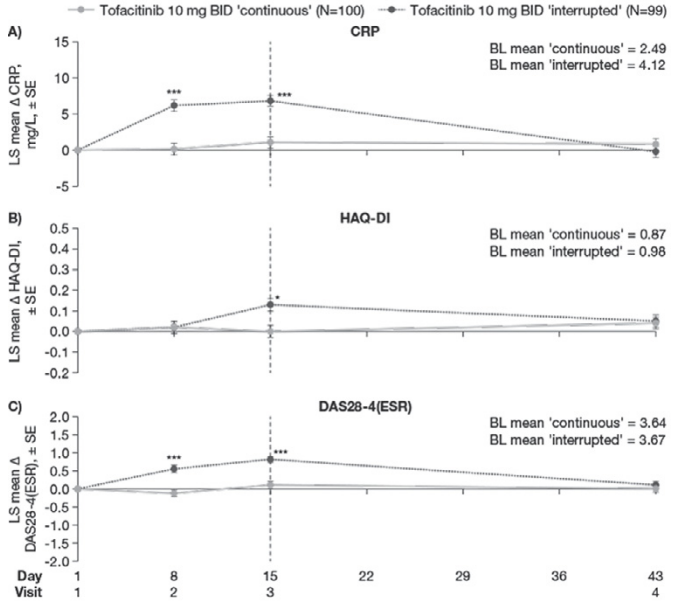
weeks post-randomisation [Day 1–Day 15; Visits 1–3], then tofacitinib 10 mg BID reinitiated as monotherapy or with MTX at Visit 3); randomisation was stratified by MTX use. Pneumococcal and influenza vaccines were administered to all pts on Day 8 (Visit 2; vaccine titers reported previously[1]). Blood samples were taken on Days 8, 15 (Visit 3) and 43 (Visit 4). Efficacy endpoints included change from baseline in C-reactive protein (CRP), Health Assessment Questionnaire Disability Index (HAQ-DI) and Disease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28-4[ESR]) at each visit. A mixed-effects model with repeated measures was used to evaluate treatment effect at each visit. Analyses for efficacy were exploratory, with no multiplicity adjustment for comparisons.

Results: Of the 199 pts in this analysis (continuous, n=100; interrupted, n=99), 117 received concomitant MTX. At LTE study baseline (BL) in the continuous and interrupted grps, respectively: 81.8/83.8% of pts were white, 84.8/86.9% were female and mean age was 55.0/53.9 years. BL (Day 1) values for CRP, HAQ-DI and DAS28-4(ESR) were generally similar between groups. At Day 8, mean CRP and DAS28-4(ESR) significantly increased from BL for interrupted vs continuous tx; HAQ-DI values were similar between grps (Figure). As expected at Day 15, mean CRP, HAQ-DI and DAS28-4(ESR) significantly increased from BL for interrupted vs continuous tx. After tofacitinib reinitiation for 28 days (Day 43), changes in CRP, HAQ-DI and DAS28-4(ESR) were similar between grps and approached BL levels. Adverse events (AEs) were experienced by 35.4% and 49.5% of pts receiving interrupted and continuous tx, respectively. The most frequent treatment-emergent AEs were bronchitis and upper respiratory tract infection (each AE: 6 pts) and vaccination-related immunisation reaction, myalgia and rash (each AE: 5 pts). Serious AEs occurred in 3 pts (3%) in each grp. In total, 1 pt (1%), in the interrupted tx grp, discontinued due to a study-drug related AE; no pts discontinued due to disease flare.

Figure. LS mean change from BL in RA efficacy endpoints over time from a vaccine sub-study with temporary tofacitinib dose interruption



*p<0.05, ***p<0.0001 for 'interrupted' vs 'continuous' tx
Dashed line indicates the end of the dose interruption period which began at BL
Δ, change from BL; BID twice daily; BL, baseline; CRP, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire Disability Index; LS, least squares; RA, rheumatoid arthritis; SE, standard error; tx, treatment

Conclusions: Efficacy of tofacitinib 10 mg BID can be reestablished following loss of efficacy during temporary (2 weeks) tx discontinuation in pts with RA. Pts receiving continuous tx maintained efficacy throughout the study. Further investigations are required.

References:

[1] Winthrop KL et al. Ann Rheum Dis 2016; 75: 687–695.

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THU0194 THE ROLE OF ENHANCED LIVER FIBROSIS (ELF) SCORE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH METHOTREXATE

J. Swierkot[1], M. Frankowski[2], M. Skoczynska[2], A. Starba[2], M.S. Gomulkiewicz[3], P. Wojtala[2], M. Bujak[3]. *[1]Department of Rheumatology and Internal Medicine, Medical University Wroclaw; [2]Department of Rheumatology and Internal Medicine; [3]Department of Radiology, Wroclaw University Hospital, Wroclaw, Poland*

Background: MTX is still a basic medicament used in treatment of patients with RA. One of its adverse reaction is its hepatoxicity. Previous studies have established high diagnostic accuracy of the ELF score to assess hepatic fibrosis in chronic viral hepatitis and fatty liver disease.

