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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SAT0217 IDENTIFICATION OF DISTINCT DISEASE ACTIVITY TRAJECTORIES IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB OVER 12 MONTHS

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Background: Persistence of active disease in patients (pts) with rheumatoid arthritis (RA) is highly variable following treatment initiation. One possible explanation is the existence of distinct disease activity/response trajectories influenced by baseline variables, such as sociodemographics, disease characteristics and health status.¹

Objectives: To identify distinct disease activity trajectories over 12 months and distinguishing baseline factors using pooled data from 3 randomised, controlled Phase 3 (P3) studies of tofacitinib 5 mg twice daily (BID) in pts with active RA who were inadequate responders (IR) to conventional synthetic (cs)DMARDs, with or without prior biologic (b)DMARDs (NCT00847613, NCT00856544 and NCT00853385).

Methods: Disease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28-4[ESR]) data from 3 P3 studies were pooled. A group-based trajectory modelling strategy was applied to find unique longitudinal groups of pts with similar disease activity over time.² Trajectories were latent models, fit as polynomials. The number of groups and polynomial degree of each group were specified and fit for all combinations of up to 6 groups and up to a 4th degree polynomial; a best-fit model was chosen using Bayesian information criteria.

Results: csDMARD-IR/bDMARD-naïve pts (n=677) were separated into 5 unique disease activity trajectories (figure 1); csDMARD-IR pts who received prior bDMARDs (n=149) were separated into 4 trajectories (not shown). In the bDMARD-naïve pts, Group 5 (3.8%) had the highest predicted baseline DAS (7.3) with minimal improvement (6.4) at Month 12; Group 4 (26.7%) had baseline DAS 7.0, improving to DAS 5.0 at Month 12; Groups 2 (30.4%) and 3 (36.6%) had baseline DAS 5.9 and 6.2, respectively, leading to low DAS (2.9) and moderate DAS (3.9), respectively, at Month 12; Group 1 (2.4%) had the lowest baseline DAS of 4.3, improving to remission (DAS 2.1) at Month 12 (figure 1). The 4 trajectories in csDMARD-IR pts who received prior bDMARDs were similar to Groups 2–5 in bDMARD-naïve pts. While baseline demographics were generally similar between bDMARD-naïve groups, there were statistically significant differences in baseline disease activity measures and pt-relevant outcomes between groups.

n = sample size of trajectory; d = degree of polynomial of trajectory
 Solid lines represent predicted values, with 95% CI indicated by shading. Percentages reflect the proportion of subjects in each group
 csDMARD, conventional synthetic DMARD; BID, twice-daily; CI, confidence interval; csDMARD, conventional synthetic DMARD; DAS28-4[ESR], Disease Activity Score in 28 joints, erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug; HDA, high disease activity; IR, inadequate responder; LDA, low disease activity; RA, rheumatoid arthritis

Figure 1. Predicted group trajectories based on DAS28-4(ESR) with 95% CI identified using group-based trajectory modeling in patients with active RA who were csDMARD-IR and bDMARD-naïve and receiving tofacitinib 5 mg BID = sample size of trajectory; d = degree of polynomial of trajectory

Conclusions: It was possible to identify heterogeneous phenotypic subgroups as distinct disease activity trajectories in csDMARD-IR pts treated with tofacitinib.

The groups were characterised by differences in disease activity and pt-relevant outcomes, including baseline pain and physical function. Very high disease activity may limit pts' ability to achieve low disease activity. The identification of distinct trajectory groups could be used to develop personalised treatment optimisation algorithms incorporating clinical and molecular phenotypes.

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SAT0218 EFFICACY AND SAFETY OF BARICITINIB IN MTX-IR PATIENTS WITH RHEUMATOID ARTHRITIS: 52 WEEK RESULTS FROM A PHASE 3 STUDY (RA-BALANCE)

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Background: Baricitinib (BARI) is an oral selective inhibitor of Janus kinase 1 (JAK1) and JAK2. In the EU and some other countries, baricitinib has been approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adult patients. This abstract reports efficacy and safety results from a phase 3, double-blinded, 52-week study (RA-BALANCE) that enrolled patients (pts) in China, Argentina and Brazil (NCT02265705).

Objectives: To assess the efficacy and safety of BARI vs placebo (PBO) in the treatment of RA.

Methods: Patients with moderately to severely active RA (tender joint counts ≥ 6 & swollen joint counts ≥ 6 & hsCRP ≥ 6 mg/L) despite stable background methotrexate (MTX), were randomized 1:1 to PBO (n=145) or BARI 4-mg (n=145) once daily (QD), stratified by country and baseline joint erosion status. Background MTX was continued. Non-responders were rescued from Week 16. At Week 24, pts receiving PBO were switched to BARI 4-mg QD. ACR20 at Week 12 was the primary endpoint and there were multiple secondary endpoints e.g., assessing physical function, low disease activity and pain.

Results: The primary ACR20 response was significantly greater for BARI than PBO (58.6% vs 28.3%, $p \leq 0.001$, Table). At Weeks 12 and 24, significant improvements were seen in pts receiving BARI vs PBO for ACR20/50/70, DAS28-hsCRP, CDAL low disease activity and SDAL low disease activity, many as early as by Week 1. At Week 16, significantly less radiographic progression was seen in pts receiving BARI vs PBO and numerical improvement was observed at Week 24. At Week 12, significant improvement in HAQ-DI minimum clinically important difference ≥ 0.3 (physical function), duration of morning joint stiffness, severity of morning joint stiffness numeric rating scale (NRS), worst tiredness NRS and reduced pain (0–100 mm VAS) were seen in pts receiving BARI vs PBO.

During Weeks 0–24, treatment emergent adverse events and infections were reported in 74.5% and 42.1% of BARI pts and 62.1% and 28.3% of PBO pts, respectively. Serious adverse events were reported in 2.8% of pts in both groups. There was 1 nonserious esophageal candidiasis in the BARI group for Week 0–24. Four herpes zoster events (1 PBO, 3 BARI) were reported for Week 0–24. No major cardiovascular events, deaths, tuberculosis, venous thromboembolic