Figure 2 Continuation rate of biological therapy in YRA and ERA

YRA: younger RA patients, ERA: elderly RA patients

Conclusions: Although continuation rate of BIO treatment in ERA was inferior to that in YRA, that in yERA was not significantly different from that in oERA. Serious infection, especially in respiratory systems, was most frequent reason for stopping BIO therapy in ERA. These results suggested that BIO therapy in ERA demands close attention to infection and special strategies might need in the treatment of ERA people.

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SAT0211

IS THERE A POTENTIAL FOR THERAPEUTIC DRUG MONITORING OF SUBCUTANEOUS TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN DAILY PRACTICE?

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Background: Tocilizumab (TCZ), is a humanized antibody that competitively inhibits membrane-bound and soluble IL-6 receptors. Subcutaneous (sc) TCZ might be a potential candidate for therapeutic drug monitoring (TDM) since a high variability in serum concentrations has been reported. Considering that TCZ concentrations above 1 µg/mL have been claimed to be sufficient for normalizing CRP production (1), there might be an overexposure in a substantial proportion of patients. We expect that patients can at least reduce to a dose aiming for a trough concentration of 5 µg/mL. Insights in serum concentrations of sc TCZ with clinical efficacy are lacking, but are necessary to reduce overexposure, potential dose-dependent adverse effects and at the same time reduce costs.

Objectives: To describe TCZ trough serum concentrations in patients with rheumatoid arthritis (RA) treated with sc TCZ.

Methods: Prospective study with consecutive RA patients starting treatment with sc TCZ between June 2015 to October 2017 who had previously failed treatment with at least two DMARDs, including MTX. TCZ was administered at a dose of 162 mg every week and patients were followed for 28 weeks. The study was conducted at the Amsterdam Rheumatology and Immunology Center | Reade. Serum trough samples were collected at baseline and at 4, 16, 28 weeks thereafter. An enzyme-linked immunosorbent assay (ELISA) was used for TCZ measurement. To analyze the concentration variability among patients at 28 weeks, a last observation carried forward approach was used.

Results: In total, 26 patients were included in the study and 94 TCZ serum concentrations were measured. Median and interquartile range (IQR) of the follow-up period was 28 (16-28) weeks and 54% of the patients accomplished week 28. Drug concentrations ranged from 0.2 to 63 µg/mL, with an overall median (IQR) of 26.0 (10.5-42.0) µg/mL. In the majority of patients, TCZ concentrations stabilized after 4 weeks of treatment. Variability in drug concentrations at 28 weeks is shown in figure 1. Median (IQR) TCZ serum concentrations at 28 weeks was 24.0 (6.4-43.0) µg/mL, 92% of the patients achieved a concentration above 1 µg/mL and 88% had a concentration > 5 µg/mL.

[TCZ] at 28 weeks with LOCF

Conclusions: The Interindividual variability among patients on sc TCZ is remarkably high. The majority of the patients achieved serum concentrations far above 5 µg/mL, suggesting overexposure in those patients. Therefore, TDM might be useful to optimize treatment, reduce (potential) side effects and achieve cost-effectiveness.

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Rheumatoid arthritis - non biologic treatment and small molecules

SAT0212

THE SAFETY AND TOLERABILITY OF INTRA-ARTICULAR INJECTION OF TOLEROGENIC DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS: THE PRELIMINARY RESULTS

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through the presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, utilization of tolerogenic DCs seems to be a promising immunotherapeutic tool to treat RA.

Objectives: The aim of our study is to evaluate the safety and tolerability of a single intra-articular injection (into the knee joint) of autologous monocyte-derived dendritic cells generated in the presence of IFN-α/GM-CSF and tolerized with Dexamethasone in RA patients.

Methods: DCs were generated by culturing blood monocytes for 5 days with GM-CSF and IFN-α in the presence dexamethasone, applied on third day. Azoximer bromide as maturation stimuli was added on fourth day. Ten RA patients with moderate and high disease activity and ultrasound-defined knee synovitis were recruited in this study. All patients fulfilled ACR/EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine or their combination. The patients received intra-articular injections of 1*10⁶, 3*10⁶, 5*10⁶, 8*10⁶ DCs in knee joints. Safety was assessed by evaluation of adverse events (AE). Acceptability was assessed by questionnaire. DAS28 and HAQ were used for assessment of treatment efficiency. This trial registered on clinicaltrials.gov (ID: NCT03337165).

