Abstract FRI0095 – Table 1

	anti-TNF α n=17	RTX n= 7	P
General features			
Sex (♂/♀)	4/2	13/5	0.79
Mean age (years)	59.1±18.3	54.28±10.7	0.49
Ocular bilateral involvement #	23.53	57.14	0.13
Duration of underlying diseases (days)	183.06±18.3	138.85±77.68	0.59
Basal			
BCVA*	0.58±0.38	0.56±0.34	0.68
Peripheral thinning #	18	9	0.77
Central keratolysis #*	4	1	0.59
Ocular perforation #	2	1	0.89
Scleritis #	3	8	0.001
Episcleritis #	3	4	0.15
Uveitis #	3	2	0.77
1st month			
BCVA *	0.67±0.31	0.56±0.27	0.67
Peripheral thinning #	5	6	0.032
Central keratolysis #*	-	-	-
Ocular perforation #	-	-	-
Scleritis #	1	1	0.54
Episcleritis #	1	0	0.45
Uveitis #	1	2	0.23
6th month			
BCVA *	0.7±0.25	0.73±0.29	0.67
Peripheral thinning #	9	3	0.14
Central keratolysis #*	0	3	0.028
Ocular perforation #	-	-	-
Scleritis #	-	-	-
Episcleritis #	-	-	-
Uveitis #	1	0	0.38
1st year			
BCVA *	0.75±0.22	0.70±0.24	0.77
Peripheral thinning #	7	3	0.25
Central keratolysis #*	1	1	0.89
Ocular perforation #	0	1	0.30
Scleritis #	-	-	-
Episcleritis #	-	-	-
Uveitis #	1	0	0.35

Comparisons were made between baseline and 1st month, 6th month and 1st year (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA). Quantitative variables were expressed as mean ±SD or median [IQR], accordingly to its distribution. They were compared with the Student t or the Mann-Whitney U test respectively. Dichotomous variables were expressed as percentages and compared by the chi-square test.

Results: We studied 24 patients/32 affected eyes. The underlying diseases in the anti-TNF α group were Rheumatoid Arthritis (RA) (n=14), Psoriatic Arthritis (n=2) and Behçet Disease (n=1); and in the RTX group: RA (n=5), granulomatous polyangiitis (n=1) and microscopic polyangiitis (n=1).

At baseline there were no significant differences between both groups in general features or in ocular involvement (table 1). Before biologic therapy they had received the following systemic drugs (anti-TNF α vs RTX) i.v. methylprednisolone (2 vs 4), doxycycline (7 vs 1), ascorbic acid (2 vs 0), MTX (11 vs 4), AZA (1 vs 2) and others (7 vs 3). In addition, 10 patients, in both groups, had required surgery: amniotic membrane (n=5), penetrating keratoplasty (n=2), conjunctival resection (n=2), tissue adhesives (n=2), conjunctival flap (n=1) and lamellar keratoplasty (n=1).

Once the treatment was initiated the ocular outcome was similar (table 1).

After a mean follow-up of 22.53±22.60 (anti-TNF α) and 22.28±8.28 months with RTX the following severe side effects were observed: supraventricular tachycardia (n=1) with RTX and pulmonary tuberculosis (n=1) with IFX.

Conclusions: In this study, anti-TNF α therapy and RTX were equally effective for the treatment of peripheral ulcerative keratitis associated to rheumatic diseases refractory to conventional treatment.

Disclosure of Interest: None declared

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FRI0096

IS SIDE EFFECTS AND TREATMENT RESPONSE TO METHOTREXATE ASSOCIATED TO COMORBIDITY IN EARLY RHEUMATOID ARTHRITIS

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Background: In Denmark approximately 0.7% (35.000) of the population is diagnosed with rheumatoid arthritis (RA). RA is a risk factor in development of comorbidity, and comorbidities are not well managed in RA patients. In addition of being first line treatment of early RA, methotrexate (MTX) gives a 70% reduction in cardiovascular disease caused mortalities, and if treatment exceeds a year, the general mortality risks are lowered by 60%. Discontinuation of MTX is therefore a bad outcome for RA. It remains unclear whether side effects and treatment response to MTX is associated to comorbidity in early RA.

Objectives: To evaluate the association between comorbidity and persistence to MTX treatment and side effects for RA patients.

Methods: Patient files from three centres were evaluated retrospectively. Inclusion criteria were: diagnosis obtained according to ACR/EULAR 2010 criteria for RA in the period 01/01/2010 to present, and MTX as first line of treatment. Medical records were reviewed for side effects, dose changes of MTX, formulation changes and persistence. Comorbidities and comedication was evaluated by usage of the Danish National Patient Registry (DNPR), and the Odense Pharmacoepidemiological Database (OPED). Comorbidities were scored according to the Charlson Comorbidity Index (CCI), and analysed by the cox proportional hazards model for discontinuation of MTX treatment and dose reduction.

