Abstract AB0488 – Table 1. Patients' Characteristics in Full and Propensity Score-Matched Cohorts according to Initiation of Igaratimod or Sulfasalazine

Characteristic	Full Cohort			Propensity Score-Matched Cohort		
	IGU (n=113)	SSZ (n=244)	SMD	IGU (n=109)	SSZ (n=109)	SMD
Sex, male (%)	17 (15.0)	45 (18.4)	0.091	17 (15.6)	18 (16.5)	0.025
Age (mean [SD])	60.21 (12.07)	60.16 (13.13)	0.004	60.48 (11.99)	60.39 (13.31)	0.007
CRP mg/dL (mean [SD])	0.64 (0.92)	0.74 (1.26)	0.082	0.66 (0.93)	0.74 (1.03)	0.087
MTX mg/wk (mean [SD])	9.00 (3.00)	9.12 (3.14)	0.037	8.93 (2.96)	8.70 (3.35)	0.074
PSL mg/d (mean [SD])	1.91 (2.68)	1.47 (2.53)	0.170	1.78 (2.56)	2.02 (3.01)	0.085
SJC 66 (mean [SD])	3.04 (4.02)	2.15 (2.94)	0.253	2.76 (3.46)	3.04 (3.32)	0.081
TJC 68 (mean [SD])	3.42 (6.69)	2.66 (4.27)	0.136	3.23 (6.52)	3.29 (5.00)	0.011
Disease duration yr (mean [SD])	11.10 (9.18)	9.41 (9.65)	0.180	11.11 (9.26)	10.40 (10.10)	0.073
PGA-0-10 (mean [SD])	3.11 (2.31)	2.91 (2.33)	0.085	3.02 (2.23)	2.99 (2.47)	0.016
mHAQ (mean [SD])	0.38 (0.51)	0.26 (0.41)	0.266	0.37 (0.51)	0.38 (0.49)	0.032

CRP: C reactive protein; IGU: igratimod; mHAQ: The modified Health assessment questionnaire; MTX: methotrexate; PGA: patient's global assessment; PSL: prednisolone; SD: standard deviation; SJC: swollen joint count; SSZ: sulfasalazine; TJC tender joint count

Conclusions: Combination therapy with IGU or SSZ and methotrexate for rheumatoid arthritis did not show a significant difference in disease activity. Further studies are needed.

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AB0489 TOFACITINIB IMPROVES LEFT VENTRICULAR MASS AND CARDIAC OUTPUT IN RHEUMATOID ARTHRITIS PATIENTS WITH CHRONIC HEART FAILURE

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Background: Rheumatologists need to develop primary and secondary prevention strategies for cardiovascular disease (CVD) in rheumatoid arthritis (RA) patients. We reported tofacitinib (Tofa) improved left ventricular mass index (LVMI) in patients with rheumatoid arthritis¹. We have experienced RA patient with chronic heart failure (CHF). We couldn't use some TNF blockers in RA patients with CHF². There is no evidence that Tofa effects on left ventricular (LV) morphology and function in RA patients with CHF.

Objectives: To study the effect of Tofa on LV morphology and function in conventional synthetic (cs) DMARDs resistant active RA patients with CHF, in a cohort study design.

Methods: RA patients with CHF were eligible if they had active disease despite treatment with cs DMARDs. Consecutive 24 patients with moderate to severe active RA patients (DAS28 >3.2) despite cs DMARDs were received Tofa plus cs DMARDs. LV morphology and function was assessed with cardio-MRI at baseline and 24 weeks follow-up. Cardiovascular risk factors and clinical data were collected at regular visits.

Results: 21 patients completed 24 weeks. New York heart association functional classification (NYHA) class 1 is 12 cases, class 2 is 7 cases, and class 3 is 2 cases respectively. Left ventricular mass index (LVMI) was attenuated significantly by Tofa (week 0 week24, -9.02 ± 5.8 g/m²; $p=0.02$). Cardiac output (CO) was attenuated significantly by Tofa (week 0 week24, -0.42 ± 1.2 l/min). DAS28 and CRP improved significantly by Tofa (week 0 week24; DAS28: -2.16 ± 0.95 ; CRP: 15.1 ± 5.7 mg/L) ($p<0.05$). Surprisingly, the change of disease activity (DAS

28 and CRP) is no correlation with the change of LVMI or CO in this study. Observationally, 2 cases significantly improved right ventricular mass as well as left ventricular mass (10% improved right ventricular mass index from baseline).

