education, and higher fatigue, whereas older age and greater pain were associated with persistent disease activity in men. Smoking cessation in men and weight reduction in women, and optimising MTX use may facilitate rapid reduction of inflammation, an essential goal of treatment in early RA.

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Fat and fatty acids: targets for therapy?

OP0107

ADIPOCYTOKINES IMBALANCE IS ASSOCIATED WITH VASCULAR DAMAGE IN SYSTEMIC SCLEROSIS

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Background: Adipocytokines are implicated in the development of fibrosis, vasculopathy and immune abnormalities through a variety of biological effects, but their role in systemic sclerosis (SSc) is not fully investigated. Chemerin is implicated in chemotaxis of immune cells, in promoting angiogenesis and it is involved in inflammation. Adiponectin (APN) has metabolic actions and anti-inflammatory properties, while Leptin (LEP) mediates actions in endothelial cells, such as angiogenesis, vasodilation, NO production and upregulates various mediators of vascular inflammation.

Objectives: In this study we investigated Chemerin, LEP and APN levels in SSc patients according to disease subtypes and clinical characteristics.

Methods: Chemerin, LEP and APN levels were evaluated in 100 SSc patients and in sex, age and BMI matched healthy controls. Clinical and demographical characteristics were available for all patients.

Results: Chemerin, APN and LEP levels were lower in SSc patients compared to healthy controls (Chemerin: 58.7±27.6 ng/ml vs 74.0±29.0 ng/ml, p=0.004; LEP: 19.6±18.3 ng/ml vs 28.5±23.8 ng/ml, p=0.03, APN: 6.5±3.9 µg/ml vs 12.8±6.0 µg/ml, p<0.001)

Chemerin levels were lower in patients with anti-topoisomerase antibodies (50.2±22.7 ng/ml) respect to patients with other autoantibodies (64.6±29.7 ng/ml), p=0.018.

Regarding capillaroscopic damage, Chemerin levels were lower in patients with late pattern (44.8±18.9 ng/ml) compared to patients with early (64.3±28.5 ng/ml) and active pattern (71.7±29.9 ng/ml), p<0.001. APN levels inversely correlate with IL-6 levels (R=-0.4, p<0.001), while directly correlate with capillary density (R=0.3, p=0.03). Patients with avascular areas presented lower levels of APN (5.3±3.9 µg/ml) compared to patients without avascular areas (7.3±3.4 µg/ml), p=0.005. LEP levels directly correlate with vascular density on nailfold capillaroscopy (R=0.3, p=0.02), confirming the role of LEP in endothelial homeostasis. Furthermore, patients with avascular areas presented lower LEP levels (15.5±13.0 ng/ml) compared to patients without avascular areas (31.1±28.4 ng/ml), p=0.003. LEP levels were lower in patients with active digital ulcers (9.3±6.6 ng/ml), compared to patients without ulcers (9.3±6.6 ng/ml), p=0.01. The anti-inflammatory and endothelium protective role of APN emerged also when we considered the lung involvement: in fact patients with DLCO >50% presented higher levels of APN (7.0±3.9 µg/ml) compared to patients with DLCO <50% (5.8±3.8 µg/ml), p=0.05.

Considering the cardiopulmonary involvement, LEP levels inversely correlate with PAPs on echocardiography (R=-0.24, p=0.02). Finally LEP levels inversely correlate with skin score (R=-0.3, p=0.009) and patients with early disease presented lower LEP levels (15.1±13.2 ng/ml) compared to patients with long lasting disease (29.9±28.7 ng/ml), p=0.006.

Conclusions: Our data suggest an imbalance of the levels of adipocytokines in SSc, their down-regulation in patients with a more aggressive pattern on nailfold videocapillaroscopy and organ damage, suggesting a possible role of Chemerin, LEP and APN in the impaired angiogenesis and in the development of vasculopathy of SSc patients.

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OP0108

DIET INDUCED METABOLIC CHANGES IN AN OSTEOARTHRITIS MOUSE MODEL

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Background: Adipose tissue is not only an energy depot, but also secretes bioactive factors such as adipokines. Several of these factors are known to regulate immune responses. Osteoarthritis (OA) is one of the most common joint diseases with obesity being a well known risk factor. Therefore, an obesity model (High-fat diet, HFD) was combined with an established model for OA (DMM, destabilisation of the medial meniscus) to evaluate the role of adipokines in this setting.

Objectives: This work evaluates the influence of different adipokines on OA progression and obesity comparing systemic vs local effects at different time points.

