Time to Discontinuation of Tofacitinib and TNF inhibitors in Rheumatoid Arthritis Patients with and without Methotrexate: Results From The Ontario Best Practices Research Initiative (OBRI)

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BACKGROUND

- Tofacitinib (TOFA) is an oral, small molecule drug which can be used as an alternative to biologic disease modifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi) for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX).

OBJECTIVES

- We aimed to evaluate the discontinuation rate of TOFA, with and without concurrent MTX, in comparison with TNFi, in patients with RA in the Ontario Best Practices Research Initiative (OBRI); a clinical registry (OBRI-RA registry) following RA patients in routine care in Ontario-Canada (www.obri.ca).

METHODS

- RA patients enrolled in the OBRI initiating their TOFA or TNFi (adalimumab, certolizumab, etancercept, golimumab, and infliximab) within 30 days prior to or anytime after enrolment between 1st Jun 2014 (TOFA approval date in Canada) and 31st Dec 2018 were included. Patients were excluded if they had < 2 visits and < 6 months follow-up.
- Time to discontinuation (due to any reason) was assessed using Kaplan-Meier survival, adjusted for propensity score using inverse probability of treatment weight (IPTW), to compare patients with and without MTX use at initiation of TOFA or TNFi.
- Covariates used for estimating propensity score: age, sex, education, annual household income, health insurance coverage, RA disease duration, number of prior biologic use, CDAI, rheumatoid factor, HAQ-DI, ESR, the presence of comorbidity (cancer, hypertension, CVD, diabetes mellitus, lung disease, depression, osteoarthritis), prior use of csDMARDs, and current use of other csDMARDs.
- To deal with missing data, Markov Chain Monte Carlo (MCMC) was used for multiple imputation (n=20) assuming that all variables in the imputation model have a joint multivariate normal distribution (MVN).

RESULTS

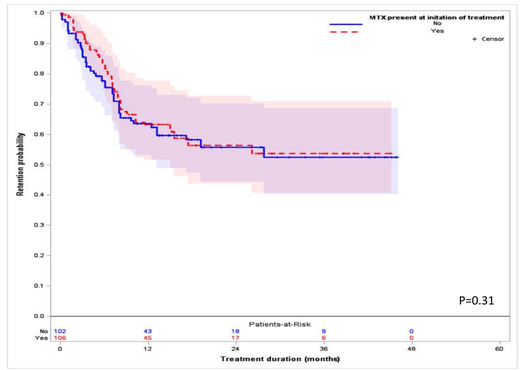
- A total of 565 patients initiated TOFA (n=208) or TNFi (n=357). Of those, 106 (51%) and 222 (62%) were treated with MTX in the TOFA and TNFi group, respectively (Table 1) and mean (SD) disease duration were 13.1 (9.4) and 9.5 (9.4) years.
- In the TOFA group, 86% were female and mean (SD) age at treatment initation was 60.4 (10.6) years. In the TNFi group 82% were female and mean age (SD) was 57.0 (12.6) years.
- The TOFA group was more likely to have prior biologic use (61.5%) compared with the TNFi group (31.0%).
- After adjusting for propensity score, patients treated with TNFi and MTX remained on treatment longer than those treated without MTX (Logrank p=0.002) while there was no significant difference in TOFA discontinuation in patients with and without MTX (Logrank p=0.31) (Figure 1).

Table 1: Patient Profile at Initiation of TOFA or TNFi With and Without MTX

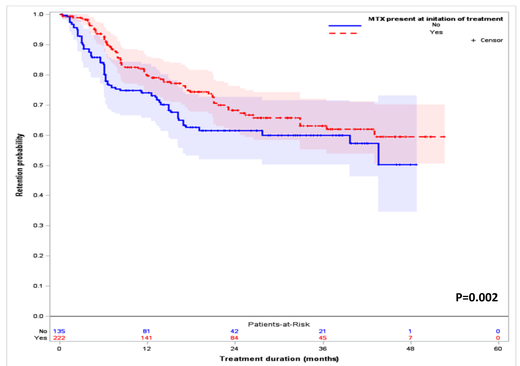
	TOFA			TNFi		
	MTX+ (n=106)	MTX- (n=102)	P-value	MTX+ (n=222)	MTX- (n=135)	P-value
Disease Duration At Treatment Initiation (years)	13.2 ± 9.6	13.0 ± 9.4	0.87	9.5 ± 9.4	9.8 ± 9.4	0.74
Age At Treatment Initiation (years)	60.5 ± 9.9	60.3 ± 11.2	0.89	57.2 ± 12.1	56.5 ± 13.4	0.62
Women	88 (83.0%)	91 (89.2%)	0.20	173 (77.9%)	120 (88.9%)	**0.01**
Concomitant MTX Start Dose	18.2± 6.3			18.6 ± 5.9		
Main Comorbidity Number	1.9 ± 2.1	2.3 ± 2.1	0.13	1.7 ± 1.9	1.9 ± 2.0	0.42
Positive Rheumatoid Factor	69 (70.4%) (N=98)	71 (77.2%) (N=92)	0.29	164 (79.2%) (N=207)	91 (71.0%) (N=128)	0.07
Positive Anti–Citrullinated Protein Antibody	28 (63.6%) (N=44)	22 (53.7%) (N=41)	0.35	82 (70.7%) (N=116	41(61.2%) (N=67	0.19
Clinical Disease Activity Index	25.3 ± 11.6 (N=90)	24.2 ± 12.7 (N=81)	0.99	20.8 ± 11.9 (N=170)	22.5 ± 12.1 (N=96)	0.08
Treatment Stopped	39 (36.8%)	36 (35.3%)	0.82	58 (26.1%)	45 (33.3%)	0.15
• **Treatment Duration (years)**	0.58 ± 0.4 (N=39)	0.51 ± 0.5 (N=36)	0.52	1.0 ± 0.7 (N=58)	0.8 ± 0.8 (N=45)	0.17
• **Reason for Treatment Cessation**			0.99			0.39
▪ **Ineffectiveness**	15 (38.5%)	14 (38.9%)		28 (48.3%)	16 (35.6%)	
▪ **Adverse Event**	16 (41.0%)	15 (41.7%)		11 (19.0%)	9 (20.0%)	
▪ **Other**	8 (20.5%)	7 (19.4%)		19 (32.8%)	20 (44.4)	
Treatment Ongoing	67 (63.2%)	66 (64.7%)	0.82	164 (73.9%)	90 (66.7%)	0.15
• **Treatment Duration (years)**	1.3 ± 0.9 (N=67)	1.4 ± 1.1 (N=66)	0.61	1.9 ± 1.2 (N=164)	1.9 ± 1.1 (N=90)	0.57
Treatment Selection						
• **First Agent**	42 (39.6%)	38 (37.3%)	0.73	168 (75.7%)	78 (57.8%)	**<0.001**
• **Subsequent Agent**	64 (60.4%)	64 (62.7%)		54 (24.3%)	57 (42.2%)	

Figure 1: Propensity Score Weighted (IPTW) Kaplan-Meier Survival Curves for Time to Discontinuation of TOFA or TNFi With MTX and Without MTX

TOFA



TNFi



CONCLUSIONS

- In this real world data study, we found that TOFA retention is similar in patients with and without MTX, while patients treated with TNFi and MTX remained on treatment longer than those treated without MTX.
- Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.

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