Results: DCs injections were safe and well tolerated. No one participants showed worsening of symptoms in targeting knee, fever, elevation of blood pressure or other AE within 7 days after injection. After one month the median pain VAS score decreased from 45 (40–65) mm to 40 (15–40) mm; $p=0.03$. Ultrasound and clinical examination did not detect synovitis. At 3 month no patients demonstrated recurrence of synovitis and median DAS28-ESR improved from baseline 5.1 to 4.4 ($p=0.008$; $n=10$). Five patients, evaluated at 6 months follow-up showed a good EULAR response (improvement of DAS28-ESR >1.2). The median DAS28-ESR in this group decreased from 5.1 to 3.3 ($p=0.04$). In addition, we detected median HAQ improvement (from 1.45 to 1.0; $p=0.04$).

Conclusions: The data obtained suggest that single intra-articular injection of autologous tolerogenic dendritic cells is safe, well tolerated, and according to preliminary data have a potential efficiency. However, the final conclusion should be done after the completion of the trial.

Disclosure of Interest: None declared

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SAT0213

TIGHT TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS IN THE EARLY STAGES OF DISEASE LEADS TO HIGH LEVELS OF REMISSION AND REDUCED USE OF BIOLOGICS

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Background: Early treatment with synthetic DMARDs has demonstrated favourable outcomes in patients with Rheumatoid Arthritis (RA). It leads to a reduction in inflammation, limits articular and extra-articular manifestations of RA, enables earlier functional improvement and causes less radiographic damage.¹ Treat to target (TTT) approaches have been used to adapt therapy according to disease activity in order to achieve clinical remission, providing a standardised treatment algorithm that allows for rapid treatment escalation when needed.

Objectives: To evaluate the remission rate of patients in a real life TTT clinic at a district general hospital in the United Kingdom and to compare our local data to the United Kingdom 2015–2016 Healthcare Quality Improvement Partnership (HQIP) audit. To evaluate the proportion of patients starting biological therapy post follow up in a TTT clinic.

Methods: The electronic records of patients referred to the TTT clinic between September 2012 and December 2015 were accessed retrospectively and data collected. All patients with a diagnosis of RA were included in data analysis. Patient demographics and clinical data were collected. Statistical analysis was performed using GraphPad Prism. Comparisons of outcomes for antibody status and smoking status were made using Fisher's exact test.

Results: 242 patients were seen at least once in the TTT clinic. Follow-up data was available for 216 patients. 65% were female with a median age of 62 years (range 19–90). 69% patients were either rheumatoid factor or anti-CCP positive and 80% were started on combination therapy (Methotrexate and Hydroxychloroquine) at their first clinic appointment. Overall 46% of patients entered remission (disease activity score (DAS) of <2.6). 49% of seropositive patients achieved remission compared to 39% of seronegative patients although this was not statistically significant ($P=0.249$, Fisher's exact test). A statistically significant fewer number of people who were current smokers achieved remission ($p=0.005$, Fisher's exact test). Only 9 patients (4.2%) required the addition of biologic drugs within the first year of treatment.

Conclusions: Our TTT clinic was successful in starting a significant proportion (80%) of patients on combination DMARDs (compared to an estimated national average of 46% based on HQIP data).² This approach also resulted in a higher proportion of patients entering DAS remission (46%, national average 31%), though understandably this was lower than the remission rate achieved in clinical trials.³ Only 4.2% of patients went onto biological DMARDs within the first year, which is far less than the proportion commencing biologics prior to TTT. This data demonstrates that TTT approaches in a real life clinical setting are important in achieving remission in patients with RA and reducing the need for expensive biological treatment.

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SAT0214

EFFECTIVENESS OF A RANDOMIZED STEP-DOWN TO METHOTREXATE OR LEFLUNOMIDE MAINTENANCE THERAPY IN PATIENTS WITH LOW DISEASE ACTIVITY, 40 WEEKS AFTER STARTING COMBINED METHOTREXATE-LEFLUNOMIDE REMISSION INDUCTION THERAPY IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE CARERA TRIAL

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Background: Combination of methotrexate, leflunomide and a short-term course of glucocorticoids is an effective initial treatment strategy for early rheumatoid arthritis (ERA) (1). However, evidence concerning further maintenance or step-down strategies after achieving remission or low disease activity is lacking.

