Longitudinal Changes in Relative Market Share Proportions of Biologic, and Targeted Synthetic, Disease-Modifying Anti-Rheumatic Drugs (DMARDs) For Treatment of Rheumatoid Arthritis: Results from the Ontario Best Practices Research Initiative (OBRI)

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BACKGROUND

- Patients with Rheumatoid Arthritis (RA) who have active disease despite treatment with conventional synthetic DMARDs can be started on either biologic DMARDS (bDMARDs) or Targeted Synthetic DMARDs (tsDMARDs) from either the Tumour Necrosis Factor Inhibitor (TNFi) or non-TNFi category.
- Over the past 10 years, multiple new agents in both classes have been developed, and guidelines do not specify the order in which these agents should be used.
- Changes in relative use of TNFi and non-TNFi agents in the biologic-naïve population and in all bDMARD/tsDMARD users is not well described.

OBJECTIVES

- We aimed to describe annual changes in relative market share of TNFi and non-TNFi in all patients using bDMARDs/tsDMARDs and in those who were biologic naïve in a real-world clinical setting.

METHODS

- Patients over the age of 18 with a diagnosis of RA enrolled in OBRI between January 2008-January 2018 who started a bDMARD or tsDMARD up to 30 days prior to, or anytime after, enrollment in OBRI were included.
- A subgroup of patients starting on their first bDMARD/tsDMARD were analyzed as a biologic-naïve cohort. Retrospectively, annual relative use of TNFi and non-TNFi therapy was described.
- TNFi included: Etanercept, Adalimumab, Certolizumab, Golimumab, and infliximab. Non-TNFi included: Abatacept, Rituximab, Tocilizumab, and Tofacitinib.

RESULTS

- 1, 057 patients were included in our analysis. 74.0% used TNFi and 26.0% used non-TNFi during the study time.
- 653 patients were biologic-naïve. 86.6% used TNFi and 13.4% used non-TNFi as their first bDMARD/tsDMARD.
- In the biologic-naive group mean age (SD) and disease duration was 56.5 (12.2) and 8.0 (8.8), respectively. Patients in the non-TNFi group had significantly more post-secondary education, more additional private drug coverage and less concurrent use of csDMARDs (Table 1).
- Overall the relative use of non-TNFi agents increased overtime in both the total population and biologic naïve population. (Figures 1 and 2).
- Non-TNFi use in biologic naïve was 0% in 2008, 12.0% in 2013, and 26.6% in 2017

Table 1: Patient profile at initiation of first bDMARD; overall and by mechanism of action.

	Total (n=653)	By Mechanism of Action		
		TNFi (n=566)	Non-TNFi (n=87)	*p*-value
Demographic Factors				
• Age, mean (SD)	56.5 (12.2)	56.1 (12.5)	58.4 (12.9)	0.12
• Sex, female n (%)	518 (79.3%)	447 (79.0%)	71 (81.6%)	0.57
• Marital Status, married	445 (68.1%)	389 (68.7%)	56 (64.4%)	0.99
• Race, Caucasian, n (%)	538 (82.4%)	468 (82.7%)	70 (80.5%)	0.90
• Education Status, post-secondary, n (%)	371 (56.8%)	316 (55.8%)	55 (63.2%)	**0.04**
• Annual Income, (≥ 50,000 CD), n (%) [√]	260 (39.8%)	223 (39.4%)	37 (42.5%)	0.90
• Smoking History, n (%)				
Never Smoking	295 (45.2%)	259 (45.8%)	36 (41.4%)	0.24
Former Smoking	223 (34.2%)	188 (33.2%)	35 (40.2%)	
Current Smoking	102 (15.6%)	93 (16.4%)	9 (10.3%)	
• Health insurance Plan, n (%)[Ω]				
Ontario Health Insurance Plan (OHIP) plus private	477 (73.0%)	409 (72.3%)	68 (78.2%)	**0.02**
Disease Factors				
• Disease Duration Since Diagnosis, mean (SD)	8.0 (8.8)	7.9 (8.6)	8.9 (9.9)	0.31
• Disease Duration ≤ 1 year, n (%)	97 (14.9%)	86 (15.2%)	11 (12.6%)	0.53
• RF positive, n (%)[π]	449 (68.8%)	395 (69.8%)	54 (62.1%)	0.65
• Swollen Joint Count (0-28), mean (SD) [±]	6.6 (4.7)	6.4 (4.5)	7.6 (5.9)	0.15
• Tender Joint Count (0-28), mean (SD) [β]	7.0 (6.3)	7.1 (6.3)	6.4 (6.4)	0.42
• Physician Global (0-10), mean (SD) [¥]	5.1 (2.3)	5.1 (2.2)	5.0 (2.6)	0.71
• Patient Global (0-10), mean (SD) [©]	5.4 (2.8)	5.3 (2.8)	5.5 (2.9)	0.76
• DAS28-ESR (0-9.4) , mean (SD) [×]	4.6 (1.4)	4.6 (1.4)	4.5 (1.5)	0.66
• CDAI (0-76) , mean (SD) [#]	24.3 (12.4)	24.3 (12.3)	24.6 (13.2)	0.87
• HAQ-DI (0-3) , mean (SD) [∞]	1.3 (0.8)	1.3 (0.7)	1.4 (0.9)	0.35
• HAQ-pain (0-3) , mean (SD) [∝]	1.7 (0.9)	1.7 (0.8)	1.8 (0.9)	0.57
• Presence of erosion, n(%)	297 (45.5%)	261 (46.1%)	36 (41.4%)	
• Number of comorbidities, mean (SD)	4.2 (2.8)	4.1 (2.7)	4.8 (3.3)	0.06
Medication Factors				
• Prior use of csDMARDs, n (%)	566 (86.7%)	486 (85.9%)	80 (92.0%)	0.16
• Concurrent csDMARDs use, n (%)	489 (74.9%)	427 (75.4%)	62 (71.3%)	**0.03**
• Concurrent steroid use , n (%)	140 (21.4%)	118 (20.8%)	22 (25.3%)	0.71
• Concurrent NSAIDs use, n (%)	136 (20.8%)	121 (21.4%)	15 (17.2%)	0.13
- Time period of first biologic used, n (%)				
2008-2010	112 (17.2%)	102 (18.0%)	10 (11.5%)	**<0.0001**
2011-2013	313 (47.9%)	287 (50.7%)	26 (29.9%)	
2014-2017	228 (34.9%)	177 (31.3%)	51 (58.6%)	

