Conclusions: In this study, we demonstrated that RF/ACPA positivity does not negatively impact on drug survival on golimumab. This may aid rheumatologists in their clinical decisions.

Disclosure of Interest: None declared


AB0226

DECLINE IN ANTI-CCP AND RHEUMATOID FACTOR LEVELS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AFTER 2 YEARS OF TREATMENT WITH INTENSIVE COMBINATION STRATEGIES, INCLUDING PREDNISOLON: THE COBRA-LIGHT TRIAL

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Background: Previous studies have proven that the COBRA-light strategy has similar effectiveness and safety as the COBRA strategy in treating early rheumatoid arthritis (RA) patients1,2. However, the effect of these strategies on anti-cyclic citrullinated peptide (anti-CCP) and rheumatoid factor (RF) levels remains contradictory.

Objectives: To investigate whether levels of anti-CCP and RF have changed after 2 years of treatment with COBRA or COBRA-light strategy.

Methods: A total of 162 early RA patients were included in a randomised, open-label, multicenter trial and treated with either COBRA or COBRA-light strategy. After 1 year, the treatment protocol ended, and physicians continued treatment according to clinical judgment, aiming at clinical remission. Log-transformation was first performed before running any analyses in case of skewed distribution, and analyses were performed with Generalised Estimated Equations to evaluate the association between the medication strategies and the change of LN anti-CCP and LN RF levels on average over time.

Results: Over 2 years’ time, median anti-CCP and RF levels decreased significantly in COBRA (6%, and 24% respectively) and COBRA-light (4%, and 13%, respectively); table 1). Of the 102 anti-CCP positive patients at baseline, 10 (10%) became anti-CCP negative during treatment (5 COBRA vs. 5 COBRA-light). No significant difference between the two treatment strategies on the change of anti-CCP and RF levels over 2 years’ time was found. Additionally, a significant association between baseline DAS44 and remaining anti-CCP positive over time was found (OR=1.8, 95% CI: 1.2–2.8).

Abstract AB0226 – Table 1. Change in anti-CCP and IgM RF levels over time

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Year 2</th>
<th>Year 2 change</th>
<th>Percentile change</th>
<th>Year 2 of treatment</th>
<th>Year 2 change</th>
<th>Percentile change</th>
</tr>
</thead>
<tbody>
<tr>
<td>COBRA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CCP</td>
<td>140 (1012)</td>
<td>81 (717)</td>
<td>-59 (-27.9)</td>
<td>0.04</td>
<td>108 (1077)</td>
<td>-4 (13.4%)</td>
<td>-6</td>
</tr>
<tr>
<td>RF</td>
<td>77 (1093)</td>
<td>39 (486)</td>
<td>-38 (-24.3)</td>
<td>0.04</td>
<td>85 (1380)</td>
<td>-5 (13.8%)</td>
<td>-1</td>
</tr>
<tr>
<td>COBRA-LIGHT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CCP</td>
<td>128 (1086)</td>
<td>81 (108)</td>
<td>-47 (-20.8)</td>
<td>0.04</td>
<td>102 (164)</td>
<td>-6 (13.4%)</td>
<td>-12</td>
</tr>
<tr>
<td>RF</td>
<td>40 (1232)</td>
<td>12 (40)</td>
<td>-28 (-8.6)</td>
<td>0.04</td>
<td>13 (18)</td>
<td>-3 (13.4%)</td>
<td>-12</td>
</tr>
</tbody>
</table>

Conclusions: Both COBRA and COBRA-light strategies lead to substantial decreases in anti-CCP and RF levels over 2 years of treatment. Patients with a higher DAS44 at baseline have higher odds of being anti-CCP positive over 2 years’ time.

REFERENCES:

Disclosure of Interest: None declared


AB0227

TRANSCRIPTIONAL PROFILING OF SYNOVIAL MACROPHAGES USING MINIMALLY INVASIVE ULTRASOUND-GUIDED SYNOVIAL BIOPSIES IN RHEUMATOID ARTHRITIS

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Background: Despite the many therapies for patients with rheumatoid arthritis (RA), there is little information to guide selection of the most effective treatment for an individual patient. Forty-sixty percent of patients with RA respond (defined by ACR50 response criteria) to conventional disease modifying anti-rheumatic drugs (cDMARDs) or cDMARDs plus anti-tumour necrosis factor (TNF) therapy. Moreover, 20%–40% of subjects in clinical trials never demonstrate even a minimal response (ACR20 response criteria). Based on a population of over 300 million in the United States, a disease prevalence of 0.6%, and a course of 3–4 months per biologic DMARD therapy, as much as $2.5 billion is wasted annually on inequitable therapy. There is a clear need to develop precision-based therapy for patients with RA, whereby clinical information such as novel biomarkers will enhance our ability to predict the therapeutic response and thereby limit ineffective therapy.

