A10.22 RESPONSE TO MTX PLUS PREDNISONE IN CAMERA II USING A MULTI-BIOMARKER DISEASE ACTIVITY (VECTRA™ DA) TEST AND DAS28-ESR

doi:10.1136/annrheumdis-2013-203224.22

¹JWJ Bijlsma, ¹MS Jurgens, ¹JWG Jacobs, ¹M Bakker, ¹FPJ Lafeber, ¹PMJ Welsing, ²G Cavet, ²D Chernoff, ²EH Sasso, ²W Li, ²DJ Haney. ¹University Medical Center Utrecht, Utrecht, The Netherlands; ²Crescendo Bioscience, Inc., South San Francisco, CA, USA

Background and Objectives The CAMERA II study (Computer Assisted Management in Early RA) demonstrated that the addition of prednisone versus placebo to a MTX-based tight-control strategy increased effectiveness of therapy and reduced need for biological treatment. The present study evaluated changes in biomarker levels over time with MTX+placebo and MTX+prednisone treatment, using the Multi-Biomarker Disease Activity (MBDA) blood test.

Materials and Methods Clinical and biomarker assessments were performed at monthly visits to 1 year for 92 patients who had MBDA test results available at baseline and ≥ 1 subsequent visit. Average number of visits with non-missing disease activity measures was 3.7 per patient. Concentrations of 12 serum biomarkers were combined to produce a score between 1 and 100 using the MBDA algorithm, which generates a validated measure of disease activity. Biomarker responses were also assessed individually but only to 5 months, to avoid subsequent protocol-mandated exposures to non-MTX DMARDs for insufficient responders. Association between DAS28-ESR response and MBDA response was assessed using Spearman's correlation. Changes from baseline and comparisons of change over time for MTX+placebo versus MTX+prednisone were analysed by t-tests. Biomarker concentrations were analysed as fractions relative to baseline using Mann Whitney U tests.

Results Changes from baseline to 1 year in DAS28-ESR and MBDA scores showed a significant correlation in the MTX+placebo arm ($r = 0.57$, $p < 0.001$, $n = 31$) and the MTX+prednisone arm ($r = 0.57$, $p = 0.002$, $n = 28$). Improvements in DAS28-ESR ($p < 0.001$) and MBDA ($p = 0.01$) scores were observed as early as 1 month post-BL in the MTX+prednisone arm. Significant reduction in disease activity in the MTX+placebo arm was first observed at 2 months for DAS28-ESR ($p = 0.02$) and 4 months for MBDA ($p = 0.03$). Overall, DAS28-ESR and MBDA response profiles were similar, with mean changes at month 5 for MTX+placebo and MTX+prednisone being $-2.2/-4.2$ for DAS28-ESR, and $-13/-21$ for MBDA score. Individual biomarker response profiles differed: for some biomarkers, MTX+placebo had little/no effect but MTX+prednisone had significant effect (e.g., MMP-1, TNF-R1, VCAM-1); for others, MTX+placebo had a significant effect that was augmented (e.g., CRP, IL-6, VEGF) or not affected (SAA) by prednisone.

Conclusions Responses assessed with the biomarker-based MBDA test and DAS28-ESR were greater and more rapid for therapy with MTX+prednisone than MTX+placebo, even though individual biomarkers differed in their response profiles. The MBDA test may be useful in combination with clinical assessment to evaluate early response to therapy with MTX or MTX+prednisone.

