sex/age-matched healthy controls: 50 in Cohort 1, 50 in Cohort 2, and 100 in Cohort 3. Among these 446 subjects, 75% were females and the average age was 52.5 years. Amine/phenol-containing metabolites were labeled by 13C-dansyl chloride to improve the LC-MS detection. For each cohort, a pooled sample was prepared and labeled by 13C-dansyl group to serve as the reference sample for relative quantification. Then the individual samples and the pooled sample were mixed and 1:1. Finally, an LC-QTOF-MS platform analyzed the mixtures and output the intensity ratios of 13C/13C peak pairs.

**Results:** 1,149 amine/phenol-containing metabolites were commonly detected across the three sample sets. Among them, 134 were positively identified by our dansyl-labeling standard library, and 141 were matched to predicted retention times and mass values of dansyl-labeled human metabolites. Visualized by the partial least squares discriminant analysis (PLS-DA), the overall amine-phenol-submetabolome demonstrated clear and consistent differences between healthy controls and the RA groups, with cross-validation Q2 ≥ 0.785, 0.745, 0.793, respectively. The selection of significant metabolites was conducted according to the fold change and false-discovery-rate-adjusted Welch's t-test. Cohort 1 demonstrated 85 metabolites having higher concentrations in the RA samples than the controls, and 89 metabolites with lowered concentrations. The numbers of increased/decreased metabolites in Cohort 2 and 3 were 87/26 and 90/53, respectively. Importantly, there were 59 significantly discriminatory metabolites commonly found in the three data sets (49 increased and 9 decreased). We picked the top three with the highest univariate classification performance to form a biomarker panel. We implemented the linear support vector machine (SVM) to build the classifier and the receiver operating characteristic (ROC) analysis to measure the performance. The area-under-the-curve (AUC) values (95% confidence interval) were 1.000 (1.000-1.000), 0.902 (0.967-1.000) and 0.902 (0.858-0.945) for the three cohorts, respectively. The results revealed the importance of examining multiple sample sets and even in the worst case (Cohort 3), our biomarker candidates could differentiate RA at 82.5% sensitivity and 82.5% specificity. Particularly, in Cohort 3, there were 30 RA patients negative for anti-cyclic citrullinated peptide and rheumatoid factor, and our metabolite panel demonstrated consistently high performance for differentiating these specific subjects from healthy controls.

**Conclusion:** Metabolites showing significant and consistent changes associated with RA have been identified with high discriminative power.

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**Table 1. Multivariate analysis of prediction of flare with baseline variables**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Hazard ratio</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1.130</td>
<td>0.906-1.409</td>
<td>0.280</td>
</tr>
<tr>
<td>Age</td>
<td>0.996</td>
<td>0.988-1.005</td>
<td>0.414</td>
</tr>
<tr>
<td>Physician's VAS</td>
<td>1.008</td>
<td>1.002-1.013</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>1.002</td>
<td>0.998-1.006</td>
<td>0.34</td>
</tr>
<tr>
<td>EGSQD</td>
<td>0.952</td>
<td>0.934-1.000</td>
<td>0.96</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.407</td>
<td>1.109-1.786</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Poor adherence</td>
<td>1.008</td>
<td>1.002-1.014</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>1.272</td>
<td>1.047-1.545</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Conclusion:** RA patient who have risk factors for flare, even though their disease activity was low, require more proactive treatment.

**References:**


**Disclosure of Interests:** None declared

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**THU0107 OBESITY PREDICTS RESPONSE TO NOT ALL BUT CERTAIN BIOLOGICAL / TARGETED DISEASE MODIFYING ANTI-RHEUMATIC DRUGS FOR RHEUMATOID ARTHRITIS - RESULTS FROM KANSAI CONSORTIUM FOR WELL-BEING OF RHEUMATIC DISEASE PATIENTS (ANSWER COHORT)**


1Kyoto University Graduate School of Medicine, School of Medicine, Department of Rheumatology and Clinical Immunology, Kyoto, Japan
2Kyoto University Graduate School of Medicine, Department of Advanced Medicine for Rheumatic Diseases, Kyoto, Japan
3Kurashiki Sweet Hospital, Health Information Management, Kurashiki, Japan
4Nara Medical University, the Center for Rheumatic Disease Patients (ANSWER COHORT), which was the real-world retrospective cohort of clinical data-base for rheumatic diseases, RA patients who initiated biological / targeted disease modifying anti-rheumatic drugs were included and consecutively followed. Obesity was defined as BMI over than 25, and patients were divided between
obese ("Ob") and non-obese ("non-Ob") patients. SDAI (simplified disease activity index) was compared between non-Ob and Ob at month 0, 3, 6, 9, 12 after the indicated drugs were administered. Using logistic regression analysis, odds ratio (OR) and their corresponding 95% confidence intervals (95% CIs) were further calculated to estimate achievement rate of SDAI remission defined as lower than 3.3 by obesity and other relevant clinical parameters. Once after the drugs were discontinued by any unfavorable reason, disease activity was no more scored and the Last Observation Carried Forward (LOCF) imputation method was used for SDAI at month 3 and thereafter.

Results: A total of 1936 patients met in the inclusion criteria were under the analysis. Each drug's remission rate (non-Ob, Ob, p-value by Chi-square test) at month 12 was as follows: Infliximab (IFX, n=135): 43%, 38%, (not significant); Etanercept (ETN, n=188): 44%, 19%, p=0.012; Adalimumab (ADA, n=169): 50%, 56%, NS; Golimumab (GLM, n=315): 36%, 30%, NS; Certolizumab pegol (CZP, n=131): 33%, 56%, p=0.0287; Tocilizumab (TCZ, n=423): 41%, 29%, p=0.0436; Abatacept (ABT, n=144): 26%, 23%, NS; Tofacitinib (TOF, n=69): 27%, 23%, NS. In multivariate analysis to predict SDAI remission at month 12, obesity was an independent protective factor in CZP (OR: 0.29, 95% CIs: 0.10 – 0.83), but was an independent risk factor in TCZ (OR: 1.9, 95% CIs: 1.01 – 3.61) irrespective of age, sex, disease duration, SDAI at month 0 or number of previous bDMARDs. Any other drug including ETN did not show significant result between non-Ob and Ob in the multivariate analysis.

Conclusion: Obese patients were more resistant to TCZ but more effective in CZP than non-obese patients.

References:

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