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POS0448 DISCONTINUATION RATE OF TOFACITINIB AS MONOTHERAPY IS SIMILAR COMPARED TO COMBINATION THERAPY WITH METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS: POOLED DATA FROM TWO RHEUMATOID ARTHRITIS REGISTRIES IN CANADA

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Background: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). We previously reported the similarity in retention between TOFA monotherapy and TOFA with MTX using data from two different registries separately; the Ontario Best Practices Research Initiative (OBRI) and the Quebec registry RHUMADATA.
Objectives: To increase the study power, we propose to evaluate the discontinuation rate (due to any reason) of TOFA with and without MTX, using pooled data from these two registries.
Methods: RA patients enrolled in the OBRI and RHUMADATA initiating their TOFA between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Concurrent MTX use was defined as MTX use for more than 75% of the time while using TOFA. Multiple imputation (Imputation Chained Equation method, N=20) was used to deal with missing data for covariates at treatment initiation.
Time to discontinuation was assessed using Cox regression models. To deal with confounding by indication, we estimated propensity scores for selected covariates with an absolute standard difference greater than 0.1. We then adjusted Cox regression models for propensity quantile to compare the discontinuation of TOFA with MTX versus TOFA without MTX.
Results: A total of 493 patients were included. Of those, 244 (49.5%) and 249 (51.5%) were treated with MTX and without MTX, respectively. Compared to TOFA monotherapy, the TOFA with MTX group had a significantly lower mean HAQ-DI, fatigue score, and the number of prior biologic use at the time of TOFA initiation. A lower proportion of positive ACPA (59% vs. 66%), prevalence of hypertension (31% vs 37%), and concomitant use of Leflunomide (11% vs. 23%) were also observed for patients using TOFA with MTX.
Over a mean follow-up of 19.0 months, discontinuation was reported in 182 (36.9%) of all TOFA patients. After adjusting for propensity score quantile across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 1.12, 95% CI: 0.83-1.51; p=0.49).
Conclusion: In this pooled real-world data study, we found that in patients with RA, the retention of TOFA is similar if it is used as monotherapy or in combination with MTX.
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POS0449 BIOLOGICS INITIATION IN MODERATE VS SEVERE RHEUMATOID ARTHRITIS PATIENTS: PROSPECTIVE OBSERVATIONAL STUDY FROM A CANADIAN REGISTRY

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Background: Prior studies have shown that in the real-world setting, rheumatoid arthritis (RA) patients have lower disease activity than those studied in clinical trials. However, randomized controlled trials for biologics continue to mainly recruit patients with severe disease.
Objectives: To assess the implications of this practice, our study investigates the proportion of patients achieving remission (DAS28-ESR ≤ 2.6), in RA patients with moderate disease activity and severe disease activity, at 12 months post starting their first biologic, and identifies baseline predictors of biologic response.
Methods: This study included RA patients who have never been treated with a biologic and initiated their first biologic while enrolled in the Ontario Best Practices Research Initiative (OBRI) registry, between 2008 and 2019. Patients selected had either moderate RA (DAS28 ≥ 3.2 to ≤ 5.1) or severe RA (DAS28 > 5.1). Comparisons were made between the moderate and severe disease groups using the student's t-test for continuous variables, and the chi-square test for categorical variables. Multivariable logistic regression was used to test potential predictors of remission. Backward stepwise model selection was applied to select variables with *p*-value ≤0.10. Multiple imputation (MCMC method; n=20) was used to impute missing data.
Results: Overall, 641 patients initiated their first biologic, 483 had follow up data at 12 months (moderate disease activity=264; severe disease activity=219). In the moderate group, the mean age (SD) was 55.7 (13.1) and 80% were female. In the severe group, mean age (SD) was 58.4 (12.3) and 81% were female. At time of biologic initiation, the mean DAS28 for the moderate group was 4.1 (0.5), and 6.0 (0.6) for the severe group. After 12 months of starting a biologic, the proportion of patients achieving remission was 50% in the moderate group, and 23% in the severe group ($p<0.0001$). In contrast, the proportion of patients achieving significant clinical change from baseline (improvement in DAS28 ≥ 1.2) was 78% in the severe group, compared to 66% in the moderate group ($p=0.0049$). More specifically, the absolute improvement in DAS28 after 12 months was higher in the severe group at 2.2 (1.5), compared to a change of 1.4 (1.3) in the moderate group ($p<0.0001$). Negative predictors of remission include female gender (odds ratio (OR), 0.57, 95% confidence interval (CI), 0.33-0.97; $p=0.039$), and higher HAQ-DI score (OR 0.49, 95% CI 0.36-0.68; $p<0.001$). In turn, moderate disease at time of biologic initiation (OR 2.38, 95% CI 1.50-3.79; $p=0.0390$) was identified as a positive predictor of remission.
Conclusion: This prospective cohort study found RA patients with moderate disease activity are more likely to reach targeted states (remission and low disease activity), whereas severe patients have greater absolute improvements in DAS28 and HAQ-DI but are less likely to achieve remission. Moderate disease is a positive predictor for remission, whereas female gender and a higher HAQ-DI score are negative predictors.

