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 Igaratimod 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.

Results: To detect the most effective JAKi in blocking the inflammatory response induced by IL-1 β , RA-FLS were first pretreated with different JAKi for 2 hour with concentrations of 1 μ M and 10 μ M and then additionally stimulated with IL-1 β (20 ng/ml) for 18 hour. Even at the highest concentration of 10 μ M Tofacitinib and Baricitinib did not change the IL-6 levels, whereas Peficitinib and Filgotinib reduced the IL-6 release at 10 μ M. Tofacitinib and Baricitinib reduced the cytokine release if the RA-FLS were stimulated with OSM, a factor directly inducing the JAK-dependent IL-6-pathway (n=3).

To obtain a dose-response curve for the clinically relevant range of concentrations between 0.01 μ M and 5 μ M, RA-FLS were pretreated with Filgotinib and Peficitinib for 2 hour and then stimulated with IL-1 β (10 ng/ml) for 17 hour. In contrast to Filgotinib, Peficitinib at 5 μ M caused a reduction of IL-6 levels of 66% compared to control with IL-1 β (p<0.01, n=5). The MMP-3 release was decreased by both substances at 5 μ M: In comparison to the control with IL-1 β , Peficitinib caused a reduction of 92% (p<0.0001, n=5) whereas Filgotinib only reduced the levels by 43% (p<0.05, n=3). Furthermore, Peficitinib at 1 μ M decreased the MMP-3 release by 46% (p<0.01).

The treatment with Peficitinib did not affect the viability, cytotoxicity or apoptosis of RA-FLS (n=3). Therefore, the effects of Peficitinib on the inflammatory response were not caused by cell death.

Conclusions: Peficitinib reduced the release of proinflammatory cytokines and of matrix metalloproteinases after activation of RA-FLS with IL-1 β and appeared to be superior to Tofacitinib and Baricitinib in targeting the pro-inflammatory and matrix destructive properties of RA-FLS.

Disclosure of Interest: None declared

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AB0493 EFFECTIVENESS OF SUBCUTANEOUS PRESENTATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is one of the most used drugs for the treatment of rheumatoid arthritis (RA) and has become the gold standard of therapy. It can be given via oral, intramuscular or subcutaneous (SC). MTX is a highly effective therapy for patients with RA; however, oral MTX has been associated with gastrointestinal intolerance diminishing the adherence of patients to treatment and increasing the switching to biological therapy. Thus, the use of SC methotrexate can improve its efficacy compared to oral MTX.

Objectives: The aim was to determine the effectiveness and safety of SC MTX in patients with rheumatoid arthritis.

Methods: We performed a retrospective descriptive analysis; our main goal was to provide real-life data regarding effectiveness of SC MTX in patients with RA. We excluded patients who were in remission. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 $\geq$ 3.1 and $\leq$ 5.1), and every 11–13 weeks (DAS28 <3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it; regarding the effectiveness of SC MTX we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We performed a bivariate analysis using Pearson's χ^2

Abstract AB0493 – Table 1. DAS28 and CDAI in patients with RA receiving SC MTX

	BASELINE		12 MONTHS	
	n	%	n	%
Remission			44	33
LDA	36	28	29	22
MDA	84	63	50	38
SDA	12	9	9	7
CDAI	n	%	n	%
Remission			38	29
Low	87	66	62	47
Moderate	34	26	25	19
High	11	8	7	5

Results: A total of 132 patients meet our inclusion criteria, 88% were female and 12% male. Mean age was 61 years $\pm$ 9. Mean DAS28 at baseline was 3.8 $\pm$ 0.83, while at 12 months mean DAS28 was 3.28 $\pm$ 1.12. Clinical disease activity CDAI at baseline had a mean of 9.6 $\pm$ 7.2 and at 12 months 7.8 $\pm$ 7.5. We achieved

remission in 33% of patients according to DAS28 and 29% according to CDAI, also it was a significant decrease in patients with moderate disease activity see table 1. Finally, there was a statistical significance between disease activity at baseline compared to disease activity at 12 months (p<0.005). It was not observed major complaints with SC MTX, only 5% of the patients reported some mild and transient discomfort at the local application site.

Conclusions: Subcutaneous MXT is an effective and safe alternative for the treatment in patients with RA and intolerance to oral MTX, and could be a good option to prevent a premature switching to biological therapy.

Disclosure of Interest: None declared

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AB0494 USABILITY OF A PRE-FILLED PEN FOR SELF-ADMINISTRATION OF SUBCUTANEOUS METHOTREXATE

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Background: Methotrexate (MTX) is the first-line DMARD for the treatment of rheumatoid arthritis (RA).¹ It is also of high significance in the treatment of psoriasis arthritis (PsA) and psoriasis vulgaris (PsV).^{2,3}

Studies in RA patients found that there are advantages in terms of bioavailability and efficacy when MTX is administered subcutaneously (SC) as compared to orally.^{4,5}

Since the introduction of MTX pre-filled syringes, patients are principally enabled to self-administer methotrexate subcutaneously, however not all patients are able to use syringes easily. Auto-injection using a pre-filled pen can facilitate administration by the patient. Results of a comparative crossover study showed that SC self-injection with a pre-filled pen is mainly preferred to a pre-filled syringe with regard to use, acceptability, and satisfaction⁶. Usability of the pre-filled pen was proven in an actual-use study⁷, however no comprehensive data from routine clinical use is available so far.

Objectives: The aim of this practice documentation was the evaluation of the usability of a MTX pre-filled pen under everyday clinical conditions.

Methods: This multicentric non-interventional practice documentation, which took place from 2013 to 2015 in Germany, was open to naïve patients and to those who had already been treated with the pre-filled pen in accordance with the approved indications. Usability was evaluated by the patient and the physician through assessment of the individual steps of two self-injections in an interval of approximately 12 weeks (V1, V2) and through a final overall assessment using ordinal scales. Data analysis was carried out descriptively by means of standard statistical methods. Calculation of a total usability score allowed for comparison of V1 and V2.

Results: The 478 participating patients had a mean age of 56.2 $\pm$ 13.7 years, 57.1% were female; 39.3% suffered from RA, 34.7% from PsV, 23.4% had PsA, and 12.6% were diagnosed with other conditions. 87.7% received treatment with the pre-filled pen for the first time, and 61.5% had previously received MTX. The individual steps of self-injection, removing of a protective cap, placing the device onto the skin, pressing the injection button, removing the pen, and ergonomics of the pen, were rated as "very good" and "good" by more than 90% of patients as well as of physicians in both visits. Comparing V1 and V2, usability was assessed to be even better at the second visit (p<0.0001 in the total score). Injections were carried out accurately by more than 93% of the patients.

Conclusions: Autoinjection with a pre-filled pen enables patients to self-administer subcutaneous MTX easily and comfortably in routine clinical practice.

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