GC group than in the N group. The patients in both groups equally recognized the reduction in arthritis, morning stiffness, fatigue and the recovery of activities of daily living (ADL). Anxiety regarding adverse events was eliminated in the GC group as GC administration was restricted to a low dose for a short term. Almost identical results were obtained from the two groups.

Figure 2. questionnaire results

Conclusions: The treatment of early RA patients with low and short GC enables earlier improvement of disease activity, particularly VAS and CRP. Patients also reported that low and short GC were an improvement effect from the early stage, particularly regarding pain and anxiety about adverse events. These data confirm that the treatment with low and short GC in RA patients leads to improved patient satisfaction.

REFERENCE:

- 1) Vibeke Strand, et al. J Rheumatol 2015.

Disclosure of Interest: None declared

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SAT0228

STEP-DOWN METHOTREXATE THERAPY IN RHEUMATOID ARTHRITIS (STEMETRA): A PILOT STUDY TO ASSESS THE SAFETY AND THE TOLERABILITY OF HIGH-DOSE METHOTREXATE.

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Background: Methotrexate (MTX) remains the cornerstone of the treatment of rheumatoid arthritis (RA). However, MTX is frequently underutilized in terms of suboptimal dosage, insufficient duration of treatment, and route of administration.

Objectives: To evaluate the tolerability and the safety of higher-dose, subcutaneous methotrexate (MTX) in patients with rheumatoid arthritis (RA).

Methods: The STEP-down Methotrexate Therapy in Rheumatoid Arthritis (STEMETRA) was an open-label, monocentric, pilot study of 12-week duration. The protocol treatment schedule consisted of subcutaneous (SC) MTX 50 mg/week for 4 consecutive weeks, followed by 25 mg/week for 4 weeks and then 15 mg/week for 4 weeks. All patients received oral supplementation of folic acid (leucovorin) 12 mg, administered twelve hours after the injection of SC-MTX.

Results: Ten patients (7 females and 3 males), with a mean age of 58.1 (±12.1), were enrolled in this study; one of them withdrew consent before taking study drug. Therefore, nine patients were treated. MTX was well tolerated: a total of 5 adverse events (AEs) occurred in 4 patients, none of which was severe. AEs consisted in: transient elevation of alanine aminotransferase (<2 ULN), which resolved spontaneously, and vertigo, in the same patient; moderate fatigue in one patient; one case of urinary tract infection; low back pain in one patient. At week 12, four patients (44.4%) achieved DAS28(ESR) remission, two (22.2%) reached

low disease activity, one (11.1%) patient showed moderate disease activity, and two (22.2%) had still had high disease activity. Overall, 8 out of 9 patients (88.8%) showed a reduction in DAS28>1.2 from baseline.

Table 1 Adverse events in patients who received study drug. MTX: methotrexate; ALT: alanine aminotransferase; ULN: upper limit of normal; UTI: urinary tract infection. *: this adverse event resolved by the time of the next visit. +: at week 12, this patient decided to withdraw MTX. §: this patient was taking MTX 20 mg/week instead of 15 mg/week as an escape treatment for insufficient disease control (see main text).

	Baseline	Week 2	Week 4	Week 8	Week 12
MTX dose	-	50 mg/week	50 mg/week	25 mg/week	15 mg/week
Patient #1	none	none	none	none	none
Patient #2	none	none	none	none	none
Patient #3	none	none	none	none	none
Patient #4	none	none	none	none	none
Patient #5	none	none	none	none	none
Patient #6	none	none	Increased ALT (<2 ULN)*	Vertigo	Vertigo+
Patient #7	none	none	none	Fatigue*	none
Patient #8	none	none	none	none	UTI§
Patient #9	none	none	none	Low back pain*	none

Conclusions: In this study, short-term higher dose MTX was well tolerated. Based on the tolerability observed in this preliminary study, a randomized controlled study of higher dose induction therapy versus traditional dosing will be conducted.

Disclosure of Interest: None declared

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SAT0229

RHEUMATOID ARTHRITIS TREATMENT WITH COMBINATION OF THREE CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (CSDMARDS) AND ITS EFFECTIVENESS ON DISEASE CONTROL IN A SHORT TERM COMPARED TO BIOLOGIC DMARDS TREATMENT AFTER PROPENSITY SCORE MATCHING PROCEDURE IMPLEMENTED

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Background: Rheumatoid arthritis (RA) treatment has now many variations with use of biologic or targeted synthetic disease modifying anti-rheumatic drugs (b/tsDMARDs) and conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). In these, triple csDMARD combination therapy (tri-TX), that has comparable disease activity control effectiveness compared to anti-TNF therapy is one of alternative [1].

Objectives: Aim of this study is to evaluate the effectiveness of tri-TX compared to bDMARD with methotrexate treatment (bm-TX) for RA statistically, with the use of propensity score matching (PSM) technique.

