Why Do Patients with Chronic Inflammatory Rheumatic Diseases Discontinue Their Biologics? An Assessment of Patients' Adherence Using a Self-report Questionnaire

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ABSTRACT. Objective. Concerns have been raised about nonadherence behavior among patients with chronic inflammatory rheumatic diseases (CIRD) receiving biologics. This nonadherence may be caused by various factors. The main objective was to explain why patients discontinue their biologics of their own accord.

Methods. A quantitative and descriptive study was performed using a self-report questionnaire that was sent through the Internet to members of different patient associations. Sociodemographic data, medical and therapeutic history, management of biologic administration, previous experiences, and patients' beliefs and perceptions about treatment efficacy and side effects were studied to explain self-discontinuation (SD).

Results. A total of 581 patients answered the questionnaire between June 16, 2012, and July 4, 2012, including patients with ankylosing spondylitis (351/581, 60.4%), rheumatoid arthritis (196/581, 33.7%), psoriatic arthritis (30/581, 5.2%), and other CIRD (4/581, 0.7%). More than 1000 different biologics were described by the 581 patients, with a median of 2 lines per patient. Eighty-six patients discontinued their biologics of their own accord (14.8%). In a multivariate analysis, factors that were significantly related to SD were low level of pain, more than 1 line of biologics tried, self-administration of biologics, negative beliefs about the treatment, and a lack of medical and social support. Conclusion. Five predictive factors of this SD were identified, which should be assessed in routine with patients with CIRD receiving biologic treatment: pain, treatment history, self-administration of injections, negative beliefs about treatment, and a lack of perceived medical and social support. (First Release February 15 2016; J Rheumatol 2016;43:724–30; doi:10.3899/jrheum.150414)

Key Indexing Terms: RHEUMATIC DISEASE ADHERENCE

BIOLOGICS BELIEFS DISCONTINUATION PATIENT EDUCATION

Compared with conventional disease-modifying antirheumatic drugs (DMARD), biologics have brought significant therapeutic advantages to the treatment of chronic inflammatory rheumatic diseases (CIRD): rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), and others. The high effectiveness of biologics on the evolution of CIRD has been demonstrated by randomized controlled trials and described in clinical practice 1,2,3,4,5,6.

However, many studies have also reported high discontinuation rates with biologics^{7,8,9,10}, the main causes being side effects and lack of efficacy¹¹.

Given these results, the issue of self-discontinuation (SD), discontinuation that is decided by the patient himself/herself, needs to be addressed. There is ample literature describing "adherence," a term that covers the 2 aspects of medication taking: regularity, which refers to "patient compliance," and

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Funded by a grant from the French Society of Rheumatology.

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Accepted for publication January 6, 2016.

continuity, which refers to "persistence" ¹². Adherence is an emerging aspect in the field of rheumatology, particularly among patients with CIRD treated with biologics ¹³. In a review by Koncz, *et al*, compliance rates ranged between 63% and 90% and persistence decreased steeply over time ¹⁴. Another review from Blum, *et al* gave an overall range of persistence of 32.0% to 90.9% after 12 months of treatment ¹⁵.

Poor adherence may undermine the potential therapeutic benefits of biologics by contributing to treatment failure, progression of disease, and potential comorbidities^{16,17}. Moreover, the economic burden of nonadherence is high given the high cost of biologics and the lack of benefits from partial treatment¹⁸. Therefore, identifying the reasons for this lack of adherence is a priority. Several authors have studied the association between adherence to biologics (estimated from pharmacy records) and some factors related to patients with CIRD, the disease, or the treatment^{19,20,21,22}, but to our knowledge none have used patient self-report to assess reasons for SD.

Between December 2011 and February 2012, we performed a preliminary qualitative analysis of medication adherence of patients receiving biologic therapy²³ and revealed 5 main categories to explain this behavior. The main objective of our present study was to confirm the previous figures and identify predictive factors of SD among patients with CIRD. We expected that chronology of the disease and treatments, healthcare organization, previous experiences, beliefs, relationship between the patient and the healthcare provider, perception of social support, and self-efficacy were related to SD.

