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## Two-Year Abatacept Retention Rate in Clinical Practice in the French ACTION Cohort

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## **ABSTRACT**

**Objectives:** Abatacept retention rates were evaluated in the French cohort in the prospective ACTION study (2010-2013), which included patients with moderate-to-severe rheumatoid arthritis managed in everyday clinical practice and started on intravenous abatacept therapy.

**Methods:** Two-year abatacept retention rates were evaluated in 455 patients classified according to treatment line, body mass index (BMI), and status for rheumatoid factor (RF) and anti-citrullinated peptide antibody (ACPA).

**Results:** After 2 years, the overall abatacept retention rate was 44%. The retention rate was nonsignificantly higher in the patients with vs. without a history of unresponsiveness to at least one biologic (48.1% vs. 41.8%, respectively). No significant retention rate differences were found across BMI categories (444 patients; <25, 45.5%;  $\geq$ 25 to <30, 48.9%; and  $\geq$ 30, 36.6%). Neither were any significant differences demonstrated according to RF and ACPA status (RF+ and ACPA+, 45.7%; RF+ or ACPA+, 43.8%; and RF- and ACPA-, 39.1%).

**Conclusion:** The 44% 2-year retention rate in the French ACTION cohort supports the usefulness of abatacept therapy. In this study, retention was not associated with treatment line, BMI, or antibody status.

**Keywords:** Abatacept. Biologic. Real-life study. Drug retention rate. Rheumatoid arthritis. National specificity.

## 1.Introduction

Rheumatoid arthritis (RA) is the most common inflammatory joint disease in adults [1]. The large strides made over the past 15 years in the management of RA include the optimization of conventional synthetic disease-modifying antirheumatic drug (csDMARD) therapy, licensing of biologic agents, parsimonious use of glucocorticoids, and development of strategies that combine several drug classes.

The recommendations for the management of RA issued by the EULAR [2] and the 2018 updated guidelines of the French Society for Rheumatology (*Société Française de Rhumatologie*) [3] indicate that DMARD therapy should be initiated early, starting with methotrexate alone or, if needed, combined with a brief course of glucocorticoid therapy [3]. If methotrexate is inadequately effective or poorly tolerated, targeted treatments are in order in patients with adverse prognostic factors [3] such as early erosions; positive tests for rheumatoid factor (RF) and/or anti-citrullinated peptide antibodies (ACPAs), particularly in high titers ( $\geq 3N$ ); persistent moderate-to-high disease activity with high erythrocyte sedimentation rate (ESR) and C-reactive protein values and/or high tender and swollen joint counts despite csDMARD therapy; and failure of two or more csDMARDs [3,4,5]. The presence of comorbidities and preferences of the patient also influence the treatment decisions [3].

All the available biologic DMARDs (bDMARDs) have been proven to alleviate the symptoms and to slow structural disease progression in patients with RA who have an inadequate response to methotrexate. However, among patients given TNF $\alpha$  antagonist therapy, 30% to 50% stop the treatment within 1 year, due to either poor tolerance or inefficacy [6]. Many of these patients are then given a different bDMARD, which produces

improvements in 60% to 70% of cases. The bDMARD retention rate decreases gradually as the number of previous bDMARDs used increases.

Abatacept in its intravenous formulation was approved in Europe in May 2007 for the treatment of adults with moderate-to-severe RA and an inadequate response to one or more TNF $\alpha$  antagonists. In July 2010, the approved indication was extended to include methotrexate failure or intolerance. A subcutaneous abatacept formulation was introduced in 2014 after it was found non-inferior to intravenous abatacept [7].

The drug retention rate is a simple parameter that reflects treatment efficacy and tolerance. Only observational studies and real-life registries can provide information on drug retention rates. Prospective registries have been set up in several countries to evaluate the retention rate of abatacept, such as the ORA in France (2008-2010) [8] and the pan-European registry collaboration for abatacept (PANABA) [9].

