AB0486 SUBCUTANEOUS METHOTREXATE DISCONTINUATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Safety of methotrexate (MT) therapy remains the most important issue of early rheumatoid arthritis (RA) therapy.

Objectives: A prospective evaluation of most common causes of MT discontinuation in RA patients with disease duration <3 years.

Methods: An open 1 year study included 106 patients with active RA meeting ACR/EULAR 2010 or ACR 1987 (DAS28 >3.2) criteria, naïve to subcutaneous (SC) MT. All pts were administered SC MT, starting with 10–15 mg/week dose, and following 5 mg up-titration each 1–2 weeks (to max 30 mg/week) until achieving the target (remission or minimum disease activity) or emergence of adverse reactions (AR). Pts' monthly monitoring procedures included physical examination, blood analysis and biochemistry panel. T. Woodworth et al. inventory was used to assess the severity of ARs, and Naranjo scale was used to assess casual relationship of MT with an AR.

Results: Totally 12 (11%) MT discontinuations for the period of >3 weeks were analysed. Permanent discontinuation occurred in 9 pts (8%), and temporary (from 4 weeks to 4 months)—in 3 (3%). 83% of all cases of withdrawal took place during the first 3 months. In 3 patients MT was discontinued because of an AR and inefficiency. Combination of drug failure with AR was the reason for permanent SC MT discontinuation in 3 pts.

The causes led to SC MT discontinuation were: skin reactions in 3 pts (25%), "after-dose reactions"—in 2 (17%), allergic rash—in 2 (17%), diarrhoea—in 2 (17%), elevated liver enzymes—in 3 (25%), leukopenia—in 1 (8%), breast abscess—in 1 (8%). Some patients manifested multiple ARs. Two ARs (17%) were serious (grade 4 severity). Grade 3 ARs were documented in 4 cases (30%), Grade 2 ARs—in 4, and Grade 1 (mild) ARs—in 2 (17%) pts.

Skin lesions became the underlying cause for SC MT discontinuation, such as active dermatitis (n=1) and lichenoid skin reaction (n=1).

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Conclusions: Skin reactions were the most common cause for SC MT discontinuation. Therapeutic failure as the leading cause for drug discontinuation was not documented in a single patient.

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AB0487 MULTICENTER 24-WEEK STUDY TO ASSESS THE EFFICACY AND SAFETY OF TACROLIMUS IN ACTIVE RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is characterised by persistent synovitis and structural joint damage with T cell-driven inflammation. Tacrolimus suppress activation of T cells through the inhibition of calcineurin.

Objectives: We evaluated the efficacy and safety of tacrolimus in Korean active RA patient who had inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) including Methotrexate (MTX).

Methods: During the study period from Aug. 2012 to Jan. 2016 in this open labelled, multicenter study, 115 patients were enrolled with DAS28 ≥3.2. Patients received tacrolimus during 24 weeks. The initial dose was 1 mg once daily and was increased to 3 mg by every 4 weeks. The disease activity and safety was assessed.

Results: Data from 97 patients were evaluated in full set analysis. At week-24, EULAR response rate were 83.5% (81 of 97) with improvements from week-16 in 74.2% (72 of 97). Mean DAS28-ESR was continuously decreased of 5.64 at baseline, 4.14 (±1.22, p<0.001) at week-16 and 3.66 (±1.39, p<0.001) at week-24. Efficacy rates according to SDAI were 89.7% (87 of 97) and KHAQ-20 score decreased -2.42 (±4.37, p<0.001) from baseline 7.27 (±4.59) at week-24. Mean ESR was decreased -10.97 (±24.16, p<0.001) at week-16, -14.77 (±24.57, p<0.001) at week-24 from baseline 46.05 (±23.22). Mean CRP was decreased from 2.86 (±7.85, p=0.0578) at baseline to 1.34 (±3.02, p=0.0367) at week-24. In serious adverse events (6 of 108, 5.56%), two cases (pneumonia, high glucose level) were related with tacrolimus and recovered with treatment.

Conclusions: This study demonstrated the efficacy of add on tacrolimus therapy to MTX in patients with active RA patients.

Disclosure of Interest: None declared

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AB0488 DISEASE ACTIVITY AT ONE YEAR AFTER ADDITION OF IGURATIMOD OR SULFASALAZINE TO METHOTREXATE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: PROPENSITY SCORE ANALYSIS

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Background: Igratimod (IGU) is a small-molecule disease-modifying anti-rheumatic drug (DMARD) that has been shown to suppress inflammation via the inhibition of nuclear factor-kappa B activation *in vitro*. The efficacy of combination therapy with IGU and methotrexate (MTX) has been demonstrated in comparison with that of placebo in rheumatoid arthritis (RA). However, its efficacy in comparison with other DMARDs such as sulfasalazine (SSZ) has not been elucidated.

Objectives: To assess the disease activity at one year after addition of IGU in comparison with SSZ to MTX in typical clinical practice.

Methods: We analysed data from 16,988 RA patients registered in a large database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan) from April 2012 to March 2017.¹ In this study, we compared the two groups who received IGU or SSZ in addition to methotrexate in the earlier year. We excluded patients who started receiving biologic DMARDs, and IGU or SSZ the year prior to the study period, and those whose regimens were changed to other DMARDs such as tacrolimus and bucillamine.

Baseline characteristics were compared using the *t* test, Wilcoxon test, or chi-square test. Fisher analysis was conducted for both outcomes. The predicted probability of IGU treatment was calculated by fitting a logistic regression model using all clinically relevant variables as presented in table 1. Moreover, to reduce the effect of treatment-selection bias and potential confounding in this observational study, we performed rigorous adjustment for significant differences in the baseline characteristics of patients with propensity-score matching using the following algorithm: 1:1 optimal match with a ±0.2 calliper and no replacement. We used the standardised difference to measure covariate balance, whereby a standardised mean difference of >0.1 represents meaningful imbalance. The outcome was remission rate with disease activity score 28 CRP (DAS28-CRP) in the year after initiation of IGU or SSZ therapy.

Results: The group that received IGU in addition to MTX included 113 patients; the other group that received SSZ in addition to MTX included 244 patients. Table 1 shows the results of the pre- and post-propensity score matching of patients' characteristics.

One hundred and nine patients were compared in each group after score matching. The remission rates of DAS28-CRP in the following year was 45.0% (49/109 patients) and 54.1% (59/109 patients; p=0.22), and drug retention rate was 79.8% (87/109 patients) and 78.9% (86/109 patients; p=1.00), in the IGU and SSZ groups, respectively.

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: iganatimod; 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