MATERIALS AND METHODS

Design and study population. Ours was a prospective descriptive study. A self-report questionnaire was developed in March 2012 based on the initial qualitative phase²³. The questionnaire consisted of closed-ended and multiple choice questions grouped into 5 categories: (1) disease-induced impairment, (2) drug regimen complexity, (3) demographic and socioeconomic characteristics of the patient, (4) relation between the patient and the healthcare system, and (5) the patient's own resources (knowledge, beliefs, experience, motivation). The questionnaire was tested in May and June 2012 on 10 patients from the Rheumatology Clinic of the Grenoble University Hospital. After validation, the questionnaire was posted on the Internet and the link was sent by e-mail to the members of 3 major French patient associations: Association Nationale de Défense contre l'Arthrite Rhumatoïde (3500 members), Association Française de Lutte Anti-Rhumatismale (3000 members), and Association France Spondylarthritites (750 members). Data were collected between June 16, 2012, and July 4, 2012. Inclusion criteria were age > 18 years and CIRD treated (or formerly treated) with at least 1 biologic DMARD. All concomitant treatments were allowed.

We left the questionnaire posted online until we reached around 10% of respondents from the initial potential pool of targeted patients.

Measurements. Various methods, direct or indirect, are approved to measure medication adherence²⁴. In our quantitative analysis, we decided to look at the "SD" of biologics, which was better adapted to our self-declaration model than "nonadherence."

Assessment of discontinuation and SD. We defined discontinuation as stopping injections of a biologic either definitively, with possibly a switch

to another biologic, or temporarily. Discontinuation was assessed in 2 distinct parts of the questionnaire. First, patients were asked to name their first biologic and whether this therapy was still in progress. If not, they were asked to explain the reason for the discontinuation and who had decided on it ("the physician," "in agreement with the physician," "alone and then validated by the physician," or "alone without validation by the physician"). These questions had to be answered for each biologic used. Second, patients were asked if they had already tried to space out the injections of their biologic(s). If so, they were asked the name of the specific biologic and to explain the reason behind the interruption, who made the decision, and the duration of the break (questionnaire available from the authors on request).

SD was defined as the patient's decision to stop biologic injections. Patients were considered "SD patients" if they declared having discontinued their biologic injections by themselves ("alone" or "alone and then validated by a physician"), with the exception of patients who declared having spaced out their injections because of a sign of infection or planned surgery (situations where the action was considered appropriate).

Exploration of reasons for SD. A total of 21 different factors grouped into 3 domains were tested with SD patients in the univariate analysis:

- (1) Sociodemographic data (6 factors): age, sex, marital status, work status, highest level of study, and place of residence.
- (2) Pain, type of CIRD, disease duration, time to diagnosis, time since first biologic, number of biologic lines, number of physicians consulted since first symptoms.
- (3) Medical and therapeutic history (7 factors): pain over the last 8 days assessed by a visual analog scale (VAS) from 0 (no pain) to 10 (maximum pain), type of CIRD (RA, AS, PsA, or other), disease duration, time to diagnosis, time since first biologic, number of biologic lines, and number of physicians consulted since first symptoms. We defined a "biologic line" as each biologic drug treatment 1 patient had during their medication history (1 patient could accumulate several biologic lines).
 - (4) Management of biologics in daily life (8 factors):
 - Management of biologic administration: the person who administered the biologic ("myself," "a carer," "a nurse," or "other").
 - Previous experience of treatment: Side effects with biologic drugs and consequences on daily life (4-level scale); and use of complementary and alternative medicines (CAM).
 - Beliefs and perceptions about the efficacy of the biologic and side effects. From the qualitative analysis data, a series of 14 questions were developed to assess beliefs about disease and treatment among patients with CIRD receiving biologics. After a factorial analysis, questions were grouped into 5 factors:
 - Beliefs about treatments (3 statements: "In the past 3 months, I sometimes did not take my biologics because I feel that my treatment hurt me more than did good to me," "In the past 3 months, I sometimes did not take my biologics because certain weeks I was not convinced of its benefits," "In general, I find that drug treatment is poison.")
 - Perception of self-efficacy of self-injection (2 statements: "I'm afraid to make injections by myself," "I feel capable of making my injections.")
 - Perception of treatment efficacy (3 statements: "Concerning my daily routine I globally need help of a third person," "Thanks to my biologics, I was able to go back to a regular activity," "With the treatment I see things in a positive way.")
 - Medical and social support (3 statements: "In general, I feel involved by my doctor in the choice of my medical care," "My objective with the treatment is to be cured," "Close relatives and friends help me to pursue my treatment.")
 - Expected objective of the treatment (3 statements: "When I stop my biologics, I feel consequences in my body," "The perspective of suffering frightens me," "My objective with the treatment is to run a normal life.")