To complement these registry data, the international prospective observational study ACTION (AbataCepT In rOutiNe clinical practice) was conducted in Europe and Canada in 2008-2015 [10]. Under real-life treatment conditions, the overall 2-year abatacept retention rate was 47.9% (95% confidence interval [95%CI], 45.7%-50.0%). Retention was significantly higher in bDMARD-naïve patients than in patients having failed at least one bDMARD (54.5% [95%CI, 50.5%-58.3%] vs. 45.2% [95%CI, 42.7%-47.7%], respectively;  $P < 0.001$ ) [11].

Here, we examined the data from the patients included into the ACTION study in France with the objectives of identifying possible country-specific features of abatacept retention and of describing the treatment regimens used in everyday clinical practice. Patient inclusion into the ACTION study in France occurred after the French ORA registry was closed, and the present study therefore adds to the information available from other French nationwide investigations.

## 2. Methods

### Study design and population

ACTION (NCT02109666) was a 2-year prospective international observational study conducted in 11 European countries (Austria, Belgium, the Czech Republic, Denmark, France, Germany, Greece, Italy, The Netherlands, Spain, and Switzerland) and Canada. The objective was to assess the 2-year abatacept retention rate under the conditions of everyday practice. Inclusion criteria were age above 18 years, fulfillment of revised 1987 ACR criteria for moderate-to-severe RA, and initiation within the past 3 months of intravenous abatacept therapy in compliance with local marketing authorizations. The only non-inclusion criterion was simultaneous participation in another clinical study.

Changes in the approved indications of abatacept therapy in the participating countries during the patient recruitment period led to the differentiation of three cohorts, as follows: patients naive to bDMARD therapy or having failed at least one bDMARD ( Cohort A, May 2008-December 2010), patients naive to bDMARD therapy (cohort B, September 2010-December 2013), and patients having failed at least one bDMARD (ohort C, October 2011-December 2013)

The patients were followed-up for 2 years or for 6 months after abatacept discontinuation. Mean follow-up was 460 days. Data collection was stopped on January 25, 2016. No patients were included into the cohort A in France, as the ORA registry was open at the time. The 2-year abatacept retention rates were evaluated in the overall population and in the subgroups defined by treatment line (i.e., B vs C), body mass index category (BMI; <25 kg/m<sup>2</sup>, 25-30 kg/m<sup>2</sup>, or ≥30 kg/m<sup>2</sup>), and antibody status category (RF+ and ACPA+, RF+ or

ACPA+, and RF- and ACPA-). In addition, comorbidities were collected by completion of a box for additional information and a predefined list of health conditions.

## **Statistical analysis**

### *Abatacept retention rate*

Abatacept retention after 2 years was defined as continuous abatacept therapy (via the subcutaneous or intravenous route) for 2 years. Reasons for abatacept discontinuation included primary and secondary inefficacy and any other reasons. Switching from the intravenous to the subcutaneous route was not classified as discontinuation. The nonparametric Kaplan-Meier method was applied to assess treatment duration with its 95% confidence interval (95%CI) in the overall population. Abatacept treatment duration was defined as the time between the first abatacept infusion date + 1 day and the date of a reported event, such as death, date of last contact or date of last FU available). Abatacept discontinuation was defined as a period of more than 84 days without an abatacept dose, i.e., as missing two consecutive intravenous infusions, regardless of whether abatacept therapy was re-started subsequently. In a sensitivity analysis, patients who resumed abatacept therapy within 6 months after at least 84 days without a dose were classified as having continued their abatacept therapy. As observed data were analyzed, without imputation for missing data.

### *Efficacy*

The 2-year clinical response rate to abatacept was evaluated in each subgroup using the EULAR criteria based on the Disease Activity Score on 28 joints (DAS 28). Patients were categorized as good responders, moderate responders, or nonresponders. Remission was defined according to the EULAR criteria as a DAS 28 (ESR or CRP) <2.6 or a DAS 44 <1.6 or a Simple Disease Activity Index (SDAI)  $\leq$ 3.3 or a Clinical Disease Activity Index (CDAI)  $\leq$ 2.8 or presence of the Boolean remission criteria.

## *Safety*

During this observational study, all serious adverse events that occurred during follow-up were collected until the study completion date.