[√] available number =459 [Ω] available number =615 [π] available number =606 [±] available number =528 [β] available number =520 [¥] available number=437 [©] available number =470 [×] available number =476 [#] available number =467 [∞] available number =463

SD=standard deviation

DAS28 ESR=Disease Activity Score 28-erythrocyte sedimentation rate, csDMARDs=conventional synthetic disease-modifying antirheumatic drug, HAQ-DI=Health Assessment Questionnaire -Disability Index, RA=rheumatoid arthritis, RF=rheumatoid factor, TNFi=tumour necrosis factor inhibitor.

Figure 1: Frequency of biologic use according to mechanism of action by calendar year (n=1057)

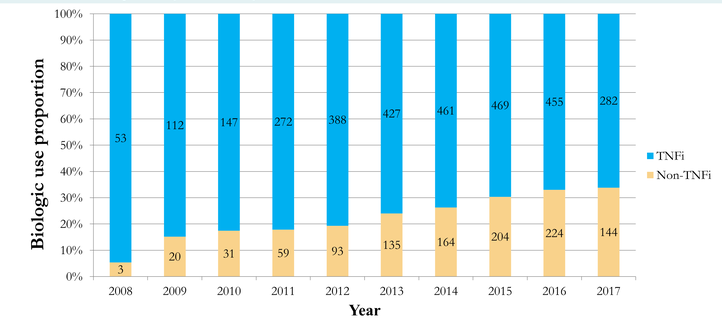
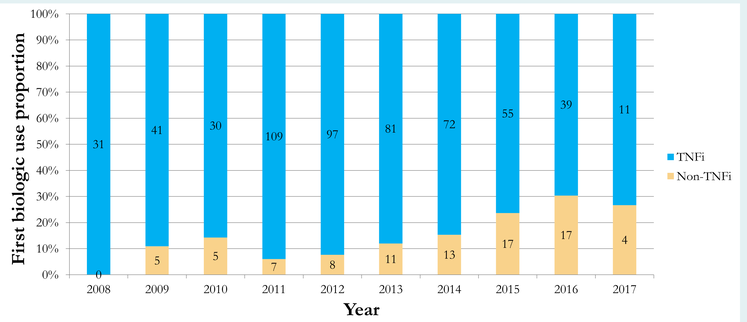


Figure 2: Frequency of first biologic use according to mechanism of action by calendar year in biologic-naïve patients.



CONCLUSIONS

- The analysis demonstrates an overall increase in the uptake of non-TNFi therapy over time in both the total population and the biologic-naive population. The increase in non-TNFi use in the biologic-naive population seems to follow the relative broadening of the ACR/EULAR guideline suggestions in 2012/13 and 2015/16.
- Future analysis to identify predictors of non-TNFi use in biologic naïve patients and assessment of relative non-TNFi use after discontinuation of initial TNFi are planned.

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