Objectives: Currently, there are no reliable biomarkers for predicting therapeutic response in patients with rheumatoid arthritis (RA). The synovium may unlock critical information for determining efficacy as reduction in numbers of sublining synovial macrophages remains the most reproducible biomarker. Thus, a clinically actionable method for collection of synovial tissue, which can be analysed using high-throughput methods, must become a reality.

Methods: Rheumatologists at six United States academic sites were trained in minimally invasive ultrasound-guided synovial tissue biopsy. Histology, fluorescence-activated cell sorting and RNA-seq were performed on biopsy synovial tissue from patients with RA and compared with osteoarthritis (OA) samples. An optimised protocol for digesting synovial tissue was developed to generate high quality RNA-seq libraries from isolated macrophage populations. Associations were determined between macrophage transcriptional profiles and clinical parameters of RA patients.

Results: Patients with RA reported minimal adverse effects in response to synovial biopsy. Comparable RNA quality was observed between synovial tissue and isolated macrophages from patients with RA and OA. Whole tissue samples from patients with RA demonstrated a high degree of transcriptional heterogeneity. In contrast, the transcriptional profile of isolated RA synovial macrophages highlighted a subpopulation of patients and identified six novel transcriptional modules that were associated with disease activity and therapy.

Conclusions: Performance of synovial tissue biopsies by rheumatologists in the United States is feasible and generates high-quality samples for research. By utilising cutting-edge technologies on synovial tissue biopsies with corresponding clinical information, a precision-based medicine approach for patients with RA is attainable.

Disclosure of Interest: None declared


AB0228

INCREASE IN GLOBAL DNA METHYLATION AT 3 MONTHS OF METHOTREXATE USE IS NOT ASSOCIATED WITH RESPONSE IN EARLY RA PATIENTS

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Background: Methotrexate (MTX) is a first-line therapy in early Rheumatoid Arthritis (eRA). Still, up to 40% of treated patients do not adequately respond to MTX. MTX interferes with the folate cycle, where it indirectly inhibits the global DNA methylation donor S-adenosylmethionine (SAM). Thus, we hypothesised that global DNA methylation changes during MTX use are associated with treatment response.

Objectives: To examine whether there is a change in global DNA methylation (δΔMeth) upon MTX use and if this change is associated to MTX response (ΔΔMeth) in eRA patients.

Methods: DNA was isolated from whole blood (n=120) and Peripheral Blood Mononuclear Cells (PBMCs, n=83) of eRA patients, before and 3 months after MTX use. Samples were collected from the Treatment in the Rotterdam Early Arthritis Cohort (REACHE), a multicenter, stratified single-blind clinical trial of eRA patients. Selected patients received triple (MTX + SSZ + HCQ) or monotherapy (MTX) combined with corticosteroids. 7 CpG sites within Long-Interspersed Nuclear Elements (LINE1), a proxy for global DNA methylation, were quantified by Sequenom Epityper. Paired t-tests or Wilcoxon Signed Rank tests were conducted to assess a change in methylation. ΔΔMeth score over 3 months was used as a measure for response. Associations between ΔΔMeth and δΔMeth were corrected for baseline DAS28 in a linear regression model.

Disclosure of Interest: None declared


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Results: In leukocytes, %Meth did not significantly change over time. However, in PBMCs, %Meth in CpG1 (\Delta %Meth\text{=2.61}, p=0.008) and CpG2 (\Delta %Meth\text{=0.73}, p=0.039) and CpG11.12 (\Delta %Meth\text{=0.56}, p=0.016) significantly increased over 3 months of MTX use after Bonferroni correction. \Delta %Meth in CpG8 was significantly associated to the \Delta DAS28 (B=0.29, p=0.039), yet this was no longer significant after Bonferroni correction. \Delta %Meth was not significantly associated to \Delta DAS28 in any of the other LINE1 CpG sites tested.

Conclusions: PBMC global DNA methylation in LINE-1 CpG sites increased upon 3 months of MTX use. However, this change in methylation is not associated to MTX response. Further research is needed to investigate the role of global DNA methylation in these patients.

Disclosure of Interest: None declared


AB0229 WHAT WARRANT COMPREHENSIVE DISEASE REMISSION (CDR) AT LONG TERM – PROBABILITY OF DAS28-CRP REMISSION AT SIX MONTHS –

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Background: Comprehensive disease remission (CDR) for rheumatoid arthritis (RA) patient is an ultimate challenge in treatment. Several reports suggested initial treatment with CDAI or 100 mm VAS was essential for attaining CDR, what means it is necessary to indicate treatment is essential for attaining CDR, what means it is necessary to indicate.

