Development, Princeton, United States of America;⁶Bristol Myers Squibb (at the time of analysis), Translational Medicine, Princeton, United States of America;⁷Bristol Myers Squibb, Japan Translational Medicine, Research and Development, Tokyo, Japan

Background: Effective biomarkers are needed to guide RA treatment selection, and the importance of evaluating synovial tissue is increasingly recognised.¹ Markers of extracellular matrix (ECM) turnover (e.g. C3M, a marker of interstitial tissue degradation)² may have clinical utility as disease-relevant and surrogate biomarkers of synovial joint pathophysiology.

Objectives: To evaluate baseline (BL) correlations of ECM biomarkers with disease activity and the predictive value of ECM biomarkers in patients (pts) with seropositive early RA in the exploratory head-to-head Early AMPLE study (NCT02557100), and to explore the impact of shared epitope (SE) status.

Methods: Biologic-naïve, MTX-inadequate responder adults with early (≤12 months' duration), active, moderate-to-severe RA were enrolled if they were anti-cyclic citrullinated peptide 2+ and RF+. Pts were randomised 1:1 to receive SC abatacept (ABA) 125mg weekly or SC adalimumab (ADA) 40mg every 2 weeks (wks) for 24 wks (single-blind period). Linear correlations between levels of ECM serum biomarkers (Nordic Biosciences) and disease activity (DAS28 [CRP], SDAI) at BL and change from BL (CfB) at Wk 24 were assessed in the overall population and by SE status (+/-); early (Wk 4) changes in biomarkers were also assessed.

Results: For SE+ (n=61) and SE- (n=18) pts at BL, mean (SD) DAS28 (CRP) was 5.3 (1.2) and 5.0 (1.0), and SDAI was 35.9 (16.2) and 34.0 (13.8), respectively. At BL in the overall population, significant medium correlations between C1M, C3M and C4M and disease activity were seen (Table 1). Correlations were generally higher in SE+ vs SE- pts, with C1M highly correlated with DAS28 (CRP) in SE+; correlations between C1M, C3M and C4M and disease activity were all significant in SE+ but not SE- pts. At Wk 24, overall CfB in C3M showed higher correlation with CfB in disease activity in pts receiving ABA (n=36; DAS28 [CRP]: 0.66 [p<0.0001]; SDAI: 0.53 [p=0.0009]) vs ADA (n=32; DAS28 [CRP]: 0.33 [p=0.0644]; SDAI: 0.39 [p=0.0267]); this was more pronounced in SE+ pts (ABA, n=27; DAS28 [CRP]: 0.70 [p=0.0001]; SDAI: 0.63 [p=0.0005] vs ADA, n=25; DAS28 [CRP]: 0.33 [p=0.1120]; SDAI: 0.41 [p=0.0445]). Changes at Wk 4 in C3M showed higher correlation with response to ABA vs ADA (Figure 1). Correlations between CfB (at Wks 4 and 24) in other biomarkers and response were generally similar between treatment groups.

Table 1. BL correlation of ECM biomarkers with BL disease activity

	Overall (N=77)		SE+ (n=60)		SE- (n=17)	
	DAS28 (CRP)	SDAI	DAS28 (CRP)	SDAI	DAS28 (CRP)	SDAI
CRPM	0.26 0.0207	0.20 0.0777	0.20 0.1324	0.12 0.3583	0.41 0.0981	0.41 0.1001
Osteocalcin	0.24 0.0380	0.23 0.0416	0.23 0.0763	0.20 0.1293	0.28 0.2818	0.33 0.1890
CTX-1	0.23 0.0440	0.20 0.0844	0.21 0.1104	0.17 0.1932	0.26 0.3089	0.28 0.2703
C1M	0.54* 0.0000	0.34* 0.0028	0.60* 0.0000	0.38* 0.0029	0.34 0.1822	0.26 0.3216
C2M	-0.05 0.6774	0.00 0.9759	-0.06 0.6565	0.01 0.9567	-0.02 0.9441	0.01 0.9813
C3M	0.44 0.0001	0.30 0.0080	0.47 0.0001	0.30 0.0199	0.33 0.1943	0.31 0.2301
C4M	0.39 0.0004	0.32 0.0049	0.47 0.0001	0.36 0.0047	0.10 0.7012	0.11 0.6767