Conclusions: Tofa improved LVMI and CO in active RA despite cs DMARDs with CHF. Tofa improves LVMI and CO independently of its effects on disease activity. Tofa might be improved right ventricular mass. JAK-STAT pathway might be an important role of LV hypertrophy. Tofa, JAK-STAT pathway blocking, may prevent cardiovascular morbidity and mortality in RA with CHF.

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AB0490 EVALUATION OF INHIBITORY FACTOR OF RADIOGRAPHIC PROGRESSION BY IGURATIMOD ADD-ON THERAPY IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSES TO DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Igaratimod (IGU) is one of csDMARDs (Conventional synthetic Disease modified anti-rheumatoid arthritis drug) for RA patients in Japan. It was reported to suppress the production of inflammatory cytokines by inhibiting NFκB pass-way. IGU add-on therapy was efficient in patients with RA who were previously designated MTX-monotherapy inadequate responders (MTX-IR). The efficacy of IGU add-on therapy in bDMARDs (Biological DMARD)-IR patients was also reported. In this study, we showed disease activity and safety, and showed also radiographic evaluation for the first time by adding IGU.

Objectives: To obtain DAS28-ESR and adverse event data about adding IGU on RA patients with poor response to csDMARDs and/or bDMARDs in single-centre, open label and retrospective study. Furthermore, to show the radiological evaluation after one year.

Methods: Clinical and radiographic efficacy was assessed by disease activity score of 28 joints (DAS28) ESR (n=68) and the modified total Sharp score (mTSS) (n=44), respectively. We evaluated which factors are important in determining a prognosis of clinical response and mTSS. For safety, adverse events (AE) were investigated on all patients (n=89).

Abstract AB0490 – Table 1

	Non Response	Response	p		Non Response	Response	p
SEX	76%	74%	ns	CRP	0.92±0.20	2.38±0.59	<0.05*
AGE	60.19±1.64	61.58±2.44	ns	ESR	24.48±2.96	35.61±3.98	<0.05*
DUR	86.67±10.11	101.03 ±15.76	ns	TJC	3.52±0.54	5.03±0.62	ns
a-CCP-Ab	180.11 ±50.79	153.25 ±40.11	ns	SJC	3.67±0.42	5.32±0.60	<0.05*
RF	133.10 ±28.67	161.39 ±47.20	Ns	VAS	32.74±3.34	47.19±4.43	<0.05*
DAS28-CRP	3.85±0.15	4.83 ±0.15	<0.05*	MMP-3	149.33 ±27.60		
	181.01 ±46.48	ns					
CDAI	13.63±0.94	20.06±1.28	<0.05*	PreTSS	5.72±1.07	5.26±0.82	ns
mHAQ	0.34±0.07	0.54±0.11	ns				

Results: 89 RA patients were recruited, and male was 28% (n=25). Mean age was 61.5 years old and mean of disease duration was 87 months. Main csDMARDs were MTX (72%). The mean dose of MTX was 7 mg/week (The average dose in Japan). Observational period was 13 months (range, 1 to 30). DAS28-ESR changed from 4.3±1.1 to 3.6±1.2 after adding IGU for 6 months ($p<0.0001$). The relation with the predictive factors before treatment and the response by using Igaratimod. CRP, ESR, swelling joint, DAS28-ESR, CDAI and

VAS at the baseline were all significantly high in Response (good response+ moderate response) group than No-response group (table 1). Yearly mTSS was 0.60 and rate of structural remission (mTSS ≤ 0.5) was 87%. Rapid radiological progression was not seen even if yearly mTSS at the baseline was 5.52. The relation between yearly mTSS and disease duration was shown in Figure ($r=0.33$, $p=0.029$). Adverse AE were observed such as transaminase elevation, stomatitis and dizziness. All AE was not serious. DAS28-ESR, CRP, ESR and swelling joint were prognostic factors of the group of good and moderate response against no response group.

Abstract AB0490 – Figure 1

Conclusions: Adding IGU to csDMARDs with poor response in RA patients is effective, but AE should be considered. Radiographic progression by Iguratimod might be inhibited in early phase of RA.

