarkers for disease activity (SAA1, IL6, TNFRSF1A, VEGFA, PYD, MMP1, ICAM1, calprotectin, YKL40, MMP3, EGF, IL1RA, VCAM1, leptin, resistin, CRP, IL8, ApoAI, ApoCIII, CCL22, IL1B, IL6R and IL18) were measured by customized immunoassays in 120 serum samples from the CAMERA study (Computer Assisted Management in Early Rheumatoid Arthritis). 72 samples were from baseline visits and 48 were from 6 month visits. The associations between individual biomarkers and disease activity were assessed by Pearson correlation (r) for log-transformed concentrations. False discovery rates (FDR) were estimated by the method of Benjamini and Hochberg. A pre-specified algorithm using a subset of biomarkers was applied to calculate RA Disease Activity Test scores. The performance of the algorithm was evaluated by Pearson correlation (r) and area under the ROC curve (AUROC) for identifying high and low disease activity at the baseline and 6 month visits. The reference classification for ROC analysis was based on a threshold DAS28CRP of 2.67.

Results: 14 proteins were correlated with DAS28CRP4, 11 with swollen joint count and 9 with tender joint count (FDR<0.05). IL6 was the protein most strongly correlated with all of these disease activity measures. The individual biomarkers associated with disease activity represented a range of pathways associated with RA pathophysiology.

A pre-specified Disease Activity Test algorithm, developed previously on independent data and using a linear combination of protein biomarkers, was tested for its ability to measure disease activity, relative to DAS28CRP4. The test algorithm performed well at assessing disease activity in CAMERA samples with a Pearson correlation of $r=0.65$ (95% confidence interval 0.53-0.73) and AUROC of 0.84 (95% confidence interval 0.75-0.90) relative to the DAS28CRP4. To ensure that performance was not overestimated due to inclusion of 2 samples for some patients, we analyzed subsets including only one randomly selected visit per patient; algorithm performance was equally good in these subsets.

Conclusion: Serum protein biomarkers representing a variety of biological pathways are consistently associated with RA disease activity in different cohorts. A pre-specified Disease Activity Test algorithm that combines information from multiple biomarkers performed well when evaluated in CAMERA as an independent test set.

References: 1. S M M Verstappen et al. *Ann Rheum Dis* 2007 66:1443-1449

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