### **3. Results**

#### **Baseline patient Characteristics**

Of the 456 patients included by 77 rheumatologists in France, 455 were assessable (**Figure 1**), including 153 (33.6%) naive to bDMARDs (cohort B) and 302 (66.4%) having failed at least one bDMARD (cohort C). Mean age was  $61.7 \pm 11.8$  years in the cohort B and  $58 \pm 12.2$  years in the cohort C. In both cohorts, over 70% of patients were female. The BMI was available for 444 (97.6%) patients, of whom over half were in the overweight or obesity range (30.9% and 21.7% of B-cohort patients and 32.5% and 23.6% of C-cohort patients, respectively). Of the 390 patients whose RF and ACPA status was available, 277 (71%) were RF+ and ACPA+, 46 (12%) were RF+ or ACPA+, and 67 (17%) were RF- and ACPA-.

In the cohort B, mean disease duration was  $9.4 \pm 10.5$  years, and 92.8% of patients had previously taken methotrexate. At abatacept initiation, 16.9% of patients were taking a csDMARD (other than methotrexate) and 67.3% a glucocorticoid. The cohort C had a longer mean disease duration of  $13.8 \pm 9.9$  years and a mean number of previous csDMARDs of  $1.3 \pm 1.1$  per patient, with 94.4% of patients having taken methotrexate; 46.7% and 53.3% having taken one and two TNF $\alpha$  antagonists, respectively; and 84.8% having received a glucocorticoid (**Table 1**). The reason for discontinuation of the most recent treatment was primary inefficacy in 25.5%, secondary inefficacy in 44.0%, and adverse effects in 26.8% of patients.

## **Treatment regimens**

Abatacept was used as single-drug therapy in 15% of cohort B and 27.2% of cohort C patients. Corresponding proportions of patients given abatacept in combination with other drugs were 85% and 72.8%, respectively. Glucocorticoid therapy was given concomitantly to 67.3% of cohort B and 65.6% of cohort C patients, in a mean daily dosage of 5 mg.

Comorbidities in the cohort B and C , respectively, were as follows: smoking, 19% and 19.2%; chronic obstructive pulmonary disease, 9.2% and 11.9%; cardiovascular disease, 8.5% and 8.6%; psychiatric disorders, 2% and 4.3%; neurological disorders, 2.6% and 3.3%; and malignancies, 2.6% and 1.3%) (**Table 1**).

## **Two-year abatacept retention rate**

After 2 years, 83/455 (18%) patients had been lost to follow-up, leaving 372 patients for the analysis. The overall 2-year abatacept retention rate was 44.0% (95%CI, 39.2%-48.8%). The 2-year retention rate was nonsignificantly higher in the cohort B than in the cohort C (48.1% [95%CI, 39.8%-56.0%] vs. 41.8% [95%CI, 35.8%-47.7%]; log rank test,  $P=0.22$ ) (**Figure 2**).

The reasons for abatacept discontinuation were similar in the two cohorts. Inadequate efficacy was the reason for discontinuation in 63.3% of cohort B patients and 68.5% of cohort C patients; corresponding proportions for discontinuation due to adverse events were 16.3% and 17.6%.

A period longer than 84 days without an abatacept dose was recorded for 57 cohort B patients and 107 cohort C patients, who were classified as having discontinued abatacept therapy in the per protocol analysis. Among these patients, the proportion with abatacept treatment resumption within 6 months was higher in the cohort B than in the cohort C (27/57, 47.4% and 41/107, 38.3%, respectively). In the sensitivity analysis, these patients who

resumed treatment within 6 months were not classified as having discontinued abatacept therapy. The 2-year abatacept retention rates were then 67.2% (95%CI, 59.0%-74.2%) in the cohort B and 62.3% (95%CI, 56.2%-68.4%) in the cohort C (**Figure 2**). **Table 2** reports the main features of these patients at abatacept interruption and resumption. At resumption, 37% of patients had CDAI values indicating low disease activity or remission compared to 46.2% at the last evaluation preceding the interruption; corresponding proportions of patients with DAS 28 values indicating low disease activity were 10.3% and 18.4%, respectively. The proportions of patients also taking glucocorticoid therapy were higher at abatacept resumption than at the last evaluation preceding the interruption (51.5% and 57.4%, respectively).