Statistical analyses. Categorical data are reported as frequency and percentage, and continuous data as average or median when appropriate.

Regarding data on patients' beliefs and perceptions about treatment efficacy and side effects, an exploratory factor analysis of the questionnaire was conducted using the nonorthogonal (Direct Oblimin) method of rotation as recommended by Kline²⁵ and Cattell²⁶. Results showed a 5-factor solution as suggested by factor scree plot explaining 59% of the variance. Then scores were calculated by adding items from each factor (or subgroup), with the hypothesis that the higher the score, the more likely patients were to self-discontinue. Univariate analyses were performed to compare characteristics between patients with RA and patients with AS, and between SD patients and other patients. The chi-square test was used for categorical data or the Fisher's exact test when appropriate, and the Student t test was used for continuous data (only for belief scores) or the Mann-Whitney U test when appropriate. The independent SD factors were tested using multivariate logistic regression, entering only variables associated with SD with a p value < 0.2 in univariate analysis. A backward stepwise selection was then performed to give the final model, which included only significant variables. The OR for SD against no SD and the associated 95% CI are reported for these variables. We considered p values < 0.05 significant. Statistical analyses were performed with STATA 12.0 (StataCorp).

This research was approved by the CECIC ("comité d'éthique des centres d'investigations cliniques") Rhône-Alpes Auvergne (No. IRB: 5891).

RESULTS

Characteristics of the population. Out of the 606 patients who responded to the questionnaire during the inclusion period, 581 were retained. Twenty-five patients were excluded: 15 answered twice, 9 gave inconsistent and/or inadequate data, and 1 was under 18 years old. From the majority of patients, 60.4% had AS (351/581), 33.7% RA (196/581), 5.2 PsA (30/581), and 0.7% other CIRD (4/581). Results were reported according to 3 groups: AS group (n = 351), RA group (n = 196), and other CIRD group (n = 34).

Sociodemographic data. The median age was 46 (42 for AS, 55 for RA, and 49 for other CIRD). Sociodemographic characteristics are presented in Table 1. All counties in France except 8 were represented, indicating a good geographical distribution of our sample throughout the country.

Medical and therapeutic history. The mean duration of the disease since first symptoms was 14.9 years for the AS group, 16.5 years for the RA group, and 18.5 for the other CIRD group. The mean time between first symptoms and diagnosis for the AS, RA, and other CIRD groups was 5.9 years, 2.5 years, and 5.9 years, respectively. Finally, the mean period between diagnosis and the first biologic line tried was 5.3 years, 8.5 years, and 6.1 years, respectively.

