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.

REFERENCES:

- [1] Raza K, Buckley CE, Salmon M, Buckley CD. Treating very early rheumatoid arthritis. Best practice & research Clinical rheumatology 2006;20 (5):849–863.
- [2] Healthcare Quality Improvement Partnership. National clinical audit for rheumatoid and early inflammatory arthritis. 2016.
- [3] Grigor C, Capell H, Stirling A, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised control trial. Lancet 2004;364(9430):263–269.

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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.

Conclusions: Step-down to methotrexate monotherapy instead of leflunomide monotherapy seems more efficacious, is well tolerated and has a good drug retention rate in ERA patients in LDA after combination therapy with methotrexate and leflunomide.

REFERENCE:

- 1) Verschueren P, et al. *Ann Rheum Dis* 2017;76(3):511–520.

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SAT0215 LIVER BLOOD TEST ABNORMALITIES ARE RARE IN PATIENTS ON METHOTREXATE: EVIDENCE FROM A LARGE COHORT OF INFLAMMATORY ARTHRITIS PATIENTS

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Background: National British Society of Rheumatology guidelines for monitoring non-biologic disease-modifying anti-rheumatic drugs (DMARDs) suggest reducing the frequency of blood monitoring for patients on stable doses of methotrexate to 12 week intervals.¹ Implementation of this recommendation would reduce pressure on services, reduce costs and enhance patient experience. However, it remains unclear whether patient safety would be compromised with 12 week interval blood monitoring in a real world setting.

Objectives: The primary objective was to establish whether reducing blood monitoring frequency from monthly to 12 week intervals would compromise the safety of patients on methotrexate by either late detection or missing signs of transaminitis on blood results.

Methods: Between June 2016 and July 2017, monthly liver function test results were monitored in 1,964 patients on methotrexate. Demographic data were collected and abnormal results were reviewed. Patients with raised alanine aminotransferase (ALT) (>34 U/l) were categorised as either: isolated (only one abnormal result), persistent (at least two consecutive abnormal results) or intermittent (more than one abnormal result separated by at least one normal result). For those with an ALT>100 U/l, medical records were reviewed to determine causality.

Results: ALT results for 1,964 patients were reviewed (F=1288, M=676). 775 were on one concomitant DMARD, 82 were on triple DMARD therapy (hydroxychloroquine and sulfasalazine) and 396 were on biologic therapy. Indications for methotrexate were rheumatoid arthritis (n=1262), psoriatic arthritis (n=611) and spondyloarthritis (n=91). Ten patients (0.51%) had an ALT>100 U/l over 13 months: 8 were persistent, 1 was intermittent and 1 was isolated. Further investigations revealed fatty liver in one patient (necessitating methotrexate discontinuation) and a weakly positive anti-smooth muscle antibody in another (both with persistent ALT>100), but were unremarkable in the other 8. A further 48 patients had at least one ALT rise of 35–100 U/l which did not alter therapy.

Conclusions: Over 13 months monitoring 1,964 patients on methotrexate, only 0.51% developed an ALT>100 U/l of whom only one patient discontinued methotrexate. In this patient the ALT rise was persistent for more than 12 weeks. Therefore 12 week interval blood monitoring would have reliably detected this abnormality. In those with intermittent and isolated ALT rises >100 U/l, there were no concerning features requiring cessation of methotrexate. This suggests that although a proportion of ALT rises would not be captured on 12 week blood monitoring intervals, isolated or intermittent rises are unlikely to pose harm to patients. Reducing the frequency of blood monitoring to 12 week intervals would be an efficient use of resources whilst being safe for patients. Furthermore this study provides evidence that less frequent blood monitoring may be feasible in patients on combination DMARDs, particularly relevant in an era where combination treatment is the standard of care in inflammatory arthritis.

REFERENCE:

- [1] Ledingham J, et al. BSR and BHPH guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. *Rheumatology* 2017;56:865–868.

