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.

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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.

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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		p	Week 12		p
	MTX	MTX +CCH		MTX	MTX +CCH	
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.

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