Average pain over the previous 8 days was estimated as 4.2/10 on the VAS, 4.5/10 for the AS group, 3.8/10 for the RA group, and 4.1 for the other CIRD group (p = 0.002). Patients reported having consulted an average of 4.7 different physicians since their first symptoms. A total of 1044 biologic lines were described (for each patient, this corresponded to a sequence of 1 or more biologic drugs), with a median of 2 biologic lines per patient (range from 1 to 7). The most cited biologics were etanercept (37.4%, 390/1044 biologics), adalimumab (29.8%, 311/1044), and infliximab (19.6%, 205/1044) for the AS group (39.8%, 33.6%, and 23.2%, respectively), RA group (33.7%, 23.4%, and 12.9%), and other CIRD group (36.4%, 31.8%, and 25.8%).

Management of biologic administration. A large majority of patients self-administered their biologic: 72.5% (235/324) for the AS group, 58.3% (102/175) for the RA group, and 76.7% for the other CIRD group (23/30; p = 0.003).

Previous experiences. Seventy-four percent of patients with AS (243/326), 63.6% of patients with RA (112/176), and 86.7% of patients with other CIRD (26/30) reported having already felt side effects (p = 0.006), and more than 85% agreed that it had disrupted their daily activities. CAM use was reported among 55.7% of patients with AS (177/318), 42.9% of patients with RA (72/168), and 66.7% of patients with other CIRD (20/30; p = 0.007).

Patients' beliefs and perceptions about the efficacy of biologics and side effects. Scores were calculated for each factor with the hypothesis that the higher the score, the more patients actually experienced SD (Table 2).

Discontinuation. About 74% of patients discontinued their biologics (431/581) at least once, and 79% of biologic lines were discontinued (823/1044). Among these discontinuations, 56.7% involved a switch to another biologic (467/823), 13.1% were definitive (108/823), and 30.1% were restarted (248/823). Regarding patients who restarted biologics, 39.6% (203/581) declared having spaced out their biologic injections, with a mean gap of 24.1 days. Among the 431 patients who discontinued their biologics at least once, 86 patients were included in the SD group, which means that 20% of discontinuations were the patient's decision.

Among the 581 patients of our study, 14.8% experimented with SD. Fifty-seven percent (49/86) were patients with AS, 36% (31/86) were patients with RA, and 7% (6/86) were patients with other CIRD (p = 0.638), representing about 10% of biologic lines (112/1044). Reasons for these SD are presented in Table 3.

Factors related to SD. Factors significantly related to SD by univariate analysis (for a p value < 0.05) were more than 1 line of biologics tested, self-administered biologics, use of CAM, negative beliefs about treatment, and lack of medical and social support (Table 4 and Table 5). Significant factors related to SD in the univariate model for a p value < 0.2 were entered into the multivariate model. Factors associated with SD in our sample of patients with CIRD (for a p value < 0.05) were lower level of pain, more than 1 line of biologics tried, self-administered biologics, negative beliefs about treatment, and lack of perceived medical and social support.

Type of CIRD or sex were not associated to adherence.

DISCUSSION

In our study, 14.8% of patients with CIRD self-discontinued their biologics. Five predictive factors of this SD were identified: pain (low level), treatment history (more than 1 line of biologics tried), self-administration of injections, negative beliefs about treatment, and lack of perceived medical and social support.

Table 1. Sociodemographic characteristics. Values are n (%) unless otherwise specified.

