ASSOCIATION OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE WITH ARTERIAL INFLAMMATION, ASSESSED WITH 18F-FUROUREDODEOXYGLUCOSE PET/CT EMISION TOMOGRAPHY, IN RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Biomarkers

J. Giles1, D. Solomon2, K. Liao3, P. Rist4, L. Santacroce4, Z. Fayad5, A. Tawakol4, J. Bathon4. 1Columbia University, Department of Medicine, New York, United States of America; 2Brigham & Women's Hospital, Department of Medicine, Boston, United States of America; 3Mount Sinai Medical Center, Translational and Molecular Imaging Institute, New York, United States of America; 4Massachusetts General Hospital, Department of Medicine, Boston, United States of America.

Background: Rheumatoid arthritis (RA) and atherosclerosis share many common inflammatory pathways. Reducing the activity of inflammatory pathways with immunomodulators may lessen the risk of cardiovascular disease in RA. As such, a multi-biomarker of RA disease activity (MBDA; AKA the Vectra Score) could serve as an indicator of treatment-associated improvements in atherosclerotic plaque inflammation.

Objectives: To prospectively evaluate the association of an MBDA score and its components with the change in arterial inflammation in RA patients enrolled in a clinical trial of two different RA treatment strategies.

Methods: In the TARGET Trial, patients with active RA despite methotrexate were randomly assigned to the addition of either a TNF inhibitor (TNFi) or sulphasalazine+hydroxychloroquine (triple therapy). Baseline and 24-week follow-up (18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT)) scans were assessed for change in arterial inflammation measured as the maximal arterial target-to-background ratio (TBR) of FDG uptake in the most diseased segment (MDS) of either the carotid arteries or aorta (TBRmax MDS). The MBDA score, measured at baseline and weeks 6, 12, and 24, was assessed for its association with the change in arterial inflammation. The MBDA score was categorized as low, moderate, and high disease activity (LDA, MDA, and HDA; LDA<30, MDA 30-44, HDA>44 units).

Results: Among the 150 randomized TARGET participants, 112 had an interpretable TBR at baseline and trial conclusion (24 weeks) (mean age=60 years; 71% female; RA duration=1.4 years; baseline DAS28-CRP=4.8). The MBDA score at baseline and trial conclusion (24 weeks) (mean age=60 years; 71% female; RA duration=1.4 years; baseline DAS28-CRP=4.8). The MBDA score at week 24 was significantly correlated with the change in TBRmax MDS (Spearman's rho=0.239; p=0.011), while the baseline and interim MBDA scores were less strongly and not significantly correlated with the change in TBRmax MDS.

Conclusions: Achieving low disease activity by the MBDA at 24 weeks was associated with a clinically meaningful reduction in arterial inflammation, similar to high-intensity statins, in a way not predicted using other RA disease activity measures, suggesting that treatment-associated improvements in arterial inflammation may be indicated by specific biomarkers that overlap those used to track arthritic disease activity.

HUMORAL RESPONSES AGAINST HDL ARE LINKED TO LIPOPROTEIN TRAITS, ATHEROSCLEROSIS, INFLAMMATION AND PROTEOMIC PATHOGENIC PATHWAYS DURING EARLY ARTHRITIS STAGES

Keywords: -omics, Cardiovascular disease, Autoantibodies

J. Rodríguez-Carrio1,2, M. Alperi-López3,4, P. López1,2, Á. Pérez-Alvarez2, G. Robinson2, S. Alonso Castro2, N. Amigo5,6, F. Atzeni2, A. Suárez2,1, 1University of Oviedo, Department of Functional Biology, Oviedo, Spain; 2Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Department of Metabolism, Oviedo, Spain; 3Central University Hospital of Asturias, Rheumatology, Oviedo, Spain; 4University College London, Centre for Adolescent Rheumatology versus Arthritis, London, United Kingdom; 5Biostere Teslab, Biostere Teslab, Reus, Spain; 6Fundación Instituto de Investigación Sanitaria Pere Virgili, Department of Basic Medical Sciences, Tarragona, Spain; 7Universidad de los Studi di Messina, Rheumatology, Messina, Italy.

Background: Cardiovascular (CV) risk excess in rheumatoid arthritis (RA) cannot be solely attributed to traditional CV risk factors. Chronic inflammation and immune dysregulation are crucial mechanisms for atherosclerosis development in RA. Recent evidence suggests a link via humoral responses against high-density lipoproteins (HDL) and its components. However, their exact specificity, clinical relevance and emergence along disease course are unknown, especially during the earliest phases of arthritis.

Objectives: To characterize the specificity and clinical relevance as predictors of anti-HDL responses along during the earliest phases of arthritis.

Methods: IgG and IgM serum levels of antibodies against HDL (anti-HDL) and Apolipoprotein A1 (anti-ApoA1) were measured in 82 early RA patients (EULAR/ACR classification criteria), 14 arthralgia individuals (EULAR definition) and 96 controls. Established RA patients (n=42) were included for validation. Atherosclerosis occurrence and vascular stiffness were measured by Doppler-ultrasound. Lipoprotein content, particle numbers and size were measured by H-NMR. Cytokines were measured by immunoassays. A cytokinemtabolic-related protein panel was evaluated using high-throughput targeted proteomics.

Results: IgG and IgM anti-HDL and anti-ApoA1 responses were increased in early RA compared to controls (both p<0.001) and were comparable to established disease. Only IgG anti-ApoA1 antibodies were increased in arthralgia compared to controls (p<0.050). IgG anti-HDL and anti-ApoA1 were associated with unfavourable lipoprotein traits (particle content, number and size distribution) in RA and arthralgia, respectively. A similar picture was observed for positive correlations with inflammatory mediators (IFNα, MIP-1α, IL-6, IL-8 and IFNg). No associations with clinical features or traditional risk factors were found. IgG anti-HDL were independently associated with atherosclerosis occurrence (p=0.012) and extension (r=0.274, p=0.016) in early RA. This association remained after adjusting for traditional CV risk factors in multivariate models (OR 1.001 [95% CI: 1.000 – 1.002], p=0.004). The addition to IgG anti-HDL to the mSCORE chart improved patient classification and outperformed patient stratification over mSCORE alone (Table 1). The addition of IgG anti-ApoA1 levels resulted in low-to-moderate improvements (Table 1). IgG anti-HDL antibodies correlated with serum proteomic signatures involved in immune activation, remodelling, and lipid metabolism pathways in early RA (Figure 1).

Acknowledgements: We would like to acknowledge the investigators of the TARGET Trial Consortium and the patients that participated in the trial. The trial was funded by NIH-NIAINS U01-AR068043; Abbvie and Amgen supplied study drug. Crescendo Biosciences funded and performed the assays for the MBDA testing.

Disclosure of Interests: Jon Giles Consultant of: AbbVie, Pfizer, Eli Lily, Gilead, Novartis, UCB, Bristol Myers Squibb, Grant/research support from: Pfizer, Dani- el Solomon Grant/research support from: Abbvie, Amgen, Jansen, Moderna, Katherine Liao: None declared, Pamela Rist: None declared, Leah Santacroce: None declared, Zahi Fayad: None declared, Ahmed Tawakol: None declared, Joan Bathon: None declared.

DOI: 10.1136/annrheumdis-2023-eular.4188