DISEASE AND TREATMENT CHARACTERISTICS THAT MIGHT INFLUENCE LONG-TERM RETENTION WITH BIOLOGICS IN THE REAL-WORLD CLINICAL SETTING: EXPERIENCE FROM THE RHUMADATA CLINICAL DATABASE AND REGISTRY

D. Choquette[1], L. Bessette[2], J. Brown[2], B. Haraoui[1], F. Massicotte[1], J.-P. Pelletier[1], J.-P. Raynauld[1], M.-A. Rémillard[1], D. Sauvageau[1], A. Turcotte[2], E. Villeneuve[1], and L. Coupal[1]

[1]Institut de Rhumatologie de Montréal (IRM), [2]Centre d'ostéoporose et de rhumatologie de Québec (CORQ)

INTRODUCTION

- Patient adherence and sustainability of the regimen plays an important role in the long term outcomes.
- Biologic disease-modifying antirheumatic drugs (bDMARDs) have revolutionized the treatment of rheumatoid arthritis (RA), yet drug discontinuation is common.[1]

OBJECTIVES

- We aim to investigate factors that might influence long-term retention with biologics in a RA cohort.

METHODS

- RA patients treated at the Institut de Rhumatologie de Montréal (IRM) and the Centre d'Ostéoporose et de Rhumatologie de Québec (CORQ) with either abatacept (ABA) or an anti-TNF inhibitor, adalimumab (ADA), etanercept (ETA), or infliximab (INF) were grouped according to their experience with biologics.
- The first cohort included patients receiving first line biologic and the second cohort included patients on their second biologic.
- Patients were enrolled after January 1st 2007 and were followed until they discontinued their treatment or February 23, 2015.
- Patient characteristics were compared using ANOVA with Bonferroni correction.
- Kaplan-Meier methods were used to compute the cumulative incidence of biologic agent discontinuation. Differences in the discontinuation rates of biologic agents were tested using the log-rank tests.

RESULTS

- 403 patients received first line biologic therapy and 189 patients were on their second biologic, Table 1.
- No clinically significant differences in baseline characteristics were noted between treatment groups. As expected the disease duration was longer in patients on second vs first biologic (10.8 years vs. 6.9 years).
- Approximately 66% (66.7% first; 66.1% second cohort) of patients were rheumatoid factor (RF) positive. Anti-cyclic citrullinated peptide antibodies (anti-CCP) were detected in 62.0% and 55.4% of patients in the first and second cohort, respectively.
- Neither the RF status, use of corticosteroids, or the use of biologics as monotherapy vs in combination with non-bDMARDs had a significant impact on long term retention rates.