Data are Spearman correlation coefficient, p value. Linear correlations by shading: light grey, low (0<-0.3); medium grey, medium (0.3<-0.6); dark grey, high (0.6-1). Pts with missing SE allele data not included.^an=75.^bn=58.C1M, C2M, C3M, C4M=MMP-mediated degradation products of collagen type I, II, III and IV, respectively; CRPM=neo-epitope of MMP-mediated degradation of CRP; CTX-1=neo-epitope of cathepsin-mediated degradation of type I collagen; MMP=matrix metalloproteinase; SE=-0 SE alleles; SE+≥1 SE allele.

Conclusion: Significant BL correlation between C1M, C3M and C4M and disease activity was seen and was generally numerically higher in SE+ vs SE- pts. Early (Wk 4) change in C3M and later (Wk 24) treatment response were more highly correlated in pts receiving abatacept vs adalimumab. The predictive value of ECM biomarkers for treatment response warrants study in a larger population.

REFERENCES:

- [1] Ouboussad L, et al. *Front Med (Lausanne)* 2019;6:45.
[2] Gudmann NS, et al. *Clin Exp Rheumatol* 2018;36:462-470.

Figure 1. Correlation between early changes in C3M and Wk 24 changes in efficacy parameters in the overall population and SE+ subpopulation

Acknowledgements: Professional medical writing and editorial assistance was provided by Joanna Wright at Caudex and was funded by Bristol Myers Squibb.

Disclosure of Interests: S. Louis Bridges Grant/research support from: Bristol Myers Squibb, Jane Buckner Consultant of: Bristol Myers Squibb, Grant/research support from: Bristol Myers Squibb, Janssen, Michael A Maldonado Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Vivian Bykerk Consultant of: Grants from Amgen, Bristol Myers Squibb, Novartis, and UCB (given to institution); grants from the NIH, PCORI, and CIHR (given to institutions with whom she is affiliated); and personal fees from Amgen, Bristol Myers Squibb, Gilead, Pfizer, Regeneron, Roche, Sanofi Aventis, and UCB outside the submitted work., Grant/research support from: Grants from Amgen, Bristol Myers Squibb, Novartis, and UCB (given to institution); grants from the NIH, PCORI, and CIHR (given to institutions with whom she is affiliated); and personal fees from Amgen, Bristol Myers Squibb, Gilead, Pfizer, Regeneron, Roche, Sanofi Aventis, and UCB outside the submitted work., Neelanjana Ray Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Sumanta Mukherjee Shareholder of: Bristol Myers Squibb, GlaxoSmithKline, Employee of: Bristol Myers Squibb, GlaxoSmithKline, Nobuhisa Ohtsuka Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.873

AB0108 USING RNA SEQUENCING TO IDENTIFY GENE EXPRESSION SIGNATURES ASSOCIATED WITH RESPONSE TO ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

H. H. Chen¹, W. C. Chao², J. R. Wang³, T. M. Ko³. ¹Taichung Veterans General Hospital, Department of Medical Research, Taichung, Taiwan, Republic of China; ²Taichung Veterans General Hospital, Department of Critical Care Medicine, Taichung, Taiwan, Republic of China; ³National Chiao Tung University, Department of Biological Science and Technology, Hsinchu, Taiwan, Republic of China

Background: Rheumatoid arthritis (RA) is a common chronic autoimmune disease. Abatacept (CTLA4-immunoglobulin) is one of the biological disease-modifying antirheumatic drug (bDMARD) for RA patients with inadequate response to methotrexate. Recently, Yokoyama-Kokuryo et al. compared gene expression levels between abatacept responders and non-responders in RA patients using a microarray and found that type I IFN score and expression levels of nine genes may be used as a biomarker to predict response to abatacept. However, little study used RNA sequencing (RNA-seq) to identify whole blood gene expression signatures to predict therapeutic response to abatacept.