Table 1. Outcomes at 12 months among patients with RA who initiated the first biologic

	Moderate-RA (n=264)	Severe-RA (n=219)	*P*-Value
Remission, *n* (%)	111 (50)	45 (23)	<0.0001
Low disease activity, *n* (%)	151 (59)	74 (35)	<0.0001
Change in DAS from baseline ≥ 1.2, *n* (%)	168 (66)	164 (78)	0.0049
HAQ-DI change >0.22, *n* (%)	98 (53)	83 (52)	0.7974
Change in DAS28 from baseline, mean (SD)	-1.4 (1.3)	-2.2 (1.5)	<0.0001
Change in HAQ-DI from baseline, mean (SD)	-0.29 (0.57)	-0.30 (0.66)	<0.0001
Change in fatigue from baseline, mean (SD)	-0.98 (3.2)	-1.11 (3.2)	<0.0001
Change in sleep from baseline, mean (SD)	-0.85 (3.6)	-1.05 (3.9)	0.0004

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POS0450 INCIDENCE RATES OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS IN REAL-WORLD CLINICAL PRACTICE

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Background: A definition of difficult-to-treat rheumatoid arthritis (D2T RA) was recently proposed by the European League Against Rheumatism (EULAR) [1]. However, information on the incidence rates of D2T RA in real-world clinical practice is lacking.
Objectives: The aim of this retrospective cross-sectional study was to evaluate the incidence rates of D2T RA in clinical practice in Japan.
Methods: Data from the Toyohashi RA database (TRAD) was used. The TRAD is a collection of single-center retrospective data. Patients with RA who fulfilled the following three requirements were included in this study: (1) had been treated with >1 biological or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD); (2) >1 year had passed since b/tsDMARD treatment was initiated; and (3) regularly visited our institute at the time of investigation. The number of targeted patients was 363. The criteria of D2T RA used in this study were modified from the EULAR definition for simplification of the investigation as follows: (a) ≥2 b/t DMARDs with different mechanisms of action had been administered; (b) at least moderate disease activity (DAS28-ESR > 3.2 or clinical disease activity index [CDAI] > 10) at the time of investigation; and (c) 7.5-mg/day of prednisolone (PSL) or more was administered at the time of investigation. In this study, D2T RA was defined as criteria (a) + (b) or (a) + (c) or (a) + (b) + (c). The 363 patients were categorized into four groups as follows: group A, DT2 RA; group B, patients with RA who had been treated with ≥2 b/tsDMARDs and did not fulfill the D2T RA definition; group C, RA patients who had been treated with one kind of b/tsDMARD with the same mechanism of action (e.g., two kinds of tumor necrosis factor inhibitors) and fulfilled either or both criteria (b) and (c); and group D, patients with RA who had been treated with one kind of b/tsDMARD with the same mechanism of action (e.g., a tumor necrosis factor inhibitors or two interleukin 6 inhibitors) and did not fulfill either or both criteria (b) and (c). The incidence rates of D2T RA were calculated, and the patients' characteristics at the time of initiation of the b/tsDMARD treatment were compared between the groups.
Results: The number of patients in groups A, B, C, and D were 34, 53, 94, and 182, respectively. Of all the patients included in this study, 9.4% were categorized into group A, those with D2T RA, and 39.1% were treated with ≥2 b/tsDMARDs and categorized into group A (Fig 1). The patients' characteristics were as follows (group A/B/C/D): mean age (57.1/54.3/61.4/56.2 years), RA duration (10.0/6.7/13.8/8.2 years), %Steinbrocker stage III+IV (%; 84.0/60.0/77.3/54.3), %Steinbrocker class 3+4 (%; 68.0/33.3/43.4/23.0), methotrexate (MTX) concomitant rate (%; 79.4/92.5/74.5/91.8), PSL concomitant rate (%; 91.2/52.8/55.3/43.4), DAS28-ESR score (5.5/5.0/5.5/4.7), and CDAI score (12.3/13.7/22.7/16.9). There were statistically significant differences in RA duration, %stage III+IV, %class 3+4 and PSL concomitant rate between group A and B.
Conclusion: D2T RA occurred in 9.4% of patients treated with b/tsDMARDs. Incidence rate was increased to 39.1% after the treatment with ≥2 b/tsDMARDs. The patients with D2T RA tended to be older, have a long RA duration, be treated without concomitant MTX, be treated with concomitant PSL, and have higher disease activity at the time of starting the b/tsDMARD treatment. The baseline patient characteristics in group C were similar to those in group A. In the future, we suggest that patients with D2T RA be included in group C.
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[1] Nagy et al. Ann Rheum Dis 2021; 80: 31-35.