Table 1. BASELINE CHARACTERISTICS

	First biologic agent					Second biologic agent				
	ABA	ADA	ETA	INF	ALL	ABA	ADA	ETA	INF	ALL
	n=62	n=111	n=195	n=35	n=403	n=76	n=47	n=47	n=19	n=189
Age (years)	57.3 (11.9)	52.1 (13.7)	54.9 (13.2)	55.8 (10.9)	54.6 (13.0)	57.5 (11.8)	52.8 (12.8)	57.5 (14.1)	53.0 (15.9)	55.9 (13.2)
Women, n (%)	50 (80.7%)	84 (75.7%)	150 (76.9%)	27 (77.1%)	311 (77.2%)	62 (81.6%)	32 (68.1%)	38 (80.9%)	12 (63.2%)	144 (76.2%)
Disease Duration (years)	7.2 (7.7)	5.3 (6.9)	7.9 (8.7)	6.3 (7.8)	6.9 (8.1)	12.6 (9.7)	10.3 (6.5)	10.3 (9.5)	6.9 (6.6)	10.8 (8.8)
Number of previously used DMARDs	2.5 (1.1)	2.1 (0.8)	2.3 (0.8)	2.5 (1.0)	2.3 (0.9)	2.8 (1.0)	2.7 (1.1)	2.5 (1.1)	2.8 (1.2)	2.7 (1.1)
Number of concurrently used DMARDs	1.4 (0.8)	1.4 (0.7)	1.3 (0.7)	1.5 (0.7)	1.4 (0.7)	1.0 (0.7)	0.9 (0.7)	0.9 (0.7)	1.2 (0.6)	0.9 (0.7)
No DMARDs used	9 (14.5%)	9 (8.1%)	28 (14.4%)	2 (5.7%)	48 (11.9%)	20 (26.3%)	13 (27.7%)	14 (29.8%)	2 (10.5%)	49 (25.9%)
Methotrexate	38 (61.3%)	85 (76.6%)	117 (60.0%)	27 (77.1%)	267 (66.3%)	41 (53.9%)	28 (59.6%)	23 (48.9%)	13 (68.4%)	105 (55.6%)
Hydroxychloroquine sulfate	37 (59.7%)	47 (42.3%)	96 (49.2%)	16 (45.7%)	196 (48.6%)	21 (27.6%)	10 (21.3%)	14 (29.8%)	6 (31.6%)	51 (27.0%)
Leflunomide	5 (8.1%)	9 (8.1%)	13 (6.7%)	5 (14.3%)	32 (7.9%)	6 (7.9%)	2 (4.3%)	2 (4.3%)	4 (21.1%)	14 (7.4%)
Sulfasalazine	4 (6.5%)	6 (5.4%)	11 (5.6%)	2 (5.7%)	23 (5.7%)	3 (3.9%)	2 (4.3%)	1 (2.1%)	0 (0.0%)	6 (3.2%)
Other	0 (0.0%)	3(2.7%)	5 (2.6%)	1 (2.9%)	9 (2.2%)	2 (2.3%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	3 (1.5%)
Use of corticosteroids	12 (19.4%)	17 (15.3%)	53 (27.2%)	8 (22.9%)	85 (22.0%)	34 (44.7%)	14 (29.8%)	14 (29.8%)	5 (26.3%)	67 (35.4%)
Duration of morning stiffness (minutes)	119.7 (248.6)	46.4 (162.1)	65.0 (191.4)	119.0 (286.1)	72.1 (203.5)	110.9 (268.8)	116.8 (281.9)	72.9 (174.2)	129.0 (378.8)	104.6 (263.1)
HAQ-DI, range 0-3	1.3 (0.5)	1.1 (0.6)	1.2 (0.6)	1.2 (0.5)	1.2 (0.6)	1.4 (0.7)	1.2 (0.8)	1.2 (0.6)	1.1 (0.8)	1.3 (0.7)
Fatigue VAS, range 0-10	5.0 (3.1)	3.6 (3.4)	3.6 (3.4)	4.9 (3.4)	3.9 (3.4)	5.4 (3.0)	4.8 (3.8)	4.2 (3.3)	4.4 (3.0)	4.9 (3.3)
Pain VAS, range 0-10	5.1 (3.1)	4.4 (3.2)	4.5 (3.3)	4.8 (3.2)	4.6 (3.2)	5.5 (3.0)	5.1 (3.4)	4.5 (3.4)	4.4 (2.6)	5.1 (3.2)
CRP (mg/L)	13.3 (16.4)	11.4 (18.3)	12.8 (21.3)	8.6 (11.7)	12.1 (19.1)	16.5 (24.8)	19.5 (29.0)	6.8 (9.9)	14.8 (27.7)	14.6 (23.8)
ESR (mm/hr)	20.6 (17.1)	22.7 (16.3)	24.8 (25.0)	16.8 (14.0)	22.9 (21.0)	27.8 (22.1)	25.6 (19.3)	19.9 (15.8)	23.9 (27.1)	24.9 (20.7)
RF positive (%)	71.2%	65.1%	64.4%	75.8%	66.7%	71.6%	65.9%	65.9%	44.4%	66.1%
Anti-CCP positive (%)	61.5%	64.1%	62.0%	56.7%	62.0%	57.8%	64.3%	47.4%	50.0%	55.4%
Tender joint count (TJC), range 0-28	8.2 (6.4)	6.4 (6.6)	6.8 (6.5)	8.9 (6.9)	7.1 (6.6)	6.3 (6.1)	5.8 (6.5)	5.8 (5.4)	5.0 (7.2)	6.0 (6.1)
Swollen joint count (SJC), range 0-28	7.8 (5.5)	7.2 (6.1)	7.8 (5.5)	8.4 (5.5)	7.6 (5.7)	7.9 (6.1)	5.5 (4.9)	6.3 (5.6)	6.8 (8.2)	7.0 (5.9)
Physician global VAS, range 0-10	4.9 (2.3)	4.1 (2.2)	4.8 (1.9)	5.9 (2.2)	4.7 (2.1)	4.7 (1.9)	3.4 (2.0)	4.8 (1.6)	4.6 (3.3)	4.4 (2.1)
Patient global VAS, range 0-10	4.7 (2.5)	4.1 (2.9)	4.0 (2.9)	4.8 (2.6)	4.2 (2.8)	5.0 (2.6)	4.4 (3.2)	4.0 (2.9)	3.6 (2.4)	4.5 (2.8)
Clinical disease activity index (CDAI), range 0-76	27.1 (13.4)	21.6 (14.3)	22.4 (12.6)	27.3 (14.3)	23.3 (13.5)	21.8 (11.3)	15.8 (10.0)	20.1 (13.7)	17.3 (17.0)	19.8 (12.3)