### **Subgroup analyses of the 2-year treatment response and retention rates**

The treatment response was similar in the cohort B and cohort C patients still taking abatacept therapy after 2 years, with good-to-moderate EULAR response rates of 90.9% vs. 78.6%, respectively ( $P=0.08$ ). The proportions of patients in remission, defined as DAS 28-ESR and DAS 28-CRP values  $<2.6$  and as meeting Boolean remission criteria (**Table 3**), were also similar in the two groups (DAS 28-ESR: 50.0% and 45.2%,  $P=0.64$ ; DAS 28-CRP: 55.4% and 58.1%;  $P=0.64$ ; Boolean criteria: 25.0% and 28.4%,  $P=0.593$ ).

In the 444 patients with available BMI data, 2-year abatacept retention rates were as follows:  $<25$  kg/m<sup>2</sup>, 45.5% (95%CI, 38.1%-52.6%); overweight, 48.9% (95%CI, 39.9%-57.2%); and obese, 36.3% (95%CI, 26.7%-46.0%). The differences across the three subgroups were not statistically significant ( $P=0.147$ ).

In the 390 patients for whom RF and ACPA data obtained before abatacept initiation were available, 2-year abatacept retention rates were not significantly different across antibody status subgroups ( $P=0.418$ ): RF+ and ACPA+, 45.7% (95%CI, 39.5%-51.8%); RF+

or ACPA+, 43.8% (95%CI, 28.3%-58.3%); and RF- and ACPA-, 39.1% (95%CI, 26.8%-51.2%).

### **Safety data**

During the study period, severe infections were diagnosed in 28 (6%) patients, including 3 opportunistic infections (1 case each of *Pneumocystis jirovecii* infection, candidiasis, and herpes zoster infection). In addition, 13 (3%) patients experienced immune-related disorders (psoriasis, n=3; and hypersensitivity reactions, n=7), 7 (1.5%) cardiac events, 5 (1%) vascular events, and 5 (1%) cancer. Finally, 4 (0.9%) patients died (1 case each of acute respiratory distress, cardiac arrest, and myocardial infarction; the cause of death was not recorded in the remaining patient).

## **4. Discussion**

In France, patients were included into the ACTION study between September 2010 and December 2013. The results in this country-specific cohort can be compared to the reported overall data [11-13]. The 44.0% retention rate in France was similar to the 47.9% rate internationally. Depending on the study subgroups, the retention rates in the cohort C patients were also similar in France and internationally (41.8% vs. 45.2%, respectively).

In France, abatacept retention rates have also been evaluated in the ORA registry of patients started on the drug between January 2007 and October 2010. The 2-year retention rate in ORA registry F-cohort patients was 42.5%, which was similar to the 41.8% value in French ACTION cohort C patients [14].

The 2-year abatacept retention rates in the ACTION study in France were similar to those in Germany but lower than those in the cohorts B from Austria (68.5%), Italy (67.8%), and Switzerland (64.8%) and in the cohorts C from Austria (58.0%) and Italy (54.8%) [11]. Retention rate differences across cohorts B may be related to differences in disease duration and severity in the patients included in France, who had a 2-year longer mean disease duration compared to the international population, as well as a higher mean disease activity level (SDAI, 29.1 vs. 25.4). In the cohort C, in contrast, disease activity in France was lower than internationally (SDAI, 27.2 vs. 31.9). Another possible explanation to the retention rate differences in the cohorts B and C across European countries -- and more specifically between France and Germany on one hand and Austria, Italy, and Switzerland on the other -- lies in the existence of intrinsic features of each country [9]. Thus, multivariate analyses of data from the international PANABA cohort identified associations linking retention rate differences across countries to differences in access to bDMARDs, gross domestic product, clinician perceptions, and propensity of clinicians to switch among bDMARDs. Nevertheless, in the PANABA study, inefficacy and adverse events as reasons for abatacept discontinuation were more common in the registries from France (ORA), Sweden (ARTIS), and Switzerland (SQCM). Predictors of discontinuation due to inefficacy were a higher number of previous DMARDs, younger age, worse DAS 28 at abatacept initiation, and RF- status. A higher number of previous DMARDs and older age predicted discontinuation due to adverse events.

