THU0199 TOFACITINIB IMPROVES LEFT VENTRICULAR MASS AND CARDIAC OUTPUT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatologists need to develop primary prevention strategies for cardiovascular disease (CVD) in rheumatoid arthritis (RA) patients. We reported tofacitinib (Tofa) improved arterial stiffness in RA patients. RA is associated with an increased *left* ventricular mass index (LVMI), a strong marker of cardiovascular mortality.There is no evidence that Tofa effects on left ventricular (LV) morphology and function.

Objectives: To study the effect of Tofa plus methotrexate (MTX) on LV morphology and function in MTX resistant active RA patients, in a cohort study design.

Methods: RA patients were eligible if they had active disease despite treatment with MTX. All patients have no steroids, and no previous history of CVD. Consecutive 28 patients with moderate to severe active RA patients (DAS28>3.2) despite MTX were received Tofa plus MTX. 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: 24 patients completed 24 weeks. Left ventricular mass index (LVMI) was attenuated significantly by Tofa (week 0-week24, –12.4±5.4 g/m^2; p=0.0002). Cardiac output (CO) was attenuated significantly by Tofa (week 0-week24,-0.87±1.2l/min). DAS28 and CRP improved significantly by Tofa (week 0-week24; DAS28: -2.26±0.91; CRP: 14.1±8.7 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, 4 cases significantly improved right ventricular mass as well as left ventricular mass (20% improved right ventricular mass index from baseline).

Conclusions: Tofa improved LVMI and CO in active RA despite MTX. TCZ 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.

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THU0200 RISK FOR DEVELOPING ADVERSE EFFECTS CAUSED BY SALAZOSULFAPYRIDINE IN RHEUMATIC DISEASES

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Background: Salazosulfapyridine is non-antimicrobial sulfonamides, which is used as a synthetic disease modified anti-rheumatic-drug (DMARD) for rheumatoid arthritis and psoriatic arthritis. Prior study suggested sulfa allergy may be more commonly seen in patients with positive anti- Ro/SS-A antibody (anti-Ro).

Objectives: To identify the risk factor for adverse effects (AEs) caused by salazosulfapyridine in patients with rheumatic diseases.

Methods: We retrospectively identified patients ≥18 years old who received salazosulfapyridine at a tertiary medical center in Japan between 2010–2015. Data were collected on the incidence of AEs, clinical features and autoantibodies.

Results: We identified 313 patients with rheumatic diseases who received salazosulfapyridine. Median age was 61 (range, 20–95); 215 of 313 (67%) were female (Table). The incidence of AEs was 15% (48/313); Median duration until developing AEs was 14 days (range, 2–50). AEs included rash (28), fever (19), elevated liver function tests (13), gastrointestinal symptoms (9), lymphadenitis (3), neutropenia and eosinophilia (1). Factors associated with AEs are female gender, positive anti-Ro or psoriatic arthritis. Multivariate logistic controlling for age, gender and anti-Ro showed that positive anti-Ro has 2.33 odds (P=0.03; 95% CI: 1.07–5.08) of having AE of salazosulfapyridine. Among patients without anti-Ro, subjects with psoriasis showed 9.95 odds (P<0.001; 95% CI: 3.51–28.2) of developing AEs than non-psoriatic patients.

Conclusions: AEs caused by salazosulfapyridine are common in patients with rheumatic diseases. Presence of anti- Ro or psoriasis may be a risk factor for AEs caused by salazosulfapyridine.

Table

	With AEs (n=48)	Without AEs (n=265)	P value
Age over 60 years — no. (%)	22 (46)	26 (56)	0.21
Female sex — no. (%)	42 (88)	173 (65)	0.002
Clinical diagnosis			
Rheumatoid arthritis — no. (%)	26 (54)	214 (81)	0.002
Sjogren's syndrome — no. (%)	15 (31)	31 (12)	0.001
Psoriatic arthritis — no. (%)	19 (40)	11 (4)	<0.001
Anti-Ro/SS-A antibody — no. (%)	14 (29)	28 (11)	0.006

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THU0201 OLDER AGE, HYPOALBUMINAEMIA AND RENAL FAILURE MIGHT BE POOR PROGNOSIS FACTORS FOR LOW DOSE METHOTREXATE-INDUCED MYELOSUPPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) serves as an anchor drug in rheumatoid arthritis (RA) and the maximal dose of MTX from EULAR recommendation is 25–30 mg/w. Small cases retrospective cohort studies reported that the mortality rate of RA patients with low dose (5–25 mg/w) MTX-induced myelosuppression was about 17–25%. However, studies of low dose MTX-induced myelosuppression are rare in Chinese RA patients.

Objectives: To perform a retrospective case series analysis of the characteristics and outcomes of RA patients with low dose MTX-induced myelosuppression in China.