Characteristics	All Diseases, $n = 581$	RA, n = 196	AS, $n = 351$	Other CIRD, $n = 34$	p	
Female sex	434 (74.7)	164 (83.7)	245 (69.8)	25 (73.5)	0.002	
Marital status						
Married	326 (56.1)	118 (60.2)	195 (55.6)	13 (38.2)	< 0.001	
Living with someone	97 (16.7)	26 (13.3)	68 (19.3)	3 (8.8)		
Single	95 (16.3)	22 (11.2)	62 (17.7)	11 (32.3)		
Divorced	49 (8.4)	19 (9.7)	23 (6.6)	7 (20.6)		
Widowed	14 (2.4)	11 (5.6)	3 (0.8)	0 (0.0)		
Children, yes	426 (73.3)	157 (80.1)	247 (70.4)	22 (64.7)	0.024	
Work status						
Active					< 0.001	
Permanent employment	258 (44.6)	55 (28.5)	189 (53.8)	14 (41.18)		
Self-employed	29 (5.0)	8 (4.1)	18 (5.1)	3 (8.8)		
Temporary employment	26 (4.5)	3 (1.5)	23 (6.6)	0 (0.0)		
Unemployed	37 (6.4)	11 (5.7)	25 (7.1)	1 (2.9)		
Others	2 (0.3)	2 (1.0)	0(0.0)	0 (0.0)		
Inactive						
Temporary or definitive cess	ation					
of work	107 (18.5)	38 (19.6)	61 (17.4)	8 (23.5)		
Retired	105 (18.2)	68 (35.2)	29 (8.3)	8 (23.5)		
In training	9 (1.6)	4 (2.1)	5 (1.4)	0 (0.0)		
Others	5 (0.9)	4 (2.1)	1 (0.3)	0 (0.0)		
Level of study						
No academic qualification, or s	chool-leaving					
certificate only	30 (5.2)	7 (3.6)	20 (5.7)	3 (8.8)	0.028	
High school graduation	238 (40.9)	90 (45.9)	138 (39.3)	10 (29.5)		
Higher education, undergradua	te degree,					
or vocational training	313 (53.9)	99 (50.5)	193 (55)	21 (61.7)		

RA: rheumatoid arthritis; AS: ankylosing spondylitis; CIRD: chronic inflammatory rheumatic diseases.

Table 2. Patients' beliefs and perceptions about the efficacy of biologics and side effects. Values are mean (median, minimum-maximum) unless otherwise specified.

Various Subgroups	All Patients	SD Patients	Other Patients	p
Beliefs about treatments, out of 12 patients, high score = negative beliefs	5.6 (5, 3–12)	6.8 (7, 3–12)	5.4 (5, 3–12)	< 0.001
Perception of SE of self-injections, out of 8 patients, high score = low SE perceived	3.8 (3, 2–8)	3.6 (3, 2–8)	3.9 (3.5, 2–8)	0.253
Perception of treatment efficacy, out of 12 patients, high score = low efficacy perceived	6.0 (6, 3–12)	6.0 (6, 3–12)	6.0 (6, 3–11)	0.927
Medical and social support, out of 12 patients, high score = lack of support Expected objective of the treatments, out of 12 patients, high score = negative	6.4 (6, 3–12)	6.9 (7, 3–11)	6.3 (6, 3–12)	0.003
expected objective expected objective	6.1 (6, 3–11)	6.1 (6, 3–9)	6.1 (6, 3–11)	0.810

SD: self-discontinuation; SE: self-efficacy.

Table 3. Reasons for self-discontinuation.

Reasons*	n = 112	%
"I felt better."	43	38.4
"I felt side effects."	32	28.6
"Treatment didn't work."	15	13.4
"I was fed up."	10	8.9
"I was afraid about health effects."	8	7.1
Other reason	4	3.6

^{*} One reason per discontinued biologic.

Only 1 study, from Bluett, et al¹⁷, used a self-reported questionnaire to quantify nonadherence, defined as whether the previously due dose of biologic therapy was reported as not taken on the day agreed with the healthcare professional. To our knowledge, even if our questionnaire was validated on a small sample, our study is the only one trying to predict nonadherence with a self-questionnaire, exploring treatment management, previous experiences, and patient's beliefs and perceptions about treatment to determine reasons for nonadherence among patients with CIRD.

Table 4. Variables associated with SD in univariate analysis for a p value < 0.2 and included in the multivariate analysis.

