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

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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 PREDNISOLONE: 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) patients^{1,2}. 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

	Baseline	Week 52	Absolute median change	Percentage median change	Week 104	Absolute median change	Percentage median change
COBRA							
Anti-CCP	143 (8-1182)	81 (7-710)	-20 (-427-0)	-14	109 (7-507)	-8 (-314-0)	-6
IgM-RF	37 (9-102)	9 (6-40)	-9 (-41-0)	-24	8 (5-46)	-9 (-36-0)	-24
COBRA-light							
Anti-CCP	229 (10-961)	80 (7-499)	-13 (-249-0)	-6	32 (7-402)	-9 (-235-0)	-4
IgM-RF	40 (10-132)	12 (6-50)	-15 (-79-0)	-38	13 (6-84)	-5 (-48-1)	-13

Data are expressed as median (IQR) as well as percentage median change from baseline. Anti-CCP, anti-cyclic citrullinated peptide; IgM-RF, rheumatoid factor type IgM.

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.

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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-six 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 inadequate 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 strategies, 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 biopsies with corresponding clinical information, a precision-based medicine approach for patients with RA is attainable.

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AB0228

INCREASE IN GLOBAL DNA METHYLATION AT 3 MONTHS OF METHOTREXATE USE IS NOT ASSOCIATED TO 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 ($\Delta\%$ Meth) upon MTX use and if this change is associated to MTX response (Δ DAS28) 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 (tREACH), 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 (LINE-1), 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. Δ DAS28 score over 3 months was used as a measure for response. Associations between Δ DAS28 and $\Delta\%$ Meth were corrected for baseline DAS28 in a linear regression model.