Disclosure of Interest: None declared

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AB0491 POSSIBLE LINKAGE BETWEEN INTESTINAL BACTERIA COMPOSITION CHANGES AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH NATURAL MILK ANTIBODIES AGAINST ENTERIC BACTERIA AND THEIR TOXINS

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Background: A growing body of research has indicated potential association between dysbiosis or imbalance of intestinal bacterial flora and RA. Previously, we demonstrated the natural milk antibody preparation containing high levels antibodies against pathogenic enteromicrobes and their toxins seems to be effective in a certain RA subset in an open labelled pilot study.¹

Objectives: To investigate the effects of natural milk antibodies (Ab) on intestinal bacteria composition, and consequent therapeutic effect on disease activity of RA by multicenter randomised double blind clinical trial (UMIN CTR: 000009492).

Methods: Eighty-seven patients with RA with disease activity score of 28 joints with ESR (DAS 28-ESR) values above 3.2 were divided into 3 groups (29 patients each), and treated with 600 mg of Ab, 300 mg of Ab plus 10 g of skim milk (prebiotics), and 20 g of skim milk alone, respectively, for 12 weeks. The therapeutic effects of milk antibody treatment were determined by DAS28-ESR, swollen joint count (SJC), tender joint count (TJC), and visual analogue score (VAS). The biological effects of milk antibodies were examined by serum and faecal LPS concentration, and faecal bacterial composition changes before and after the treatment. Bacteria composition changes was determined by quantitative PCR of bacterial 16S rRNA.

Results: A significant reduction in DAS28-ESR values from 4.6 to 4.1 was observed at 4th week in Ab 300 mg plus skim milk group (figure 1). Importantly, this effect was lasted through until 12th week ($p<0.01$), but DAS28-ESR values gradually returned to original levels after discontinuation of the treatment. On the other hand, neither high dose of milk antibody (600 mg) nor 20 g of skim milk had little effect on DAS28-ESR. Characteristic effect of milk antibody treatment observed in the Ab 300 mg plus skim milk group was the improvement of SJC, TJC, and Pain VAS. No severe adverse events have been observed. Enteric microbe analysis before the treatment indicated lower *Bacteroides fragilis* (less than 1/100 compared to healthy adults) and higher *Staphylococcus aureus* population (1000x higher) in patients with RA, indicating a dysbiosis in RA. The DAS28-ESR value reduction in the Ab 300 mg group was associated with an increase in the *Lactobacillus* population. In contrast, the improvement of Pain VAS was associated with an increase in the *B. fragilis* population. Possible improvement in the intestinal barrier function was assumed by the reduction of serum and faecal LPS concentration ratio in the Ab 300 mg groups.

* : $p<0.05$, * * : $p<0.01$ (Paired t-test), Data: mean $\pm$ SE

Abstract AB0491 – Figure 1. Therapeutic effect of natural milk antibodies on rheumatoid arthritis

Conclusions: Natural milk antibody treatment modulates the intestinal bacterial composition, and consequently may contribute to improving disease activity of RA.

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AB0492 JAK-INHIBITION WITH PEFICITINIB AND FILGOTINIB IN FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS

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Background: With the approval of the Janus kinase inhibitors (JAKi) Tofacitinib and Baricitinib for the treatment of rheumatoid arthritis (RA) in the European Union (EU), the opportunities for a successful therapy were extended by a new substance class. Other JAKi like Peficitinib and Filgotinib are currently examined in clinical trials. Peficitinib is a pan-JAKi, whereas the other substances differ clearly in the capability to block the four members of the Janus kinase family. It is unclear, if the new substances offer an additional benefit in RA treatment in comparison to the approved JAKi.

Objectives: This study characterised the effect of the different JAKi on inflammatory response of activated fibroblast-like synoviocytes from patients with RA (RA-FLS).

Methods: RA-FLS were isolated from synovial tissue of patients with RA undergoing joint replacement surgery. The cells were pretreated for 2 hour with different concentrations of JAKi or vehicle control and then stimulated with IL-1 β (10 or 20 ng/ml) or Oncostatin M (OSM, 100 ng/ml). After the indicated time (17–24 hour), the supernatants were collected and the concentrations of IL-6 and MMP-3 were measured by ELISA. An assay combining the measurement of cell viability, cytotoxicity and apoptosis was performed to exclude effects of JAKi caused by cell toxicity.