BIOLOGIC DISCONTINUATION IN RHEUMATOID ARTHRITIS: EXPERIENCE FROM CANADIAN CLINICS

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease affecting approximately 300,000 Canadians and 23.7 million individuals worldwide. Adherence and persistence to treatment is a cornerstone of treatment success in chronic diseases such as rheumatoid arthritis (RA). Identifying the predictors of adherence in Canadian patients living with RA might help optimize their therapy.

OBJECTIVES

We aim to describe biologic treatment discontinuation and assess the predictors of discontinuation in RA patients followed at Canadian clinics.

METHODS

We performed a 3-year prospective cohort study using RHUMADATA® registered RA patients followed at the IRM, the *Centre d'ostéoporose et de rhumatologie de Québec*, and the *Centre de rhumatologie de l'est du Québec*. Selected subjects were 18 years of age or older consenting to the study and had been treated with at least one biologic agent (abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or anakinra) since 2003, had been followed for a minimum of one year before biologic therapy initiation and had a minimal follow-up of six months after biologic therapy. Socio-demographic (age, sex, type of drug coverage, education, type of work, and family income), clinical (comorbidities, co-therapy, physical function), disease characteristics (duration, rheumatoid factor, anti-CCP) and activity (DAS, CDAI and SDAI scores, SJC, TJC, ESR, CRP, morning stiffness duration, global patient and physician assessments) were measured at baseline. Adherence to first biologic treatment was assessed at 6, 12, 24 and 36 months after biologic therapy initiation. Time to discontinuation and predictors of treatment discontinuation were explored using Cox proportional hazards models.

Baseline characteristics*

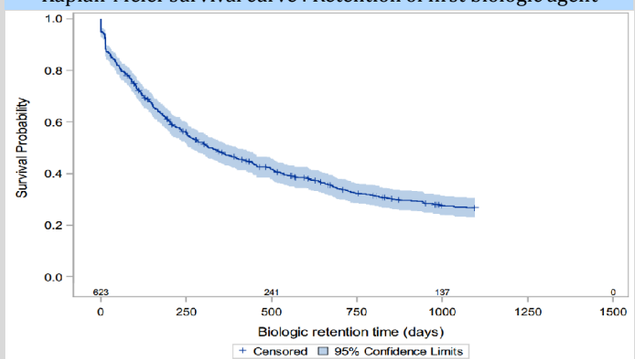
N	623
Age (years)	53.2 (12.4)
Women (%)	77.1%
Disease duration (years)	7.7 (8.3)
HAQ score	1.3 (0.6)
Fatigue (VAS)	4.5 (3.5)
Pain (VAS)	5.0 (3.3)
Morning stiffness (minutes)	92.8 (234.5)
Patient global assessment (VAS)	4.6 (2.9)
Physician global assessment (VAS)	2.0 (2.8)
CRP (mg/L)	13.0 (20.2)
ESR (mm/hr)	23.5 (20.9)
RF+ (%)	63.4%
Anti-CCP+ (%)	58.7%
DAS28-4(ESR)	4.1 (1.3)
CDAI	24.3 (13.2)

* Data are presented as means (SD), unless stated otherwise.

Selected predictors of biologic discontinuation

Variable		HR (95% CI)
Age (years)		1.00 (0.99-1.00)
Gender	Women vs Men	1.10 (0.90-1.35)
Disease duration (years)		1.00 (0.99-1.01)
Smoking	Yes vs No	0.98 (0.76-1.27)
Income	20 000$ to 39 999$ vs less than 20 000$	1.35 (1.01-1.80)
	40 000$ to 59 999$ vs less than 20 000$	1.11 (0.80-1.56)
	60 000$ to 79 999$ vs less than 20 000$	1.05 (0.69-1.60)
	80 000$ to 99 999$ vs less than 20 000$	2.16 (1.23-3.80)
Work	At home vs Full-time	0.85 (0.62-1.16)
	Sick leave vs Full-time	0.94 (0.56-1.59)
	Unable to work vs Full-time	1.49 (0.91-2.43)
	Retired vs Full-time	1.11 (0.85-1.45)
	Unemployed vs Full-time	0.92 (0.62-1.36)
	Part-time vs Full-time	1.57 (1.05-2.34)
	Student vs Full-time	1.01 (0.41-2.48)
Schooling	College vs Primary school	0.96 (0.63-1.47)
	Cegep vs Primary school	1.25 (0.75-2.10)
	Post graduate vs Primary school	0.91 (0.46-1.77)
	High school vs Primary school	1.00 (0.68-1.48)
	University vs Primary school	1.11 (0.73-1.68)

Kaplan-Meier survival curve : Retention of first biologic agent



RESULTS

A total of 623 eligible patients were treated with at least one biologic. The average age was 53.2 years (SD=12.4), 77% were women and patients had been diagnosed for an average of 7.7 years. The average time on treatment for the first biologic agent was 1.7 years (SD=2.1). In all, 233 (37%), 326 (52%), 405 (65%), and 438 (70%) patients had stopped their first biologic treatment after 6, 12, 24, and 36 months, respectively. In time-to-event analyses (Cox proportional hazard models), type of work [part time vs. full time; hazard ratio (HR): 1.57; 95% confidence interval (CI): 1.05-2.34] and income [$20,000 to $40,000 vs. less than $20,000 (HR: 1.35; 1.01-1.80) and $80,000 to $100,000 vs. less than $20,000 (HR: 2.16; 1.23-3.80)] were significantly associated with biologic discontinuation over the complete treatment duration. The number of disease-modifying antirheumatic drugs (DMARDs) used (HR: 0.89; 0.80-0.99) and the coconmitant use of methotrexate and hydrochloroquine (yes vs. no; HR: 0.80; 0.64-0.99) were associated with a reduced risk of biologic discontinuation.

CONCLUSIONS

In this real-life Canadian study, high biologic discontinuation rates were observed over three years. This study also suggests that income, work status, number of DMARDs used and concomitant use of MTX and hydroxychloroquine are predictors of biologic therapy discontinuation in RA patients. These results may help design interventions aiming at improving treatment adherence in RA, a chronic and progressive disease.

Dr. Denis Choquette is a full time rheumatologist and clinical researcher at Notre-Dame Hospital (*Centre Hospitalier de l'Université de Montréal*) and at the *Institut de Rhumatologie de Montréal*. He is the director of the Québec database of rheumatology (Rhumadata). Rhumadata is supported by a consortium of pharmaceutical companies including AbbVie, Amgen, Celgene, BMS Canada, Janssen, Roche and Pfizer. He has served as a speaker and consultant for all those companies. He is not a shareholder of any of those companies. Louis Coupal is a consulting biostatistician at the *Institut de Rhumatologie de Montréal*. Marie-Claude Laliberté and Olivier Desjardins are employees of AbbVie and own AbbVie shares.

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