Objectives: To evaluate efficacy and tolerability of a step-down to methotrexate versus leflunomide monotherapy in ERA patients achieving low disease activity (LDA) after induction therapy with a combination of both.

Methods: The care in ERA (CareRA) trial is a 2-year randomized pragmatic superiority trial comparing different remission induction strategies in ERA. For the purpose of the current sub-study, DMARD-naïve ERA patients initially randomized into the COBRA Avant-Garde arm (methotrexate 15 mg weekly + leflunomide 10 mg daily + prednisone step-down from 30 mg) were re-randomized, after a period of 40 to 52 weeks, to a methotrexate 15 mg weekly or leflunomide 20 mg daily maintenance therapy when achieving LDA (DAS28-CRP ≤ 3.2). Disease activity, functionality and X-ray damage were registered. Efficacy of both regimens was compared at week 65 after re-randomization as well as their safety profiles and drug retention rates (ITT analysis).

Table 1 Clinical and radiological outcomes at week 65 per treatment arm Data are presented as mean $\pm$ SD or number of patients and percentages; LDA, low disease activity; SvdH, Sharp van der Heijde score.

Table 2 Effectiveness analysis after re-randomization AE, adverse event; SAE, serious adverse event; other AEs include all other AEs less likely to be related to methotrexate or leflunomide.

	Methotrexate N=32	Leflunomide N=26	p-value
Remission DAS28-CRP <2.6	30 (93.8%)	19 (73.1%)	0.031
LDA DAS28-CRP ≤ 3.2	32 (100%)	23 (88.5%)	0.048
Δ DAS28-CRP from re-randomization	0.2 $\pm$ 0.7	-0.2 $\pm$ 1.0	0.214
Remission CDAI ≤ 2.8	21 (65.6%)	14 (53.8%)	0.362
LDA CDAI ≤ 10	32 (100%)	21 (80.8%)	0.009
Δ CDAI change from re-randomization	0.6 $\pm$ 2.7	-2.8 $\pm$ 8.1	0.462
Remission SDAI ≤ 3.3	20 (62.5%)	14 (53.8%)	0.506
LDA SDAI ≤ 11	32 (100%)	22 (84.6%)	0.021
Δ SDAI change from re-randomization	0.8 $\pm$ 3.1	-3.1 $\pm$ 8.2	0.244
HAQ (0-3)	0.3 $\pm$ 0.5	0.3 $\pm$ 0.4	0.968
Change in SvdH from baseline CareRA	0.7 $\pm$ 0.9	0.9 $\pm$ 1.8	0.702

Data are presented as mean $\pm$ SD or number of patients and percentages; LDA, low disease activity; SvdH, Sharp van der Heijde score.

	Methotrexate	Leflunomide
Patients still on monotherapy on w65	23 (71.9%)	14 (53.4%)
Patients with AE related to study therapy	10 (31.2%)	9 (34.6%)
Total number of AEs	80	79
Infection	14	16
Gastrointestinal discomfort	7	13
Liver function disturbances	3	1
Other AEs	56	49
Total number of SAEs	7	4
Number of SAEs related to study therapy	0	0

AE, adverse event; SAE, serious adverse event; other AEs include all other AEs less likely to be related to methotrexate or leflunomide.

Results: We re-randomized 58 patients to either methotrexate ($n=32$) or leflunomide ($n=26$) monotherapy. At re-randomization 81.2% of patients in the methotrexate group (26/32) was in remission (DAS28-CRP <2.6), versus 92.3% (24/26) in the leflunomide group ($p=0.225$). At 65 weeks post re-randomization significantly more patients achieved DAS28-CRP remission in the methotrexate group (93.8%) than in the leflunomide group (73.1%) ($p=0.031$). Patients re-randomized to methotrexate also achieved more frequently a state of LDA measured by DAS28-CRP, CDAI and SDAI in comparison to patients re-randomized to leflunomide (table 1). Safety analysis after re-randomization did not show differences between groups with regards to number or type of adverse events (AEs). Numbers of patients with AEs related to study medication were comparable (31.2% in the methotrexate and 34.6% in the leflunomide group). Throughout these 65 weeks 71.9% of patients in the methotrexate and 53.8% ($p=0.098$) in the leflunomide arm remained on the assigned DMARD monotherapy. At the end of the study, in patients remaining on methotrexate monotherapy the mean dose was 15.3 mg weekly versus a mean dose of 17.1 mg daily in patients remaining on leflunomide monotherapy.