Methods: RA patients hospitalized at Sun Yat-Sen Memorial Hospital from January 2001 to December 2016 were recruited. Clinical data were collected and adverse effects were recorded simultaneously. Low dose MTX-induce myelosuppression was diagnosed as white blood cell $<4\times10^9$/L together with hemoglobin <130 g/L and platelet count $<130\times10^9$/L after treatment of MTX without an alternative cause for pancytopenia. Data were showed as mean ± standard deviation.

Results: (1) There were 1137 RA patients recruited and 17 patients (1.5%) of them were hospitalized for low dose MTX-induce myelosuppression. Among these 17 patients, 53% were females, age was 68±5 years, disease duration was 12±11 years.

(2) Four (23.5%) patients had dose errors, taking MTX 5–10mg daily for 24 days (range: 5–80), MTX accumulated dose was 25–200mg before myelosuppression. Mean MTX dose in the other patients (n=13, 76.5%) was 11.0±1.7 mg/w (range: 7.5 –15), course of MTX was 10±11 months (range: 0.5–48). Four (30.8%) patients manifested myelosuppression within the first month after taking MTX, and 4 (30.8%) patients had been well on a stable drug dose (7.5–12.5) for more than one year before myelosuppression, 2 patients manifested myelosuppression after adding MTX dose to 15mg/w for 2 months.

(3) Fifteen (88.2%) patients had oral mucositis, eight of them had involvement of both oral mucosa and skin. Fever was noticed in 10 (58.8%) patients. Infections were recorded in 6 (35.3%) patients, manifested as pneumonia (n=4), sepsis (n=1), urinary tract infection (n=1) and skin soft tissue abscesses (n=1). Two patients experienced abdominal pain and melena.

(4) Among the patients with neutropenia [n=17, mean neutrophil count: $(0.74\pm0.76)\times10^9$/L, range: 0–1.83], 9 (52.9%) developed severe neutropenia with neutrophil counts below 0.5×10^9/L. Five patients developed severe thrombocytopenia (platelet count $<20\times10^9$/L), and severe anemia occurred in 4 patients (hemoglobin <65g/L). Hypoalbuminemia (30.0±2.8 g/L) was noted in all patients. Glomerular filtration rate (GFR)≤30 ml/min/1.73 m^2 was noted in 4 (23.5%) patients and GFR≤50 ml/min/1.73 m^2 in 12 (70.6%) patients.

(5) Pancytopenia recovered (n=17) after discontinuation of MTX and supplementation of folic acid (10–30mg/d). Only 3 (17.6%) patients were treated with rescue intravenous leucovorin. Thirteen (76.5%) were treated with granulocyte colony stimulating factor (G-CSF) and 7 (41.2%) required blood products. Fifteen (88.2%) required antibiotic therapy. Sixteen (94.1%) patients was recovered and discharged, only one patient die from acute brainstem infarction but not from myelosuppression.

Table 1 Characteristics of 17 RA patients with low dose MTX-induce myelosuppression

Case	Age (y)	Sex	Dose (mg/w)	Dose errors	Fever	Mucositis	Neutrophil count (×10^9/L)	Platelet count (×10^9/L)	Hemoglobin (g/L)	GFR (ml/min/1.73 m^2)	Albumin (g/L)	Outcome
1	74	F	10	+	-	+	0.32	107	87	50.0	34.2	Recovered
2	65	M	10	+	+	+	0.25	2	65	49.8	27.1	Recovered
3	69	M	15	+	+	+	2.43	11	53	46.9	32.2	Recovered
4	60	M	15	+	+	+	0.12	61	77	57.4	32.4	Recovered
5	71	M	10	-	+	-	0	18	78	21.3	27.3	Recovered
6	68	F	10	-	-	+	1.64	112	84	39.1	35	Recovered
7	57	F	10	-	+	+	0.13	11	109	52.2	30.3	Recovered
8	76	M	10	-	+	+	0.62	39	88	48.3	18.9	Recovered
9	75	F	10	-	-	+	1.12	106	106	28.4	32.3	Recovered
10	63	F	10	-	+	+	0.67	37	65	33.0	32.9	Recovered
11	64	F	10	-	+	+	0	69	72	32.7	30.2	Recovered
12	70	M	10	-	-	+	0.34	93	73	55.1	28.7	Recovered
13	69	M	7.5	-	+	+	1.83	112	83	47.0	34.8	Recovered
14	62	F	15	-	-	+	0.28	124	53	23.3	31.2	Recovered
15	80	M	12.5	-	-	+	1.05	49	70	42.4	28.8	Recovered
16	74	F	12.5	-	-	-	1.75	106	74	61.8	28.6	Recovered
17	57	F	10	-	+	+	0.02	11	67	17.6	26	Died