Results: 501 patients were screened, 177 were eligible and analysed at baseline for disease characteristics, medication besides MTX and comorbidities in a 5 year window before RA diagnosis baseline. The highest risk of MTX discontinuation was a CCI of 3–4, they had crude 4.18 (95% CI 1.67–10.45) increased risk compared to the reference group (RA with no comorbidities). Risk of dosage reduction was highest at CCI 1–2: 1.38 (95% CI 0.72–2.62). A CCI of 5 or higher gave a –4.83 mg (95% CI –10.24– –0.59) adjusted difference in maximum weekly tolerable MTX dosage. Side effects occurred for 23.7%. Most likely dosage causing side effect was 20 mg (IQR 15–20 mg). Nausea occurred in 29% and hepatic events 21%.

Conclusions: Patients with CCI in the range of 3–4 had an increased risk for discontinuing MTX treatment.

Disclosure of Interest: None declared

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FRI0097

EXPRESSION OF UNCOUPLING PROTEIN-1 IN SUBCUTANEOUS FAT REDUCES THE TOTAL CHOLESTEROL LEVEL AND CARDIOVASCULAR RISK IN FEMALE RA PATIENTS

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Objectives: To improve understanding of fat-related molecular mechanisms behind the increased cardiovascular (CV) morbidity in patients with rheumatoid arthritis (RA).

Methods: Transcription of uncoupling protein 1 (UCP1) was measured in the subcutaneous fat tissue and serum levels of lipoproteins, adipokines, and inflammation markers in 185 middle-aged female patients (mean age 51 years) with RA and compared between the groups stratified by the total cholesterol (TC) levels and the body mass index (BMI). The risk of dying of CV disease within 5 years was calculated electronically using the strategy proposed by Pocock et al.¹

Results: CVR was highest (risk score 27.76, 5 year CVR 0.67%) in the patients combining high TC (>5.1 mmol/L) and high BMI (>25 kg/m²), while those with low levels of TC and BMI had lowest CVR (risk score 10.82, CVR 0.11%). CVR was significantly decreased if either TC (TC^{lo}BMI^{hi}) or BMI (TC^{hi}BMI^{lo}) was low (p=0.017 and p=0.014, respectively). With the exception of TC^{lo}BMI^{lo} group, these groups had no difference with respect to age, disease duration, inflammation defined by serum IL6 and IL1, and disease activity measured by DAS28. TC^{lo}BMI^{hi} patients had an overall increase in fat expression of UCP1 (p=0.047) that has the cholesterol lowering capacity and may explain low TC levels in this

group. In contrast, TC^{hi}BMI^{lo} patients had high prevalence of cases with unmeasurable UCP1 expression and higher levels of serum adiponectin ($p=0.053$) and HDL ($p<10^{-5}$).

Measurable expression of UCP1 was found in 79%. In total cohort, the patients with measurable UCP1 had higher inflammation and RA activity presented by IL-6 ($p=0.0001$), IL1b ($p=0.037$) and DAS28 ($p=0.0086$), compared to those with no UCP1 expression. TC^{lo}BMI^{hi} patients had an overall increase in fat expression of UCP1 ($p=0.047$) and lowest prevalence of cases with no UCP1 expression (6.2%).

Conclusions: The study shows that UCP-1 expression in subcutaneous fat may be a CV protective mechanism in RA patients. The inflammation seems to be the driving force of UCP1 expression in RA.

REFERENCE:

- [1] Pocock SJ, McCormack V, Gueyffier F, Boutitie F, Fagard RH, Boissel JP. A score for predicting risk of death from cardiovascular disease in adults with raised blood pressure, based on individual patient data from randomised controlled trials. *BMJ* 2001;323:75–81.

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FRI0098

HEPATIC SAFETY IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO RECEIVED ISONIAZID FOR LATENT TUBERCULOSIS: POST-HOC ANALYSIS FROM PHASE 3 BARICITINIB STUDIES

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Background: Baricitinib (BARI) is an oral selective Janus kinase (JAK 1/2)¹ inhibitor approved in the EU, Japan, and other countries for treatment (tx) of moderately to severely active rheumatoid arthritis (RA) in adults. RA therapies may increase risk of tuberculosis (TB).² The use of isoniazid (INH) plays a vital role to control TB. However, INH may result in hepatic adverse events (AEs).³ Limited data exist on hepatic safety in TB patients (pts) with RA treated with JAK inhibitors and INH.

Objectives: To evaluate the hepatic safety in pts with RA, who were receiving INH for latent TB (LTBI) in BARI phase 3 trials.

Methods: This is a descriptive post-hoc analysis of three phase 3 studies: RA-BEAM, RA-BUILD, and RA-BEACON. All pts were screened for LTBI prior to randomisation. Pts with untreated LTBI and without documentation of prior completed tx, received INH at least for 4 weeks (wk) prior to randomisation and during the clinical trial period. Changes in ALT levels ($\geq 1X$, $\geq 3X$, $\geq 5X$, and $\geq 10X$ of ULN) from baseline up to 24 wk were analysed by tx groups (BARI 4 mg, BARI 2 mg, adalimumab [ADA], and placebo [PBO]).