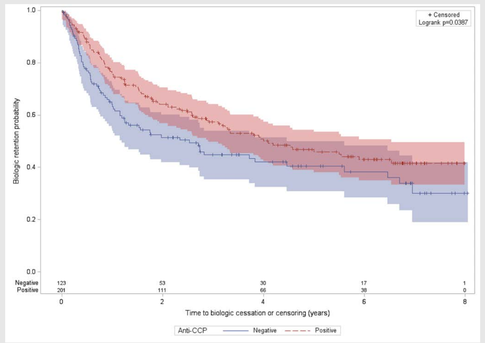

Figure 1. Retention probability of a first biologic agent. Anti-CCP positive vs Anti-CCP negative patients.

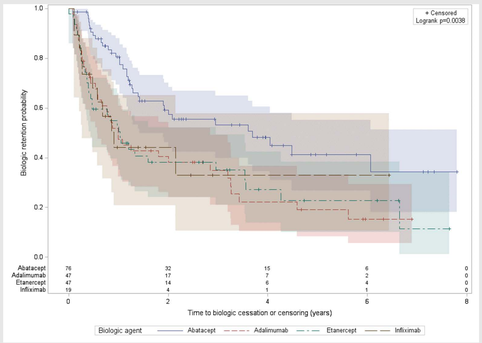

Figure 2. Retention probability of a second biologic agent.

RESULTS (continued)

- While retention probability was significantly higher in anti-CCP positive vs negative patients receiving first line biologic therapy, the anti-CCP positivity did not affect retention in patients on their second biologic, Figure 1.
- Although there were no significant differences in retention rates in the first cohort, in the second cohort treatment with ABA was associated with significantly higher retention compared to anti-TNFs, Figure 2.

CONCLUSIONS

- The anti-CCP positivity was associated with significantly higher retention when biologics were used first line. This is important as anti-CCP antibodies are predictors of an aggressive disease.[2]
- These results are compatible with other registries that indicate that anti-CCP might have an impact on retention rates.[3]
- There were no significant differences in the retention rates in the first cohort between biologic therapies.
- In the second cohort treatment with ABA was associated with significantly higher retention compared to anti-TNFs.

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CONTACT

D. Choquette MD
Institut de Rhumatologie de Montréal
1551, Ontario Street East
Montreal, Canada
denis.choquette.irm@videotron.ca