Use of bDMARDs other than TNF $\alpha$  antagonists may also affect retention rates and drug switching. A pharmaco-epidemiological study of data from a Danish and Swedish registry suggests that patients who fail a first TNF $\alpha$  antagonist should be switched to a bDMARD that has another mechanism of action, as opposed to a second TNF $\alpha$  antagonist [15]. Similarly, in a noninterventional retrospective study of data collected between 2010 and 2013 in Germany in patients having failed a first TNF $\alpha$  antagonist, 1-year retention rates were significantly

higher when the second bDMARD was not a TNF $\alpha$  antagonist [16]. Finally, in the French ROC randomized controlled trial of patients comparing a second TNF $\alpha$  antagonist to a non-TNF $\alpha$  antagonist bDMARD after failure of a first TNF $\alpha$  antagonist, low disease activity after 52 weeks was more common in the non-TNF $\alpha$  antagonist group (41% vs. 23%; odds ratio, 2.26; 95%CI, 1.33-3.86;  $P=0.003$ ) [17].

The proportions of overweight and obese patients in the French ACTION study are consistent with those expected among patients with RA [18]. In neither the French nor the international cohorts was BMI associated with the abatacept retention rate [19]. Consistently with results of the post-hoc analysis of ACQUIRE randomized controlled trial of subcutaneous vs. intravenous abatacept: pharmacokinetic or clinical outcomes were similar across patient BMI [20].

The analysis of serological status subgroups, in contrast, evidenced differences between the French and international populations. In the ACTION study patients included in France, the 2-year retention rate in the RF+ and ACPA+ subgroup was not significantly different from that in the RF+ or ACPA+ and RF- and ACPA- subgroups (45.7%, 43.8%, and 39.1%, respectively). Internationally, however, the subgroup positive for both antibodies had significantly higher 6-month and 2-year retention rates compared to the subgroup with neither antibody [21,22]. The absence of associations with serological status in the French cohort may be merely related to insufficient statistical power. A post hoc analysis of data from the randomized controlled AMPLE trial comparing abatacept to adalimumab showed that the response rates in both groups were significantly higher in the patients with very high ACPA titers [23]. This finding suggests that the ACPA status may be more relevant than the RF status and that the two should probably be investigated separately.

In the French ACTION study, 47.4% of cohort B and 38.3% of cohort C patients had an at least 84-day period without abatacept doses then resumed abatacept therapy within 6

months. The reasons for these treatment interruptions are unclear and deserve further investigation to better delineate practice patterns and to improve the evaluation of retention rates in everyday clinical practice.

This study has the limitations inherent in investigations performed under real-life conditions, including absence of active comparisons and patient attrition over time potentially resulting in a substantial amount of missing clinical data. The abatacept treatment modalities reported here reflect everyday clinical practice in France over the inclusion period from 2010 to 2013. Practices and recommendations have changed since 2013 and, therefore, the results reported here cannot be extrapolated to subsequent periods.

In conclusion, the data from the French ACTION study confirm the therapeutic value of IV abatacept on 2-year retention rates under real-life conditions [24] in adults with moderate-to-severe RA who are either naive to bDMARDs or have failed one or more bDMARDs.