Methods: Five hundred and fifty RA patient had been treated for more than one year in our clinic. In these, 74 patients had been treated with tri-TX and 135 had been treated with bm-TX, were recruited. Their sex distribution (Sex), anti-cyclic citrullinated peptide antibodies (ACPA), age, 28-joints disease activity score with C-reactive protein (DAS28-CRP), Health Assessment Questionnaire Disability Index (HAQ-DI), Sharp/van der Heijde Score (SvdHS), and pain score measured with visual analog scale (PS-VAS) at start of the treatment were measured for each patient, and their values were compared for each group. Thus, sample selection was performed with PSM technique in order to reduce bias on each of treatment groups. After selection, change of DAS28-CRP, HAQ-DI, PS-VAS for every three months until one year since start, and SvdHS at one year after were compared statistically with Mann-Whitney U test.

Results: After selection, twenty-three patients for each treatment group were harvested, and there demonstrated no significant difference in Sex, ACPA, DAS28-CRP, HAQ-DI, PS-VAS, and SvdHS at start of the treatment (table 1). Average DAS28-CRP demonstrated 2.76, 1.88, 1.91, 1.77, and 1.67 in bm-TX, while 2.71, 2.03, 2.41, 2.56, and 2.39 in tri-TX, at start, 3 month, 6 month, 9 month, and 1 year, respectively. There is no statistical significant difference between the two groups, but bm-TX demonstrated more significant improvement at every time after six month than tri-TX (<0.05), while no significant difference demonstrated in PS-VAS. Average HAQ-DI demonstrated 0.603, 0.579, 0.598, 0.609, and 0.625 in bm-TX, while 0.707, 0.654, 0.619, 0.594, and 0.567 in tri-TX, respectively. HAQ-DI showed tendency that improved more in tri-TX compared to bm-TX, whereas significant more improvement for tri-TX than for bm-TX had demonstrated at one-year (<0.05), however until then there demonstrated no statistical significance for both of absolute value and improvement. SvdHS demonstrated 62.4 to 61.6 from

start to one year in bm-TX, while 75.6 to 78.7 in tri-TX. Improvement of SvdHS demonstrated better result in bm-TX than in tri-TX significantly ($p < 0.05$).

Table 1. Average values of each parameter and their p -values

	bm-TX	tri-TX	p -value
Women	17 (73.9%)	16 (69.6%)	0.75
age	65.7	70.3	0.16
ACPA	171.1	452.6	0.14
GCs use	26.1%	21.7%	0.85
MTX use	100%	100%	1.00
DAS28-CRP	2.76	2.71	0.70
HAQ-DI	0.603	0.706	0.94
SvdHS	62.39	75.61	0.37
PS-VAS	41	39.7	0.79

bm-TX, a group of rheumatoid arthritis (RA) patient who is undertaken with biologic disease modifying anti-rheumatic drug (bDMARD) and methotrexate (MTX) therapy; tri-TX, a group of RA patient who is undertaken with combination of three conventional synthetic DMARDs therapy; p -value, statistical level of significance used with Mann-Whitney U test. Women express number and percentage in parenthesis. ACPA, anti-cyclic citrullinated peptide antibodies; GCs, glucocorticoid steroid; DAS28-CRP, 28-joints disease activity score with C-reactive protein; HAQ-DI, Health Assessment Questionnaire Disability Index; SvdHS, Sharp/van der Heijde Score; PS-VAS, pain score measured with visual analog scale.

Conclusions: PSM is useful technique to diminish artificial bias. tri-TX is one choice for RA patient, but not superior for clinical results compared to bm-TX.

REFERENCE:

- [1] Matsuno H, et al. The usefulness of a new triple combination treatment utilizing methotrexate, salazosulapyridine, and bucillamine in rheumatoid arthritis. *Modern rheumatology* 2016 Jan 2;26(1):51–6.

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SAT0230

COMPARISON OF EFFICACY OF TOFACITINIB VS. ETANERCEPT TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS WITH HIGH ACTIVITY DISEASE BY ULTRASOUND EVALUATION WITH POWER DOPPLER (1 YEAR TREATMENT PERIOD).

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Background: Modern clinical recommendations rule us to timely and rational treatment of rheumatoid arthritis (RA) patients with biologics or tofacitinib when traditional DMARDs failed in achievement of remission or low disease activity (LDA). Ultrasound power Doppler (PD) was recently recommended by some investigators for accuracy of evaluation of local inflammation in small joints to predict the possible flares of RA.

Objectives: To compare the efficacy of tofacitinib vs. etanercept in real clinical practice by complex evaluation including PD during 1-year treatment of RA patients with high disease activity.