Methods: The study was performed in C57BL/6 mice fed with HFD or ND (normal diet) prior to OA induction. Mice were sacrificed and analysed 4, 6 and 8 weeks after surgery. For systemic analysis, sera were evaluated for adipokines such as adiponectin, leptin and visfatin and inflammatory markers. Diet induced systemic changes were also analysed using a fatty liver score and evaluation of crown-like structures (CLS) in adipose tissue. OA progression was scored and quantified based on histological stainings of the joints (H/E, safranin O). Immunohistochemical stainings of the joints were performed to evaluate local distribution of adipokine positive cells and the respective cell types. Metabolic parameters were correlated to the local progression of OA.

Results: The numbers of CLS were significantly lower comparing HFD (0.2±0.1553, n=7) with ND (5.219±0.9831, n=8) in mice. Fatty-liver score was significantly higher in HFD compared to ND. OA induction was significant at every time-point vs healthy control and higher in HFD (e.g.: OA score at 6 weeks HFD 3.7 vs ND 1.4). In the OA groups, there was a positive correlation between bodyweight and OA score (r²=0.33). Correlation level of OA score with liver score or serum leptin level was low, even though leptin was significantly induced by HFD. However, DMM decreased leptin levels at all time points, independent from diet (e.g. 4 weeks: HFD healthy 18.4 ng/ml vs HFD DMM 3.7 ng/ml). The different parameters for metabolic changes (fatty liver score and bodyweight) were positively correlated with serum leptin level. HFD, DMM or the combination of both did not show significant effects on serum levels of adiponectin, visfatin or IL-6. Local adipokine secretion in the joints was independent from systemic metabolism parameters.

Conclusions: Our data show that similar to observations in humans, OA is deteriorated by HFD which correlates mainly with the bodyweight and to a lower extend with metabolic changes induced by obesity. Local adipokine expression was especially detectable in the damaged meniscus showing increased amounts of adiponectin and leptin producing cells. Interestingly, local adipokine expression was independent from systemic adipokine levels.

Disclosure of Interest: None declared

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Biologics in RA. Improving and maintaining the response

OP0109

IN RA PATIENTS WITH INITIAL RESPONSE TO RITUXIMAB, EARLY DEPTH OF B CELL DEPLETION IS ASSOCIATED WITH LONG TERM MAINTENANCE OF THERAPY

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Background: B-cell depletion is a fundamental effect of rituximab (RTX). The speed/depth of initial B-cell depletion is associated with clinical response, and non-responders largely having incomplete depletion.^{1,2} However, some patients with incomplete depletion still show clinical improvement (ID-R). Little is known about factors associated with complete depletion; the long-term outcome of the two responder groups according to their level of depletion has not been studied yet.

Objectives: To assess factors that are associated with complete depletion and clinical response (CD-R) and compare the 3 year RTX retention between the two RTX responder groups (CD-R vs ID-R), with a view to inform practice on the optimal use of RTX in RA.

Methods: A prospective observational study was conducted in patients with RA who were treated with RTX in Leeds. Each initial cycle of RTX consisted of 2 × 1000 mg infusions, repeated either on clinical relapse or fixed 6 monthly

retreatment strategy. B-cells were measured at 0, 2 weeks and every 6 months using highly sensitive flow cytometry (as previously described). Complete depletion was defined as total B cell count $<0.0001 \times 10^9/L$ at week 2. Patients were classified into 4 groups based on B-cell depletion (CD=complete,) and EULAR response (R=good/moderate, NR=no response). Multiple imputation was used for missing data. Factors for predicting CD-R in cycle 1 (C1) were tested using logistic regression analyses. In the survival analysis, an event was defined as RTX cessation either due to death, safety or switching to other biologics.

Results: A total of 693 patients were treated with RTX in Leeds. Of these, 624 had clinical data at 6 months and were included in the analysis. Total follow-up was 2826 patient-years. In cycle 1, 418/624 (67%) had EULAR response. Of these, 242/418 (58%) had CD-R. In univariable analysis, age, concomitant MTX/LEF, non-smoker, pre-RTX lower naïve, memory B-cell and plasmablasts were associated with CD-R in C1. However, in a multivariable analysis, only concomitant MTX/LEF (OR 2.1 95% CI: 1.3 to 3.5), non-smoker (1.6, 1–2.6) increased the odds while lower plasmablasts (0.89, 0.83–0.95) decreased the odds of CD-R. After adjusting for confounders including age, gender, concomitant MTX/LEF and previous exposure to TNF- α , there was a trend to longer maintenance on RTX (surrogate for response) in the CD-R vs ID-R groups; HR 0.70 (95% CI: 0.46 to 1.05); $p=0.058$ (figure 1).