Various Factors A	All Patients, $n = 581$, n (%)	SD Patients, $n = 86$, n (%)	Others, n = 495, n (%)	p
Pain, VAS between 0 and 4	316 (54.4)	55 (63.9)	261 (52.7)	0.054*
Time since first symptoms, longer than 10 yrs	361 (63.3)	58 (69.9)	303 (62.2)	0.181*
No. biologics tried, more than 1 line	299 (51.8)	55 (63.9)	244 (49.7)	0.015
Person who does the injection, self-administration	360 (68.0)	67 (77.9)	293 (66.1)	0.032
Experiences of side effects	381 (71.6)	68 (79.1)	313 (70.2)	0.096*
Consumption of alternative medicine	269 (52.1)	53 (62.3)	216 (50.1)	0.039
Factors about "patient's beliefs and perceptions about treatment efficacy and side effects"	t All Patients, Mean (Median, Min–Max)	SD Patients, Mean (Median, Min–Max)	Other Patients, Mean (Median, Min–Max)	p
Beliefs about treatments, out of 12 patients,				
high score = negative beliefs	5.6 (5, 3–12)	6.8 (7, 3–12)	5.4 (5, 3–12)	< 0.001
Medical and social support, out of 12 patients, high score = lack of support	6.4 (6, 3–12)	6.9 (7, 3–11)	6.3 (6, 3–12)	0.003

^{*} Factor not significant in univariate analysis (p > 0.05) but included in multivariate analysis (because p < 0.2). SD: self-discontinuation; VAS: visual analog scale.

Table 5. Variables associated to self-discontinuation in univariate and multivariate analysis.

Variable	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p	OR (95% CI)	p
Pain, VAS between 0 and 4	1.59 (0.99–2.56)	0.054	2.00 (1.19–3.38)	0.009
No. biologics tried, more than 1 line	1.80 (1.12-2.89)	0.015	2.01 (1.20-3.36)	0.008
Person administering biologic,				
self-administration	1.81 (1.05-3.12)	0.032	1.82 (1.02-3.26)	0.044
Experienced side effects	1.61 (0.92-2.80)	0.096	NS	NS
Use of alternative medicine	1.65 (1.02-2.66)	0.039	NS	NS
Beliefs about treatments, score 1–12	1.40 (1.25-1.57)	< 0.001	1.43 (1.27-1.61)	< 0.001
Medical and social support	1.23 (1.07-1.42)	0.003	1.17 (1.00-1.36)	0.046

VAS: visual analog scale; NS: not significant.

Our sample came from 3 patients' associations: 1 composed of patients with RA, 1 of patients with AS, and 1 of all types of CIRD. Compared with patients with CIRD in a US cohort, the median age of patients with AS and patients with RA was similar (42 and 55 years in our study vs 43 and 50 years in the US study, respectively), but the sex ratio was very different, with a predominance of women (0.4, 0.2, and 0.4 vs 1.5, 0.3, and 1.00, respectively)²⁷. Further, we also had more patients with AS in our sample than in a French cohort (60.4% vs 41.6%, respectively) and fewer patients with RA $(33.7\% \text{ vs } 50\%)^{28}$. These differences may be explained by our use of the Internet, which may be more accessible for younger people, such as patients with AS, and also by the overrepresentation of women in the patient associations we targeted. The need to use the Internet may have also selected patients with better educational and social status, which was higher in our study compared with the national data (the National Institute for Statistics and Economic Studies, 2009).

Out of the 581 patients included, about 15% self-discontinued. This estimate is in the same range as that of Bluett, *et al* (27% of self-declared nonadherence, all causes

confounded)¹⁷. Our results are in the lower range of rates found in the literature¹⁴; it may be underestimated because the rate of SD was based on self-reports that required patients to recall details of past experiences (such as dates and names of drugs). Moreover, we should not forget the social desirability bias, whereby patients report an overly optimistic estimate of their adherence to treatment²⁹.