Methods: In this randomized open study, we assign 30 patients to receive either etanercept 50 mg subcutaneous weekly (10 pts) or tofacitinib 5 mg BID orally (20 pts). There are 21 females and 9 males with severe RA (average DAS 28 >5.8) with inadequate response to methotrexate in effective dose enrolled into the study. Average age was 48.2±5.6 (42,1 for etanercept group and 51,9 for tofacitinib group), average disease history was 5,3 (1,5–25) years. Patients evaluated at baseline, after 3, 6 and 12 months of treatment: number of painful and swollen joints, ESR, C-protein, RF, anti-MCV, DAS 28, SDAI, ultrasound examination of hands and feet (German US7 score) by grey scale (GS) and power Doppler (PD).

Results: Patients in both groups had statistically significant decrease of disease activity. In etanercept group median DAS 28 decreased from 6.05 to 2.5

($p < 0.001$), 5 pts achieved remission, 3 – LDA. In tofacitinib group median DAS 28 decreased from 5.86 to 3.23 ($p < 0.001$), 5 pts achieved remission, 3 – LDA. Number of painful and swollen joints decreased to 3–8 times, ESR and C-protein normalized in 8 patients in etanercept group and 12 pts in tofacitinib group. SDAI evaluation showed lowering down the score of activity from range 37,10 to range 6,50 in etanercept group and from 40,78 to 14,25 in tofacitinib group. US dynamics: median GS score decreased from 6.5 to 2,5 ($p < 0.01$) in etanercept group and from 8 to 3 ($p < 0.01$) in tofacitinib group. Number of bone erosions still unchanged. In PD mode number of joints with hypervascularized synovium decreased from 3 to 0 ($p < 0.001$) in both groups.

Also it was noticed that by 3rd month of the treatment LDA was achieved for 2 patients (out of 10) in etanercept group and 5 (out of 15) in tofacitinib one, and relatively by 12 month – 8 in etanercept group and 8 in tofacitinib. The most significant decrease of SDAI (more than 2 times) was achieved by 3rd month and go further with the same dynamics in etanercept group and slightly less in tofacitinib group.

Conclusions: Integrated evaluation of efficacy of treatment of patients with severe RA showed that both etanercept and tofacitinib have good effect in achieving of remission or LDA (DAS28 and SDAI). Tofacitinib acts similar to etanercept in 3 months of therapy, but then its effect progressed more slowly. PD is additional method of monitoring of sinovial inflammation and shows us the significant regression of tissue hypervascularisation (activity of inflammation) by 6 months of treatment both etanercept and tofacitinib. Follow up of patients within the year and later on helps to adjust therapy.

Disclosure of Interest: None declared

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SAT0231

EFFECTS OF THE JAK1-SELECTIVE INHIBITOR FILGOTINIB ON GENE EXPRESSION PROFILE IN BLOOD OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, has shown good safety and efficacy in two phase 2b studies (background methotrexate (MTX, DARWIN 1) and as monotherapy (DARWIN 2)) in active rheumatoid arthritis (RA) patients with inadequate response to MTX^{1,2}. We conducted a large-scale RNA sequencing study of genes expressed in blood samples from these studies.

Objectives: Identify RA-associated gene transcripts that are altered in response to FIL treatment.

Methods: PAXgene blood samples from 242 RA patients receiving either a stable dose of MTX and placebo (PBO) or FIL 200 mg once daily (QD, DARWIN 1); or PBO, FIL 100 mg, or 200 mg monotherapy QD (DARWIN 2), were collected and analyzed at baseline, week 1 and/or week 12. RNA in whole blood was sequenced (Illumina HiSeq 2500) after globin depletion. Differential gene expression analysis was performed on all time-paired data after subtracting gene expression changes in the PBO group. Spearman's rank correlation of gene expression to time, dose, and disease activity score (DAS28) were calculated on samples without missing values. A false-discovery rate (FDR) of 10% was applied for all analyses

Results: Top-ranked gene sets positively associated with DAS28 disease activity at baseline over both studies included interferon alpha (IFN- α) and IFN gamma (IFN- γ) response, IL6/JAK/STAT3 signaling, and toll-like receptor signaling pathways (FDR<10%). Of 197 genes that positively correlated with disease score (increased gene expression with increased DAS28, FDR<10%), 117 (59%) trended toward reduced expression at 12 weeks with FIL in both studies. These genes were enriched in pathways which included granulocyte and macrophage activation. Conversely, of 256 genes negatively correlated with disease score (FDR<10%), 169 (66%) trended toward increased expression post-FIL (figure 1). Of 14724 genes expressed at >1CPM in at least 5% of the samples, 607 were differentially expressed following FIL treatment in either DARWIN1 or DARWIN2 with 48 genes significant in both studies (FDR<10%). Genes reaching significance in at least one study showed consistent magnitude and direction of change in both studies and were enriched in JAK/STAT, innate and adaptive immunity, and autoimmune associated pathways. CISH, SOCS2, SOCS3, VWA5a,