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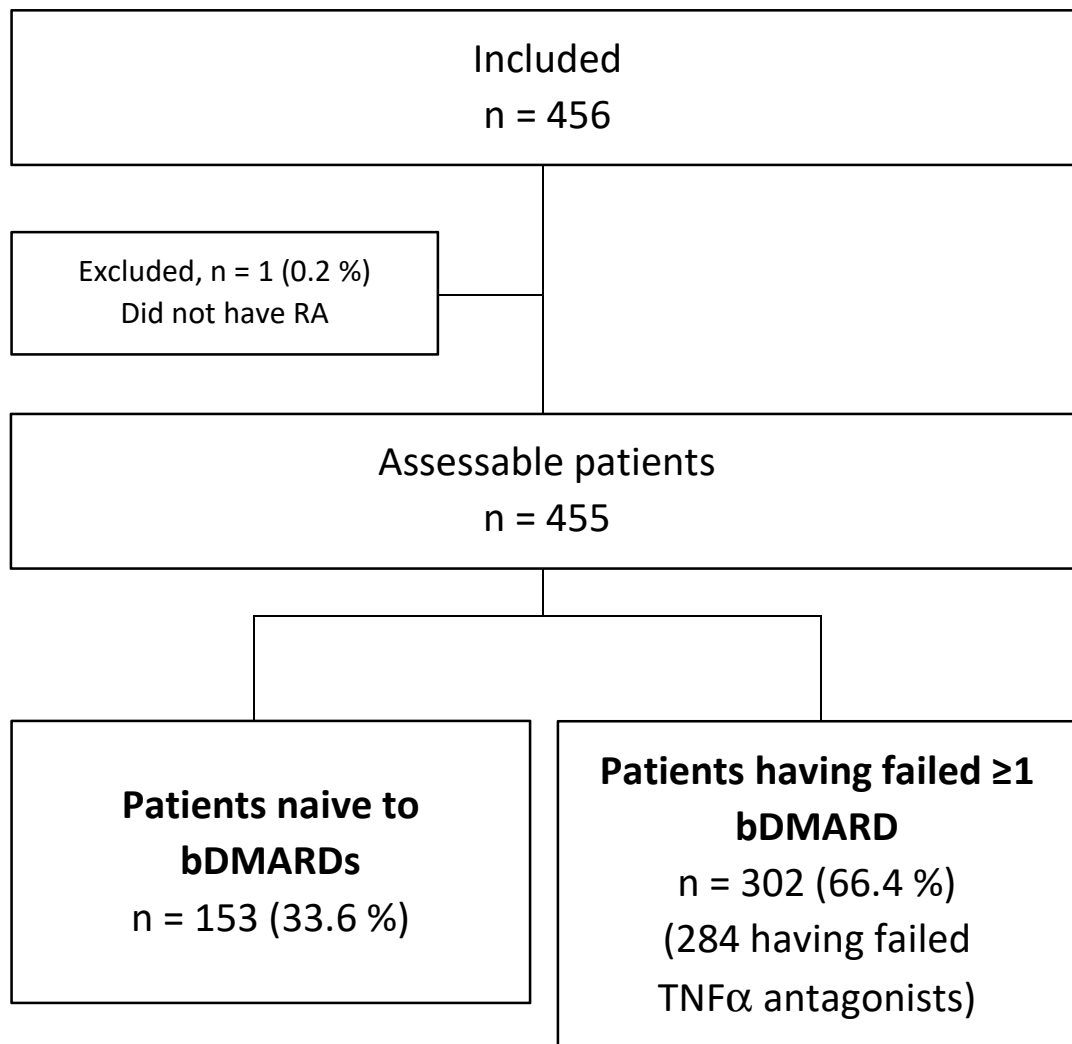
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