Objectives: The aim of this study is to identify gene expression signatures to predict therapeutic responses to abatacept in RA patients using RNA-seq.

Methods: This study is a single-center, prospective study. We used a PAX gene Blood RNA kit to collect whole blood at baseline and 4 weeks after abatacept treatment from RA patients. We also measured DAS28, physician global assessment, HAQ, ESR, CRP at baseline and 12 week to calculate EULAR response at 12 week. Patients with good EULAR response were defined as responders and those with moderate or no EULAR response were defined as non-responders.

Results: We finally conducted RNA-seq for whole blood from 7 RA patients initiating abatacept therapy. Of the 7 RA patients, one was non-responder and 6 were responders. We first use DESeq2 to analyze the differentially expressed genes of non-responder and responder before taking the drug. We used hierarchical clustering and PCA to evaluate the overall similarity of the samples, and group the patient data, and find that the nonresponder can be distinguished from responders. Subsequently, we analyzed the differentially expressed genes of the two groups of non-responder and responder patients before taking the drug. Before treatment, we found that 72 genes had a higher expression in the non-responder,

and 23 genes had a higher expression level in responders. Figure 1 showed the top 20 DEG Heatmap between the non-responder and responders. Using these two sets of genes for GO analysis, we found that most of the pathways in the non-responder are related to immune response and cytokine production, and most of the pathways in the responders are related to antigen processing and MHC class II.

Figure 1. Top 20 DEG Heatmap between non-responder and responders

Conclusion: The study showed that most of the pathways in RA patients with no EULAR response to abatacept are related to immune response and cytokine production; while most of the pathways in RA patients with moderate/good response to abatacept are related to antigen processing and MHC class II.

REFERENCES:

- [1] Yokoyama-Kokuyo W, Yamazaki H, Takeuchi T, et al. Identification of molecules associated with response to abatacept in patients with rheumatoid arthritis. *Arthritis Research & Therapy*. 2020;22:46.

Disclosure of Interests: Hsin-Hua Chen Grant/research support from: This is an investigator-sponsored trial with Bristol-Myers Squibb who provides funding support., Wen-Cheng Chao: None declared, Jing-Rong Wang: None declared, Tai-Ming Ko: None declared

DOI: 10.1136/annrheumdis-2021-eular.896

AB0109

VALIDATION OF SEPARATE PATIENT-REPORTED, CLINICAL AND LABORATORY FACTOR SCORES AS REPRESENTATION OF DISEASE BURDEN IN A POPULATION WITH ESTABLISHED RHEUMATOID ARTHRITIS

S. Pazmino¹, A. Lovik², D. De Cock¹, V. Stouten¹, D. Bertrand¹, J. Joly³, M. Doumen¹, R. Westhovens^{1,3}, P. Verschueren^{1,3} on behalf of TapERA study group. ¹Katholieke Universiteit Leuven, Skeletal Biology and Engineering Research Centre, Department of Development and Regeneration, Leuven, Belgium; ²Katholieke Universiteit Leuven, I-Biostat, Leuven, Belgium; ³UZ Gasthuisberg Campus, Department of Rheumatology, Leuven, Belgium

Background: Rheumatoid arthritis (RA) can cause important bio-psychosocial burden. When exploring disease burden evolution in the 2-year Care in early RA (CareRA) trial, 3 factor scores were extracted via exploratory factor analysis (EFA).¹ EFA uncovers the fact that multiple observed variables have similar patterns of responses because they are all associated with a latent, not directly observable, variable.

Objectives: To validate in a population with established RA, the 3 factors scores and their individual components originally extracted in CareRA.

Methods: Patients with established RA in sustained remission under treatment with etanercept (≥ 1 year) were enrolled in the TapERA (Tapering Etanercept in RA) trial between 2012 and 2014. Patients completed the Flare Assessment in RA (FLARE-RA) questionnaire.²

Components of disease activity scores (swollen/tender joint count, physician and patient global health assessment, CRP and ESR), as well as pain (question 2) and fatigue evaluation (question 8), from the FLARE-RA questionnaire, and HAQ were recorded at every visit ($v=5$).

