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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Background: Feasibility of discontinuation of biologic agents in patients with rheumatoid arthritis (RA) who have reached stable remission has been investigated. Although evidence has been accumulating regarding tumour necrosis factor inhibitors, the possibility of tocilizumab-free strategy is still unclear.

Objectives: To evaluate the sustained remission and low disease activity after discontinuation of tocilizumab in patients with RA who were treated with tocilizumab alone or in combination with methotrexate.

Methods: The SURPRISE study was a 2 year randomised, controlled study. Patients with active RA despite methotrexate were randomised to tocilizumab added to methotrexate (ADD-ON) or switch to tocilizumab alone (SWITCH). At week 52, tocilizumab was discontinued in patients who achieved remission based on disease activity score for 28 joints (DAS28-ESR<2.6). The endpoints of the second year included tocilizumab-free sustained remission rates at week 104, sustained low disease activity rates, radiological outcomes assessed with the modified total Sharp score (mTSS), and safety. The efficacy of re-instituted tocilizumab/methotrexate was also assessed.

Results: 105 patients who achieved remission at 52 week discontinued tocilizumab; 51 in the ADD-ON continued methotrexate and 54 in the SWITCH were observed without medication. Whereas sustained DAS28 remission rates at week 104 were 24% for the ADD-ON and 14% for the SWITCH ($p=0.29$), sustained low disease activity rate was significantly higher in the ADD-ON than in the SWITCH (55% vs 27%, $p=0.005$, figure 1). Radiographical progression was comparable in the 2 groups (mTSS; 0.37 vs 0.64, $p=0.36$). Re-start of tocilizumab induced remission in all patients except two irrespective of concurrent methotrexate after 36 weeks while re-start of methotrexate was effective only in a half of patients.

Tocilizumab-free low disease activity

Abstract OP0111 – Figure 1 Tocilizumab-free low disease activity

Conclusions: Sustained low disease activity after tocilizumab discontinuation could be maintained with continued methotrexate in more than half of patients. Re-treatment with tocilizumab led remission in more than 90% patients.

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OP0112 THERAPEUTIC DRUG MONITORING TO OPTIMISE SWITCHING BETWEEN BIOLOGIC AGENTS IN RHEUMATOID ARTHRITIS

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Background: Many patients with rheumatoid arthritis (RA) are treated with tumour necrosis factor inhibitors (TNFi). It is, however, unclear whether to switch to a second TNFi or to another mode of action drug in case of non-response. The detection of anti-drug antibodies (ADAs) have shown to be related to the response rate of a second TNFi.¹ The detection of ADAs is, however, to a large extent dependent of the type of assay used and, moreover, the efficacy of the drug is determined by the pharmacokinetics. Therefore, it more logical to use drug levels in daily clinical practice.

Objectives: To investigate whether serum drug concentration of patient's first TNFi, adalimumab, was related to the effectiveness of a second TNFi, etanercept.

Methods: Consecutive patients with RA treated with etanercept were followed in the Reade Rheumatology Registry, an observational cohort (NTR no.6868). Patients who were treated with adalimumab 40 mg every other week previously (switchers; n=69) were compared to patients starting etanercept without prior biologic agents (biologic-naïve; n=380). Patients received etanercept 50 mg weekly or 25 mg twice a week. Switchers were divided into three groups; respectively low- (<0.5 µg/mL), intermediate- (0.5 and 5.0 µg/mL) and high- (>5.0 µg/mL) adalimumab concentration. The last available serum sample before adalimumab discontinuation was assessed for adalimumab concentrations by enzyme linked immunosorbent assay (ELISA). ADAs were measured using the antigen binding test (ABT). Clinical endpoints were percentage of patients achieving European League Against Rheumatism (EULAR) good or moderate response and the Simplified Disease Activity Index remission criteria (SDAI <3.3) after 52 weeks.

Results: Median (IQR) adalimumab concentration of the switcher-groups with low (n=18), intermediate (n=18) and high concentrations (n=27) were, respectively 0.0 µg/mL (0.0–0.05), 2.5 µg/mL (1.5–4.3) and 7.4 µg/mL (6.0–11.8). ADAs were detected in, respectively 16 patients (89%), 6 patients (33%) and 3 patients (11%). Response rate of switchers with low adalimumab concentrations was