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SAT0216 THE ADDITION OF COLCHICINE TO METOTREXATE MIGHT HELP ACHIEVE LOW DISEASE ACTIVITY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS BY DOWNREGULATING THE ACTIVITY OF CASPASE-1.

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Background: NLRP3 inflammasome is an intracellular protein complex involved in the production of pro-inflammatory cytokines as IL-1 β and IL-18, which has been reported to have a role in the pathogenesis of RA^{1,2}. Since colchicine (CCH) is a potent inhibitor of NLRP3³, we hypothesized that it may significantly modify the expression and function of this molecular complex, reducing the inflammatory phenomenon in early rheumatoid arthritis (eRA).

Objectives: To evaluate the possible effect of CCH administration on the expression and activity of NLRP3 in patients with eRA and evaluate if it has an effect on disease activity.

Methods: Inflammasome expression by monocytes was assessed by two-color flow cytometry (CD14⁺NLRP3⁺ cells), and its function was estimated through the analysis of caspase-1 activity (colorimetric assay). Clinical activity was assessed by HAQ-DI, CDAI, SDAI and DAS28ESR at 0, 4 and 12 weeks.

Results: Twenty DMARD naive patients were recruited, 18 women, mean age 47.55 (30–72), mean time with symptoms 20 months and seropositive (RF/ACCP) in 60% of patients; all described in table 1. All patients had increased levels of caspase-1 activity and NLRP3 in week 0. At week 12, MTX+CCH patients showed decreased activity of caspase-1 and numerical difference in the expression of NLRP3. Patients with MTX+CCH at week 12 had significant clinical improvement, with low disease activity in 6/10 patients vs 2/10 patients with MTX (p<0.05). Mean change in HAQ was -0.64 in patients with MTX compared with -1.5 in patients with MTX+CCH (p<0.05).

Table 1 Demographic characteristics

	MTX	MTX +CCH
Male	1	
Female	9	
Age – years	48 ±12.85	47.1 ±7.69
Smoking	5	4
Time with symptoms – weeks	20.8±13	17.7 ±13.5
Rheumatoid factor	6	5
ACCP	5	4

Table 2 Clinical and laboratory results at week 0 and 12 in patients with eRA

	Week 0 MTX	Week 0 MTX +CCH	p	Week 12 MTX	Week 12 MTX +CCH	p
HAQ-DI	1.39 ±0.65	1.7±0.4	0.49	0.75±0.62	0.19±0.12	0.02
CDAI	39.72 ±11.94	43.08 ±9.60	0.4	21.72 ±11.7	10.6±7.3	0.04
SDAI	42.83 ±12.9	47.25 ±10.59	0.4	23.51 ±12.66	10.85±7.5	0.03
DAS28ESR	6.24 ±0.79	5.88 ±0.35	0.91	4.59±1.14	3.09±1.6	0.03
DAS28CRP	5.53 ±0.59	5.51 ±0.53	0.65	4.06±1.34	2.93±1.1	0.01
CD14+NLRP3+ Cells – %	30.63 ±11.5	27.06 ±7.85	0.47	26.12 ±14.7	17.48 + 4.34	0.1
Immunofluorescence CD14 +NLRP3+	576.8 ±267.35	514.9 ±252.44	0.62	402.6 ±236.99	319.8 ±201.7	0.3
Caspase-1 activity- nm	0.572 ±0.159	0.463 ±0.243	0.27	0.300 ±0.176	0.120 + 0.07	0.005

Conclusions: The data suggest that CCH administration is associated with decrease in the expression NLRP3 inflammasome and activity of caspase-1. This phenomenon contributes to decrease inflammation and may help to achieve low disease activity. The administration of CCH might block additional targets in patients with eRA.

REFERENCES:

- [1] Choulaki C, et al. *Arthritis Research & Therapy* 2015;17:257.
[2] Lasithiotaki I, et al. *Eur Respir J*. 2016 Mar;47(3):910–8.
[3] Martinon F, et al. *Nature* 2006 Mar 9;440(7081):237–41.
[4] Aletaha D, et al. *Arthritis Rheum* 2010 Sep;62(9):2569–81.