

## SAT0049 SERUM BIOMARKERS PREDICT PROGRESSIVE STRUCTURAL DAMAGE IN THE BEST STUDY

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**Background:** The ability to predict progressive structural damage has the potential to improve disease management and outcomes in rheumatoid arthritis (RA) patients. Blood-based biomarkers measuring the current rate of joint destructive damage could identify patients at risk for accelerated bone and cartilage damage.

**Objectives:** To identify serum biomarkers for progressive structural damage, to build and evaluate predictive models to estimate the current rate of structural damage, and to compare the performance of serum biomarkers to that of conventional measures, including DAS, CCP, CRP, and RF status.

**Methods:** We examined 105 candidate biomarkers in longitudinal serum samples (baseline and year 1) with imaging results and clinical data from 160 patients followed in the BeSt trial, a 5-year blinded study comparing four different treatment arms (sequential monotherapy, step-up combination, combination therapy with prednisone, and combination therapy with infliximab) in aggressive early RA. The concentrations of individual biomarkers were assessed for their association with change in total Van der Heijde-modified Sharp Scores (mSS) at 2 years. Statistical models using combinations of serum biomarkers were built to predict the rate of change of total mSS. Good disease control may influence the computation of mSS rate of change; hence additional analyses incorporating therapy change information into the biomarker model were also performed. Various models built by conventional measures were compared to the serum biomarker model. Performance of the models was evaluated by the Pearson correlation coefficient between actual and predicted rates of change and by the area under the ROC curve (AUC) in cross-validated test sets. Mean mSS rate of change in the test sets was used to dichotomize patients into high and low groups for AUC calculation.

**Results:** We identified serum biomarker combinations (cor = 0.52, AUC = 0.73) superior to DAS28ESR (cor = 0.33, AUC = 0.61), CRP (0.38, AUC=0.67), DAS28ESR with CCP (cor = 0.22, AUC = 0.61), or RF (cor = 0.37, AUC = 0.62) in predicting radiographic progression. In total, 35 individual biomarkers were associated with joint damage progression (false discovery rate<0.1). Incorporating therapy information into the biomarker model didn't change model performance.

**Conclusion:** The best performing models included markers of bone and cartilage destruction, pro-inflammatory cytokines and acute phase proteins. Combinations of biomarkers were able to predict radiographic outcomes despite therapy changes and good control of disease activity. Serum biomarker-based indices have the potential to improve prediction of structural damage progression over standard clinical measures of disease activity in RA patients.

**Disclosure of Interest:** Y. Shen: None Declared, G. Cavet: None Declared, L. Dirven Grant / Research Support from: Schering-Plough and Centocor , M. Centola: None Declared, B. Dijkmans Grant / Research Support from: Schering-Plough and Centocor , L. Hesterberg: None Declared, P. Kerstens Grant / Research Support from: Schering-Plough and Centocor , T. Huizinga Grant / Research Support from: Schering-Plough and Centocor, Schering Plough, Bristol Myers Squibb, Biotest AG, Wyeth/Pfizer, Novartis, Roche, Sanofi-Aventis, Abbott and Axis-Shield diagnostics, C. Allaart Grant / Research Support from: Schering-Plough and Centocor