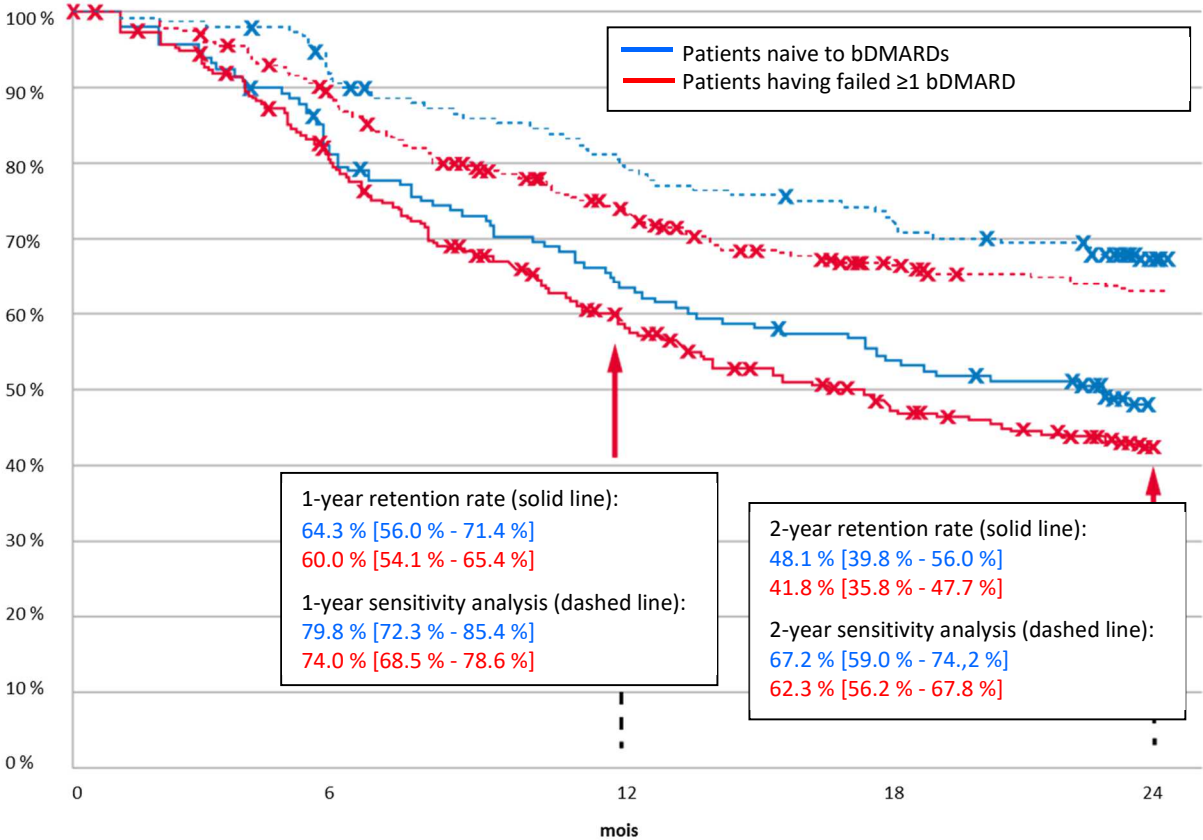
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**Figure 1:** Flow chart of patients recruited in France