A10.23 STRATIFICATION OF SLE PATIENTS FOR IMPROVED DIAGNOSIS AND TREATMENT

doi:10.1136/annrheumdis-2013-203224.23

¹Helena Idborg, ²Stefan Rännar, ¹Ganna Oliynyk, ³Jenny Forshed, ³Rui Mamede Branca, ²Magdalena Dønten, ²Kate Bennett, ¹Johanna Gustafsson, ¹Anna Vikerfors, ⁴Lennart Truedsson, ⁵Bo Nilsson, ¹Iva Gunnarsson, ^{2,6}Johan Trygg, ³Janne Lehtö, ^{2,6}Torbjörn Lundstedt, ¹Elisabet Svenungsson, ¹Per-Johan Jakobsson. ¹Rheumatology Unit, Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; ²AcureOmics AB, Umeå, Sweden; ³Clinical Proteomics Mass Spectrometry, Dept. of Oncology-Pathology, Science for Life Laboratory and Karolinska Institutet, Stockholm, Sweden; ⁴Section of Microbiology, Immunology and Glycobiology,

Department of Laboratory Medicine, Lund University, Lund, Sweden; ⁵Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden; ⁶Computational Life Science Cluster, Department of Chemistry, Umeå University, Umeå, Sweden; ⁷Organic Pharmaceutical Chemistry BMC, Uppsala University, Uppsala, Sweden

Background Systemic autoimmune diseases (SAIDs) affect about 2% of the population in Western countries. Sufficient diagnostic criteria are lacking due to the heterogeneity within diagnostic categories and apparent overlap regarding symptoms and patterns of autoantibodies between different diagnoses. Systemic lupus erythematosus (SLE) is regarded as a prototype for SAIDs and we hypothesise that subgroups of patients with SLE may have different pathogenesis and should consequently be subject to different treatment strategies.

Objectives Our goal is to find new biomarkers to be used for the identification of more homogenous patient populations for clinical trials and to identify sub-groups of patients with high risk of for example cardiovascular events.

Methods In this study we have utilised 320 SLE patients from the Karolinska lupus cohort and 320 age and gender matched controls. The SLE cohort was characterised based on clinical, genetic and serological data and combined by multivariate data analysis in a systems biology approach to study possible subgroups. A pilot study was designed to verify and investigate suggested subgroups of SLE. Two main subgroups were defined: One group was defined as having SSA and SSB antibodies and a negative lupus anticoagulant test (LAC), i.e., a "Sjögren-like" group. The other group was defined as being negative for SSA and SSB antibodies but positive in the LAC test i.e. an "APS-like" group. EDTA-plasma from selected patients in these two groups and controls were analysed using a mass spectrometry (MS) based proteomic and metabolomic approach. Pathway analysis was then performed on the obtained data.

Results Our pilot study showed that differences in levels of proteins and metabolites could separate disease groups from population controls. The profile/pattern of involved factors in the complement system supported a division of SLE in two major subgroups, although each individual factor was not significantly different between subgroups. Complement factor 2 (C2) and membrane attack complex (MAC) were analysed in the entire cohort with complementary methods and C2 verifies our results while the levels of MAC did not differ between SLE subgroups. The generated metabolomics data clearly separated SLE patients from controls in both gas chromatography (GC)-MS and liquid chromatography (LC)-MS data. We found for example that tryptophan was lower in the SLE patients compared to controls.

Conclusions Our systems biology approach may lead to a better understanding of the disease and its pathogenesis, and assigning patients into subgroups will result in improved diagnosis and better outcome measures of SLE.

A10.24 SWITCHING INFLIXIMAB FOR NEW ALTERNATIVES: A CORRESPONDENCE ANALYSIS OF BIOLOGICS, REASONS TO STOP, AND TIME PERIODS

doi:10.1136/annrheumdis-2013-203224.24

¹Julia Uceda, ²Loreto Carmona, ¹Alejandro Muñoz, ¹Jose L Marenco. ¹Rheumatology Department, Valme University Hospital, Sevilla, Spain; ²Camilo José Cela University, Madrid, Spain

Background The reason to stop the first biologic may vary from agent to agent and also from the earlier times to the more recent ones. Issues like the availability of newer alternatives or a better knowledge of the effectiveness and safety profile of individual biologics may influence treatment decisions, including the discontinuation of the biologic.