Objectives: Aim of this study is to clarify how initial treatment until 6 months affect on CDR fulfillment, and whether patient’s basic background influences.

Methods: We have 441 RA patients who had been treated consecutively for more than four years. These patients were recruited. Parameters such as 28-joints disease activity score with C-reactive protein (DAS28-CRP), modified Health Assessment Questionnaire Disability Index (mHAQ), pain score with visual analogue scale (PS-VAS), and swelling joint count (SJC) were monitored every 3 months from BL to FU.

Results: We have treated 516 RA patients for more than 3 years. Patient background data at first visit, and less reduction of TJC, SJC, EGA, and CRP. Their HAQ-DI, every component of DAS28-CRP, physician’s global assessment (EGA), number of comorbidities in throughout treatment (Com) was evaluated with MLR. 10.1136/annrheumdis-2018-eular.3434

Results: Because of lacking of data, sixty-one cases had discarded, then 488 cases was analysed in this study. The approximate equation of the relation between DAS28-CRP and PS-VAS was “DAS28-CRP=1.540+0.1565 * PS-VAS” (R=0.5050, Intercept; p=0, PS-VAS; p=0). Correlation coefficients of the approximate equation of the correlation between residuals of DAS28-CRP and the other parameters was 0.6398. Parameters that demonstrated within 1% of statistical significance were EGA (p=0), SHS (p=0.962 9-10), and Com (p=0.97110-5). Correlation coefficients of the approximate equation of the correlation between residuals of PS-VAS and the other parameters was 0.4856. Parameters that demonstrated within 1% of statistical significance were EGA (p=0.93810-3), HAQ-DI (p=0.57310-9), and SHS (p=1.59410-7). Correlation coefficients of the approximate equation of the correlation between HAQ-DI and residuals of DAS28-CRP and PS-VAS, and DD, age, EGA, and Com was 0.568. Parameters that demonstrated within 1% of statistical significance were DAS28-CRP (p=0.25610-8), residual of PS-VAS (p=0.31110-1), SHS (p=7.71310-4), and age (p=2.38910-2).

Conclusions: These results suggest that the influence of DAS28-CRP and PS-VAS on the HAQ-DI score works in commonly overlapped. However, residual (the independent part) of DAS28-CRP from PS-VAS on HAQ-DI is not statistically evidenced. We monitored every 3 months from BL to FU, and their anti-citrullinated cyclic peptide antibodies positive ratio was 70.9 years, respectively, and average follow-up term was 5.76 years. Woman’s ratio was 75.6%, and their anti-citrullinated cyclic peptide antibodies positive ratio was 77.2%.

Disclosure of Interest: None declared


AB0231 HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX (HAQ-DI) SCORE AS LESS THAN 0.5 AS A LOwer TARGET FOR REMISSION IN ELDERLY RHEUMATOID ARTHRITIS PATIENT, BUT IT IS INDEPENDENT FROM COMORBIDITIES

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Background: It is well known fact that ageing makes deep influence on Health Assessment Questionnaire (HAQ-DI) score in normalised population. We have suggested that it is also available in rheumatoid arthritis (RA) patient. However, the effect of ageing on the HAQ score is thought to be due to comorbidities.

Objectives: The aim of this study is to investigate the impact of ageing on the HAQ score statistically and to evaluate the correlation between the HAQ score and age.

Methods: We have treated 516 RA patient for more than 3 years. Patient’s Age, HAQ-DI score, 28-joints disease activity score with C-reactive protein (DAS28), Sharp/van der Heijde Score (SvdHS), pain score measured with visual analogue scale (PS-VAS) was monitored at every another year period. Their HAQ-DI, every component of DAS28-CRP, physician’s global assessment (EGA), number of comorbidities in throughout treatment (Com) was evaluated with MLR. 10.1136/annrheumdis-2018-eular.3434

Results: After exclusion of cases that lacked data, 441 patients have been analysed for this study. Their average ages at onset, BL, and FU were 60.4, 65.1, and 70.9 years, respectively, and average follow-up term was 5.76 years. Woman’s ratio was 75.6%, and their anti-citrullinated cyclic peptide antibodies positive ratio was 77.2%.

At BL, correlation coefficient of the equation (the R-value) in MLR was 0.6251. Factors that demonstrated significant correlation with the HAQ score were PS, age, SHS, EGA, and Com.

Disclosure of Interest: None declared