Results: In total, 2516 pts were included in this analysis. Of these, 891 pts were treated with BARI 4 mg, 403 with BARI 2 mg, 330 with ADA, and 892 with PBO. Background csDMARDs, mainly methotrexate (MTX) were continued. Overall, 246 pts reported LTBI at screening across all tx groups. Of these, 169 with confirmed lab data received INH as LTBI tx. At wk 24, ALT $\geq 1X$ was reported in 24 (41.4%) pts receiving BARI 4-mg+INH. None of the pts in BARI 4-mg+INH reported ALT level of $\geq 3X$, $\geq 5X$, and $\geq 10X$ ULN. For BARI 2-mg+INH, ALT $\geq 1X$ reported in 9 (33.3%) pts, ALT $\geq 3X$ in 2 (7.4%), ALT $\geq 5X$ in 1 (3.7%), and ALT $\geq 10X$ in 1 (3.7%) of the pts. Among pts treated with ADA+INH, ALT $\geq 1X$ was reported in 12 (44.4%), ALT $\geq 3X$ in 2 (7.4%), ALT $\geq 5X$ in 1 (3.7%), and ALT $\geq 10X$ in none of pts. Among pts treated with PBO+INH, ALT $\geq 1X$ was reported in 21 (36.8%), ALT $\geq 3X$ and ALT $\geq 5X$ levels were reported in 2 (3.5%, for both) of the pts. None of the pts reported ALT $\geq 10X$. One pt receiving INH in RA-BEAM PBO arm had temporary interruption of tx due to abnormal hepatic lab results. No study tx interruption or discontinuation was reported in INH users in BARI or ADA groups due to abnormal hepatic lab results.

Abstract FRI0098 – Table 1. Changes in ALT level from baseline to week 24 in patients receiving BARI, ADA, and PBO

	BARI 4-mg (RA-BEAM, RA-BUILD, RA-BEACON) N=891		BARI 2-mg (RA-BUILD, RA- BEACON) N=403		ADA (RA-BEAM) N=330		PBO (RA-BEAM, RA-BUILD, RA-BEACON) N=892	
	INH (n=58)	No INH (n=833)	INH (n=27)	No INH (n=376)	INH (n=27)	No INH (n=303)	INH (n=57)	No INH (n=835)
ALT $\geq 1X$ ULN	24 (41.4%)	260 (31.2%)	9 (33.3%)	82 (21.8%)	12 (44.4%)	91 (30.0%)	21 (36.8%)	183 (21.9%)
ALT $\geq 3X$ ULN	0	13 (1.6%)	2 (7.4%)	6 (1.6%)	2 (7.4%)	9 (3.0%)	2 (3.5%)	13 (1.6%)
ALT $\geq 5X$ ULN	0	5 (0.6%)	1 (3.7%)	1 (0.3%)	1 (3.7%)	3 (1.0%)	2 (3.5%)	3 (0.4%)
ALT $\geq 10X$ ULN	0	2 (0.2%)	1 (3.7%)	0	0	1 (0.3%)	0	0

ALT=alanine transaminase; ULN=upper limit of normal; INH=isoniazid.

All pts were on concomitant use of csDMARDs, mainly MTX.

Conclusions: The percentage of pts with $\geq 1X$ ULN ALT was numerically higher in INH group vs no INH and was consistent across PBO, BARI and ADA tx groups. The data do not suggest an increased hepatic safety risk in pts treated with BARI who were receiving concomitant INH.

REFERENCES:

- [1] Dougados M, et al. *Ann Rheum Dis.* Jan 2017;76(1):88–95.
- [2] Lim CH, et al. *PLoS One.* 2017;12(6):e0178035.
- [3] Vanhoof J, et al. *Ann Rheum Dis.* Dec 2003;62(12):1241–1242.

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FRI0099

LIVER ENZYME ABNORMALITIES AFTER TOFACITINIB TREATMENT IN PATIENTS WITH HEPATIC STEATOSIS FROM THE RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND PSORIASIS CLINICAL PROGRAMMES

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Background: Non-alcoholic fatty liver disease, characterised by hepatic steatosis (HS), is a major cause of chronic liver disease in many countries. Limited data are available on liver enzyme elevation in patients (pts) with HS who are receiving medications for inflammatory conditions, such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and psoriasis (PsO). Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA and PsA, and has also been studied in PsO.

Objectives: To describe baseline characteristics and liver enzyme abnormalities in pts from the tofacitinib RA, PsA and PsO clinical programmes with/without HS at baseline.

Methods: Pts randomised to the tofacitinib (5 or 10 mg twice daily; doses pooled) and placebo arms of 25 studies in the RA, PsA and PsO programmes were