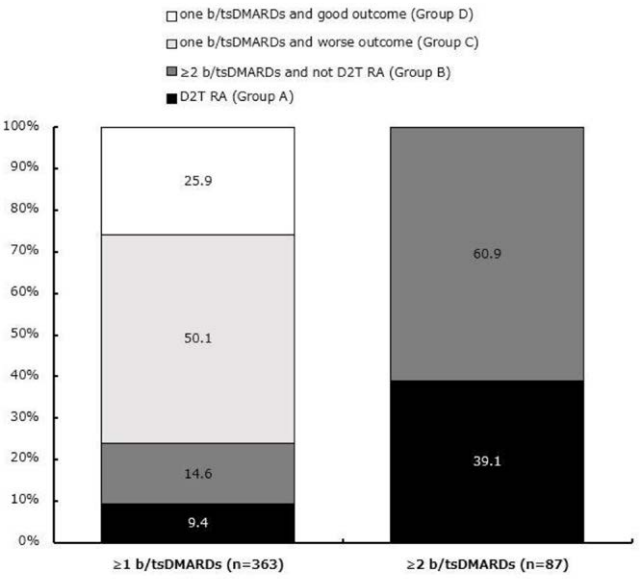

Figure1. Incidence rate of difficult-to-treat rheumatoid arthritis

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POS0451 SERUM FETUIN-A AND VISFATIN LEVELS IN WOMEN WITH RHEUMATOID ARTHRITIS DEPENDING ON DISEASE ACTIVITY

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Background: In recent years, the systemic effects of a number of cytokines have been actively studied, in particular, fetuin-A is considered a negative protein of the acute phase response, and visfatin, on the contrary, affects the activation of the cytokine cascade and has a pro-inflammatory effect. Taking into account that women suffer from rheumatoid arthritis (RA) more often, we investigated the levels of fetuin-A and visfatin in the blood serum of females in comparison with a group of healthy individuals and depending on the activity of the disease.
Objectives: to study the levels of fetuin-A and visfatin in the blood serum of women suffering from RA, depending on the activity of the disease
Methods: The study included 110 women with RA and 30 apparently healthy individuals. The inclusion criteria were: a diagnosis of RA verified based on the criteria of the American College of Rheumatology/European Anti-Rheumatic League (ACR/EULAR) 2010. The patients' age ranged from 18 to 90 years. The control group included 30 conventionally healthy individuals. Serum fetuin-A and visfatin levels were determined by indirect enzyme-linked immunosorbent assay using commercial kits. RA activity was determined by the DAS28-CRP index. Activity 0-I was in 33 (30%) patients, grade II in 67 (60.9%), grade III in 10 (9.09%) patients.
Results: The normal level of fetuin-A was calculated using the formula M±2σ in the group of conventionally healthy individuals and ranged from 653.55 to 972.19 μg/ml. In patients with grade 0-I RA activity according to DAS28, the mean serum fetuin-A level was 843.92±130.73 μg/ml, in patients with grade II activity - 742.37±98.85 μg / ml, with III the degree of activity - 663.9±123.7 μg/ml ($p<0.001$).
The average level of visfatin in the blood serum in healthy individuals was 2.43±0.17 ng/ml. The level of normal values of visfatin in healthy individuals, defined as M±2σ, ranged from 0 to 5.07 ng/ml. The average level of visfatin in patients with RA was 6.27±0.18 ng/ml, which is significantly higher than in healthy individuals ($p<0.001$).
In patients with 0-I degree of RA activity according to DAS28, the average level of visfatin in blood serum was 4.94±0.02 ng/ml, in patients with degree II activity - 5.08±0.02 ng/ml, with III degree of activity - 6.82±0.23 ng/ml ($p<0.001$).