Conclusions: This indirect comparison of different studies in cs/bDMARD-naïve RA patients, after adjusting for differences in baseline characteristics, suggest a greater pain reduction and improved physical function for BARI monotherapy vs. TCZ and ADA monotherapy. There is suggestion of greater pain reduction for BARI monotherapy vs. TOFA monotherapy, but no differences in improved physical function between the JAK inhibitors. A H2H clinical trial would be needed to confirm these results.

REFERENCES:

- 1 Fleischmann, et al. Arthritis Rheumatol 2017.
- 2 Breedveld, et al. Arthritis Rheumatol 2006.
- 3 Lee, et al. N Engl J Med 2014.
- 4 Jones, et al. Ann Rheum Dis 2010.
- 5 Burmester, et al. Ann Rheum Dis 2016.
- 6 Signorovitch, et al. Pharmacoeconomics 2010.
- 7 Bucher, et al. J Clin Epi 1997.

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SAT0226

A PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE- AND MULTIPLE-RISING DOSE STUDY OF THE BTK INHIBITOR TAK-020 IN HEALTHY VOLUNTEERS

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Background: TAK-020 is a highly selective covalent inhibitor of the Btk enzyme. Btk is involved both in B cell receptor and FcR signaling. TAK-020 showed anti-inflammatory and disease-modifying efficacy in a rat collagen-induced arthritis model and is in clinical development, with potential for immune disorders including RA and SLE.

Objectives: To assess the safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) properties of TAK-020.

Methods: The study population comprised healthy volunteers aged 18 to 55 years. The SRD had 9 cohorts and the MRD 6, each randomized 6 active- to 2 placebo-treated subjects. 72 subjects were enrolled in the SRD, with 6 each receiving 0.1 mg, 0.5 mg, 2.5 mg, 4.4 mg, 8.8 mg, 17.5 mg, 35 mg, 70 mg, or 105 mg of TAK-020; and 18 subjects received placebo. 48 subjects were in the MRD, six

each receiving 7 once-daily (OD) doses of 3.75 mg, 5.75 mg, 13 mg, 25 mg, 45 mg, or 60 mg. A total of 30 subjects received placebo.

The PD effects of TAK-020 were assessed by measuring Btk occupancy and the inhibition of FcεR1-mediated activation of basophils, a Btk-dependent process resulting in increased CD63 expression.

Results: In the SRD the same percentage of subjects (11.1%) in the pooled placebo group and the overall TAK-020 group experienced treatment-emergent adverse events (TEAE). All TEAEs were of mild intensity. Abdominal distension, upper abdominal pain, nausea, and headache were reported as drug-related TEAEs in 3 subjects in the TAK-020 group. In the MRD a lower percentage of subjects receiving TAK-020 had TEAEs than with placebo (30.6 vs 41.7%). In 4 subjects (11.1%) these were considered drug-related and included nausea, diarrhea, dizziness and headache.

There were no serious AEs or AEs leading to study drug discontinuation. No subject had clinically significant changes in laboratory tests, vital signs, or ECGs.

TAK-020 was rapidly absorbed (median Tmax 45- 60 min), and had a mean elimination half-life of approximately 3- 9 hr after single and multiple dosing. Plasma exposure was in general proportional to dose up to 70 mg administered as a single dose and up to 60 mg after 7d of OD dosing.

Single doses of TAK-020 were associated with rapid binding of Btk, with occupancy >80% and maintained for 72 hours. Sustained binding of Btk was associated with >80% reduction from baseline in the proportion of CD63-positive basophils. This PD effect was sustained throughout the entire 24 hr dosing interval after administration of the 2 highest repeat doses of TAK-020 (45 and 60 mg) but fully reversed 1 week after the last dose.

Conclusions: TAK-020 was well tolerated in healthy volunteers after single and multiple doses, and demonstrated target engagement and biological activity. The PD effects outlasted PK exposures, as expected for a covalent inhibitor.

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SAT0227

RHEUMATOID ARTHRITIS PATIENTS TREATED WITH A LOW-DOSE AND SHORT-TERM GLUCOCORTICOID WERE SATISFIED WITH EARLIER IMPROVEMENT AND REPORTED DECREASED ANXIETY REGARDING ADVERSE EVENTS.

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Background: At EULAR 2017, we reported that the treatment of early rheumatoid arthritis (RA) patients by a low-dose and short-term glucocorticoid therapy (low and short GC) enabled earlier improvement and didn't worsen the rate of new complications. Currently, in RA treatment, subjective assessment of patients as well as objective assessment of doctors is gaining more importance⁽¹⁾. What do patients think about the risks of low and short GC? Does low and short GC improve patients' satisfaction?

Objectives: In this study, we investigated the change in each factor of the disease activity index (DAI) and patients' expectation of and anxiety regarding low and short GC through a questionnaire.

Methods: We include 96 Japanese patients with RA and <2-years disease duration. Patients were treated with a T2T strategy; if the disease activity was not improved within 3 months, their DMARDs were replaced with alternatives or additional DMARDs were added. We classified patients into two groups: those treated with DMARDs alone (N group; 35 females, 10 males) and those treated with ≤5 mg/day GC for a maximum of 1 year along with DMARDs (GC group; 40 females, 11 males). The mean ages of the N and GC groups were 56.3 and 60.9 years, respectively. In the GC group, the mean GC dose was 2.46 mg/day. No significant differences were observed between the groups regarding MTX or Biologics agent use rates. We evaluated changes in the number of swollen joints and tender joints, DAS28-CRP score, CRP and VAS of pain for 3 years and compared each factor of DAI between both groups. We then asked them by a questionnaire what was beneficial from the therapies and how much paid attention to the adverse events.

Results: There were no significant differences in all factors of DAI at baseline between the groups. At 1 month after treatment, there were significant differences in the improvement rate of VAS, CRP and DAS28-CRP score in the GC group compared with the N group. However, no significant difference was observed between the groups at ≥3 months after treatment (figure 1). In the questionnaire (figure 2), pain improvement was the most expected effect from the treatment (89%), and early therapeutic effect was the second (80%) in the GC group. The pain improvement and the early therapeutic effect were significantly higher in the

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.

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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