Concerning our sample size, we consider that the maximum number of explanatory variables that can be included in a multivariate model is 1 for 10 to 15 events (to avoid the risk of overadjustment). In our study, we identified 86 events (86 patients who experimented with SD); therefore, we could include 9 variables maximum in our multivariate analysis. In practice, we included 8 variables (or factors) because these were significantly related to SD for a p value < 0.2 in our univariate analysis (on the 21 factors tested). Finally, a backward stepwise selection was then performed to give the final model, with 5 independent SD factors (for a p value < 0.05).

The first factor related to SD in our study was pain. The more pain the patient experienced, the better their adherence

to their biologic. This correlation was independent of the type of disease. Similar results have been reported in fibromyalgia³⁰. However, pain was measured over the last 8 days, while participants may have discontinued their biologics far longer ago. Further investigation should analyze the evolution of pain during time and its link to adherence. Relief from pain could be interpreted by the patient as a remission, which may lead to discontinuation^{11,31}. In contrast, pain leading up to the next injection may be perceived as a treatment efficacy, which is the most influential factor for longterm persistence according to Brod, *et al*³².

The duration of therapy seems to be a major component of adherence. Our results show that the number of different lines of therapy tried by the patient is an independent factor for discontinuation. Persistence to biologic treatments decreases with time, as Koncz, *et al* reported in a review of the literature¹⁴.

According to the literature, the previous experience of side effects is also a major driver of discontinuation ^{32,33,34}. In our study, more than 70% of patients declared having already felt side effects. However, no significant correlation with SD was found.

There is little evidence of the link between CAM and adherence. Our univariate analysis suggests that patients who self-discontinued were more likely to use CAM than others. Westhoff and Zink showed that a preference for CAM was the strongest risk predictor of lack of adherence to DMARD therapy among patients with RA³⁵. In our multivariate model, this relationship does not remain significant.

In our study, patients who self-administered their biologics were also more predisposed to discontinue their biologics compared with patients whose injection was given by someone else. A qualitative study has suggested that the most critical period concerning adherence to self-injectable treatment is the first month of therapy³². During this period, patients need encouragement and support to continue self-administered treatment.

The relationship between drug adherence and beliefs about medication among patients with RA was described by Neame, *et al* using the Belief about Medicines Questionnaire³⁶. In line with this, we concluded a significant correlation between negative beliefs and SD (impression that treatment hurts more than does good, and that it is like a poison).

Further, we found that medical and social support were significantly related to SD, which suggests that a supportive environment may improve adherence to a biologic. Regarding internal resources, we found no significant correlation between self-efficacy and SD in our study, although the literature reports this factor as an important determinant of adherence^{37,38}. However, de Klerk, *et al*³⁷ and Brus, *et al*³⁸ assessed self-efficacy among patients with conventional DMARD only and did not use the same questionnaire.

Our study identified several components of SD behavior among patients with CIRD receiving biologics. Pain, treatment history, self-administration of injections, beliefs about treatment, and medical and social support are all factors to take into consideration when a patients with CIRD is prescribed a biologic. These patterns may be useful to better target patients who are more likely to discontinue their biologics by themselves, and to adapt our patient education programs. In the light of these predictive factors of SD, we have identified 3 major educational objectives for patients with CIRD receiving biologics: (1) to improve knowledge about the efficacy and side effects of biologics, and to identify and help modify negative beliefs, (2) to enhance medical and social support, especially during the first month of self-administered therapy, and (3) to enhance motivation over the longterm with the implementation of a regular followup program to ensure longterm adherence.

ACKNOWLEDGMENT

We thank the staff of the research laboratory *Techniques de l'Ingénierie Médicale et de la Complexité - Informatique, Mathématiques et Applications, Grenoble*; the patients' associations *Association Nationale de Défense contre l'Arthrite Rhumatoïde, Association France Spondylarthritites*, and *Association Française de Lutte Anti-Rhumatismale*, and the Rheumatology Outpatient Clinic team at the Grenoble University Hospital. We also thank Dr. Alison Foote (Grenoble Clinical Research Centre) for critical reading and editing of the manuscript.

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