Objectives: The aim of the research was the evaluation of the usefulness of ELF markings, by patients treated with MTX, as an indicator which shows potential liver damage.

Methods: In the research were analyzed results of 96 patients with RA treated with MTX. Average age of patients was 60 (19–85 years old), median of body mass was 70 kg (46–140), median of BMI was 26 (16–46). Average time of taking MTX were 4 years and median of the accumulated dose was 3140 mg (12,5–27400mg). Disease activity in the moment of evaluation, evaluated by DAS 28, was 4,3 (0,98–8,42).

Achieved results ELF, PIIINP were correlated with body mass, BMI, dose of MTX, other illnesses (e.g. diabetes), taken nonsteroidal anti-inflammatory drugs and statins. In statistical analysis were used Pearson correlation and U Mann-Whitney test.

Results: The ELF values correlated with age, accumulated dose and DAS 28. Along with the increase of accumulated dose of MTX, disease activity and by older patients, were observed higher ELF values (the differences were statistically significant). The PIIINP values correlated with patients' body mass, accumulated dose of MTX and disease activity, evaluated by DAS 28. The differences were statistically significant. Along with the increase of body mass, accumulated dose and DAS 28, were observed higher values of PIIINP. Patients with diabetes had statistically higher values of PIINP (average: 11.13, median: 11,38), than patients without diabetes (average: 8.06, median: 7.15). There was observed no relationship between ELF and PIIINP results with taken nonsteroidal anti-inflammatory drugs and statins.

Conclusions: The ELF test, and one of its elements, PIIINP, may be useful in the evaluation of patients with higher probability of hepatotoxic effect of MTX. Special attention should be paid to older, obese patients, with diabetes, patients who take higher accumulated dose of MTX and with higher disease activity.

Disclosure of Interest: None declared

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THU0195 CONSISTENT EFFICACY AND SAFETY OF TOFACITINIB IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE OR INTOLERANCE TO NON-MTX CSDMARDS

J. Tesser[1], A. Gül[2], E. Olech[3], K. Oelke[4], T. Lukic[5], C.W. Murray[6], C. Zhang[6], L. Takiya[6]. *[1]Arizona Arthritis & Rheumatology Associates, Glendale, AZ, United States; [2]Istanbul University, Istanbul, Turkey; [3]UNLV School of Medicine, Las Legas, NV; [4]Rheumatic Disease Center, Glendale, WI; [5]Pfizer Inc, New York, NY; [6]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. In clinical practice, a proportion of patients (pts) with RA may not be candidates for treatment with the conventional synthetic DMARD (csDMARD) methotrexate (MTX).[1]

Objectives: To evaluate tofacitinib 5 or 10 mg BID efficacy and safety using pooled data from 8 Phase (P) 2 and 6 P3 trials in RA pts who were (1) inadequate responders (IR)/intolerant to csDMARDs, but did not have an IR or intolerance to MTX or biologic DMARDs (ie, non-MTX csDMARD-IR population) or (2) pts with an IR/intolerance to any csDMARD including MTX but not bDMARD-IR (ie, 2nd-line population).

Methods: Month 3 efficacy outcomes included proportions of pts achieving ACR20/50/70 responses, and Disease Activity Score 28-4(ESR) (DAS28-4[ESR])<2.6 (remission), as well as change from baseline in DAS28-4(ESR) and Health Assessment Questionnaire-Disability Index (HAQ-DI) scores. No multiplicity adjustments were made. Crude incidence rates (CIR; unique pts with events/100 pt-years) based on adverse event (AE) reporting through Month 24 were calculated for treatment-emergent AEs (TEAEs), serious AEs (SAEs), discontinuations (DCs) due to AEs and AEs of special interest.

Results: In the P2/3 tofacitinib RA trials, prior csDMARDs received by the non-MTX csDMARD-IR and 2nd-line populations, respectively were: chloroquine (17.7% and 37.2%), hydroxychloroquine (13.7% and 22.7%), leflunomide (19.4% and 20.9%), MTX (7.3% and 93.3%), sulfasalazine (31.1% and 27.1%) and others (8.0% and 11.1%); pts may have received >1 prior csDMARD. The non-MTX csDMARD-IR population included 208, 247 and 82 pts receiving tofacitinib 5 and 10 mg BID or placebo (PBO), respectively; the 2nd-line population comprised 1206, 1266 and 856 pts, respectively. Baseline characteristics were generally similar between populations except for mean RA duration (5.2–7.2 years, non-MTX csDMARD-IR pts; 8.2–8.5 years, 2nd-line pts). Most pts were female (80.3–85.4%), mean age range was 49.7–52.5 years and mean DAS28-4(ESR)