**Figure 2:** Two-year abatacept retention rates in the 153 patients naive to biologics and the 302 patients having failed at least one biologic, in the per protocol (solid line) and sensitivity (dashed line) analyses. In the per protocol analysis, patients who received no abatacept dose for 84 consecutive days, i.e., who missed two consecutive doses, were classified as having discontinued abatacept therapy. In the sensitivity analysis, patients who received no abatacept dose for at least 84 days but resumed abatacept therapy within 6 months were not classified as discontinuations.



Patients at risk	Month 6			Month 12			Month 18			Month 24		
	1 <sup>st</sup> line	1 previous bDMARD	> 1 bDMARDs	1 <sup>st</sup> line	1 previous bDMARD	> 1 bDMARDs	1 <sup>st</sup> line	1 previous bDMARD	> 1 bDMARDs	1 <sup>st</sup> line	1 previous bDMARD	> 1 bDMARDs
n	124	80	161	94	54	109	82	41	85	50	23	40

**Table 1:** Baseline patient characteristics in the cohort naive to biologics (cohort B) and in the cohort with failure of at least one biologic (cohort C)

	cohort B <sup>a</sup>		cohort C <sup>a</sup>	
	n		n	
Age, years, mean±SD	153	61.7 (11.8)	302	58.0 (12.2)
Females, % (n)	153	71.2 % (109)	302	78.8 % (238)
BMI, kg/m <sup>2</sup> , mean±SD	152	26.6 (5.8)	292	26.6 (6.0)
BMI, % (n)				
<25 kg/m <sup>2</sup>		47.4 % (72)		43.8 % (128)
25 - <30 kg/m <sup>2</sup>	152	30.9 % (47)	292	32.5 % (95)
≥30 - <35 kg/m <sup>2</sup>		11.8 % (18)		14.0 % (41)
≥35 kg/m <sup>2</sup>		9.9 % (15)		9.6 % (28)
RA duration, years, mean±SD	153	9.4 (10.5)	302	13.8 (9.9)
Number of previous csDMARDs <sup>b</sup>				
mean±SD	153	1.01 (1.0)	302	1.3 (1.2)
≤3, % (n)		100 % (153)		95.7 % (289)
>3, % (n)		0 % (0)		4.3 % (13)
Number of previous TNFα antagonists				
mean±SD		NA	302	1.61 (0.81)
1, % (n)		NA		46.7 % (141)
≥2, % (n)		NA		53.3 % (161)
DAS 28 (ESR)	136	4.8 (1.2)	258	4.9 (1.3)
DAS 28 (CRP)	140	4.5 (1.1)	276	4.6 (1.2)
CDAI	131	23.7 (10.1)	208	25.4 (11.9)
SDAI <sup>c</sup>	129	25.4 (11.0)	206	27.2 (12.8)
RF and ACPA status, n (%)				
RF- and ACPA-		12.4 % (18)		17.3 % (49)
RF+ or ACPA+	145	12.4 % (18)	283	9.9 % (28)
RF+ and ACPA+		66.2 % (96)		64.0 % (181)
unknown		9.0 % (13)		8.8 % (25)
Radiographic erosion, % (n)	144	63.9 % (92)	290	77.2 % (224)
≥1 comorbidity, % (n)	153	84.3 % (129)	302	74.2 % (224)
Smoking		19.0 % (29)		19.2 % (58)

COPD	9.2 % (14)	11.9 % (36)
Cardiovascular disease	8.5 % (13)	8.6 % (26)
Psychiatric disorders	2.0 % (3)	4.3 % (13)
Neurological disorders	2.6 % (4)	3.3 % (10)
Malignancy	2.6 % (4)	1.3 % (4)

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BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS 28, Disease Activity Score on 28 joints; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; CDAI, Clinical Disease Activity Index; SDAI, Simple Disease Activity Index; RF, rheumatoid factors; ACPA, anti-citrullinated peptide antibodies; COPD, chronic obstructive pulmonary disease

<sup>a</sup>The cohort B was composed of patients naive to biologics and the cohort Bof patients having failed at least one biologic.

<sup>b</sup>Other than methotrexate and glucocorticoids

<sup>c</sup>Algebraic sum of five RA parameters (swollen joint count, tender joint count, patient evaluation of disease activity, physician assessment of disease activity, and C-reactive protein level)

**Table 2:** Disease activity at abatacept interruption and resumption in the patients who received no abatacept dose for at least 84 consecutive days but resumed abatacept therapy within 6 months after the last dose

DAS 28 (ESR), mean±SD	3.6 (1.2)	4.1 (1.5) (n=58)
DAS 28 low activity, % (n)	18.4 % (9)	10.3 % (6)
DAS 28 remission, % (n)	22.4 % (11)	17.2 % (10)
CDAI, mean±SD	12.0 (7.0)	15.2 (11.8) (n=46)
CDAI low activity or remission, % (n)	46.2 % (18)	37.0 % (n=17/46)
EULAR response good or moderate, % (n)	63.3 % (31)	50.8 % (30) (n=30/59)
Boolean remission, % (n)	4.1 % (2)	11.9 % (n=7/59)
Concomitant treatments	n = 68	n = 68
Glucocorticoid therapy, % (n)	51.7 % (30)	57.4 % (39)
Methotrexate, % (n)	62.1 % (36)	54.4 % (37)

DAS 28, Disease Activity Score on 28 joints; ESR, erythrocyte sedimentation rate; CDAI, Clinical Disease Activity Index

**Table 3:** Two-year treatment response rate (% of responders)

	cohort B <sup>a</sup>		cohort C <sup>a</sup>		P value
	n <sup>b</sup>	%	n <sup>b</sup>	%	
EULAR response good to moderate	55	90.9 %	70	78.6 %	0.08
DAS 28 (ESR) <2.6	52	50.0 %	73	45.2 %	0.64
DAS 28 (CRP) <2.6	56	55.4 %	74	58.1 %	0.64
Boolean remission	56	25.0 %	74	28.4 %	0.593

DAS 28, Disease Activity Score on 28 joints; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

<sup>a</sup>The cohort B was composed of patients naive to biologics and the cohort C of patients having failed at least one biologic.

<sup>b</sup>number of patients with available 2-year data