Rituximab retention 3 years after the administration of the first cycle

Abstract OP0109 – Figure 1 Rituximab retention 3 years after the administration of the first cycle

Conclusions: Among patients with good initial clinical response to RTX, we observed differences in immunological response. This had important long term consequences: in patients with early complete B-cell depletion accompanied by good clinical response, RTX treatment was sustained over 3 years numerically, while responses of ID were less durable. Therefore, treatment with anti-CD20 mAb should aim to achieve CD for sustained maintenance on rituximab. CD-R can be predicted by concomitant use of MTX/LEF, non-smokers and those with low baseline plasmablasts.

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OP0110

SERUM TOCILIZUMAB TROUGH CONCENTRATIONS ARE ASSOCIATED WITH CLINICAL DISEASE ACTIVITY INDEX SCORES IN ADULT RHEUMATOID ARTHRITIS PATIENTS

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Background: Serum trough levels of TNF α inhibitor biologics have been found to be associated with clinical responses in rheumatoid arthritis (RA) patients. It is unknown whether serum trough levels of tocilizumab (TCZ) administered as a fixed dose subcutaneous injection, also associate with clinical disease activity responses.

Objectives: To ascertain whether serum TCZ trough levels at weeks 12 and 24 after beginning treatment with a 162 mg once weekly regimen of SC tocilizumab, were associated with clinical disease activity outcomes in RA patients.

Methods: We analysed data sets from the Israeli branch (TASC, NCT01988012) of the Roche multinational umbrella study TOZURA, which evaluated a SC TCZ treatment regimen of 162 mg once weekly as monotherapy or in combination with methotrexate or other csDMARDs in a real-life clinical setting. The study comprised of 100 patients. A paired-samples T test was used to compare mean serum TCZ levels at week 12 relative to week 24. Clinical disease activity index (CDAI) scores were natural log-transformed in order to achieve normal distribution. Generalised estimating equations were used to evaluate associations between the predictors (TCZ levels, soluble IL-6 receptor (sIL6R) levels) and the study outcomes (CDAI scores, HAQ scores, CDAI remission/low disease activity status, HAQ DI remission). Generalised estimating equations were also used to evaluate associations between age, sex, weight, BMI, baseline CRP levels, serum TCZ and sIL6R serum levels. P values below 0.05 were considered significant.

Results: Serum trough levels of TCZ at week 24 (mean 41.1, SD 23.2) were higher than at week 12 (mean 36.3, SD 18.1).

In a univariate analysis, for every increase of 1 microgram/ml in the serum concentration of TCZ there was a corresponding decrease of 1.3% (95% CI: 0.4% to 2.3%) in the CDAI score and for every increase of 100 ng/ml in the serum concentration of sIL6R there was a corresponding decrease of 12.6% (95% CI: 2% to 22%) in the CDAI score.

In a multivariate model which included age, sex, visit date and both sIL6R and TCZ levels, only the associated between TCZ levels and CDAI scores remained significant. Similarly, every increase of 10 microgram/ml in the serum concentration of TCZ was associated with an odds ratio of 1.35 (95% CI: 1.07 to 1.72) of being in a state of CDAI remission or low disease activity versus moderate/high disease activity state. TCZ and sIL6R serum levels were not associated with HAQ DI scores.

Female sex was associated with an increase of 12.9 microgram/ml in the serum TCZ concentrations (95% CI: 5.9 to 20.0). Also, every increase of 1 BMI unit was associated with a decrease of 1.5 microgram/ml in the serum TCZ concentrations (95% CI: 0.8 to 2.2) and every increase of 1 kg in weight was associated with a decrease of 0.6 microgram/ml in the serum TCZ concentrations (95% CI: 0.3 to 0.9).

Conclusions: In the first year of TCZ treatment with a fixed dose regimen of 162 mg SC injection once a week, serum trough concentrations of TCZ are associated with CDAI scores and a state of CDAI remission/low disease activity. Body weight and BMI are inversely associated with serum TCZ concentrations. These results suggest that personalising the dose of SC TCZ to body weight may improve clinical outcomes of RA disease activity.

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OP0111

TOCILIZUMAB DISCONTINUATION AFTER ATTAINING REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO WERE TREATED WITH TOCILIZUMAB ALONE OR IN COMBINATION WITH METHOTREXATE: RESULTS FROM A PROSPECTIVE, RANDOMISED, CONTROLLED STUDY (THE SECOND YEAR OF THE SURPRISE STUDY)

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