Missingness on previously mentioned variables was handled with multiple imputation (100 imputations). Pain and fatigue were re-scaled from their original Likert scale of 1-6 to 0-100 to match CareRA data. Next, timepoint clustering was

removed with multiple outputation (1000x) and each of the 100 000 datasets was analyzed by EFA with principal component extraction and oblimin rotation. The analyses were combined after re-ordering the factors by maximizing factor congruence.

Results: Sixty-six patients with a mean disease duration of 14.8 years (SD 9.03), mean age of 55.21 years (SD 12.87), 96% (63/66) positive to RF or ACPA, 77% (51/66) with erosions and 68% (45/66) female were included in this analysis.

Table 1 provides the results of the EFAs from CareRA and TapERA. The factor structure and factor components remained the same in both datasets. The factor loadings, indicating how strongly a variable relates to its factor (correlation between observed and latent score), were also comparable. The HAQ, however, did have a stronger factor loading in TapERA (0.57 vs 0.92).

Table 1. Results from the exploratory factor analyses in CareRA and TapERA

Variable	CareRA			TapERA		
	PRF	CF	LF	PRF	CF	LF
Fatigue	0.90			0.80		
PaGH	0.87			0.81		
Pain	0.86			0.75		
HAQ	0.57			0.92		
SJC28		0.92			0.82	
TJC28		0.89			0.84	
PhGH		0.76			0.60	
CRP			0.87			0.85
ESR			0.78			0.82

Factor loadings presented (correlation between the observed score and the latent factor). Cross-loadings were negligible (<0.3) -not presented. The factor order is by % of variance explained. PRF: patient-reported factor, CF: clinical factor, LF: laboratory factor, PaGH: patient's global health assessment, HAQ: health assessment questionnaire, SJC28: 28 swollen joint count, TJC28: 28 tender joint count, PhGH: physician's global health assessment, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate

Conclusion: The latent factor structure for disease burden originally found in CareRA was successfully validated in the TapERA dataset, underlining the robustness of the PRF, CF and LF scores. HAQ seems to take "greater importance" on established RA. However, deviations in factor loadings (e.g., HAQ) could be attributed to differences between study populations (e.g., early vs. established RA, sample size). Apart from traditional clinical and laboratory factors, patient-reported pain, fatigue, functionality and overall well-being determine disease burden, both in early and established RA. Using these factor scores could facilitate detection and management of patient's unmet needs.

REFERENCES:

- [1] Pazmino, et al. Does Including Pain, Fatigue, and Physical Function When Assessing Patients with Early Rheumatoid Arthritis Provide a Comprehensive Picture of Disease Burden? *J Rheumatology* 2020 Nov.
- [2] Berthelot JM, et al. A tool to identify recent or present rheumatoid arthritis flare from both patient and physician perspectives: the 'FLARE' instrument. *Annals Rheumatic Diseases*. 2012.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.915

AB0110

DETERMINING THE AMOUNT OF COPPER-CONTAINING PROTEIN, ITS BIOCHEMICAL AND IMMUNOLOGIC ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

O. Rusanova¹, A. Trofimenko¹, N. Emelyanov², O. Emelyanova¹. ¹Federal State Budgetary Institution «Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovskiy», 1, Bonnorgrad, Russian Federation; ²Federal State Budgetary Educational Institution of Higher Education «Volgograd State Medical University» of the Ministry of Healthcare of the Russian Federation, 2, Bonnorgrad, Russian Federation

Background: Production of antibodies to ceruloplasmin (CP) in rheumatoid arthritis is an issue that has not been studied well enough. It was not by chance that this copper-containing alpha 2-glycoprotein of blood plasma showing multienzymatic properties was chosen as an object of investigation. Data on the content and activity of CP in the blood of rheumatoid arthritis patients are contradictory, which has to do with different approaches to selection of patients and different measuring methods.

Objectives: Improving diagnosis of rheumatoid arthritis by determination of antibodies to CP as well as its amount and enzymatic activity.