Two-year treatment persistence with subcutaneous abatacept in rheumatoid arthritis: results from the French cohort of the ASCORE study

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Abstract

Objective

While multiple studies have investigated treatment persistence rates with intravenous abatacept, limited information is available about real-world treatment continuation with the subcutaneous form. The international ASCORE study described the characteristics and treatment persistence of real-world patients with rheumatoid arthritis (RA) receiving subcutaneous abatacept. This article presents the findings of the French cohort.

Methods

This was an observational study in French RA patients who initiated subcutaneous abatacept between August 2014 and January 2017. The primary endpoint was treatment maintenance at 2 years, analysed according to the number of previous biologic therapies.

Results

Of 546 evaluable patients, 281 (51.5%) were biologic-naive, 265 (48.5%) had experienced failure with 1 (n=134; 24.5%) or ≥2 (n=131; 24.0%) biologic therapies. At enrolment, patients who had experienced failure with ≥1 biologic therapy had more erosions and a longer duration of RA compared with biologic-naive patients, but had comparable mean disease activity scores. Overall, 43.0% of patients (95% confidence interval 38.6–47.2) were still taking subcutaneous abatacept at 2 years, which was comparable with that in other countries participating in ASCORE. The abatacept persistence rate was higher in biologic-naive patients (48.8%) than in those with 1 (40.9%) or ≥2 (32.8%) biologic therapy failures. The main reason for discontinuing abatacept was lack of efficacy (46.6%).

Conclusion

In current practice in France, the rate of subcutaneous abatacept persistence at 2 years was comparable with that of the intravenous form. Treatment persistence was higher when abatacept was used as first-line versus later-line biologic therapy.

Key words

abatacept, rheumatoid arthritis, disease-modifying anti-rheumatic drugs, real-world study, treatment persistence

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Competing interests: see page 1384.

Introduction

Rheumatoid arthritis (RA) is the most common form of chronic inflammatory rheumatism in adults, with an estimated prevalence of 0.31% in France and 0.54% in Europe (1, 2). According to French and European recommendations updated in 2019, RA management is based on the early first-line use of methotrexate monotherapy, possibly combined with short-term corticosteroid therapy (3, 4). If the patient has an inadequate response to, or cannot tolerate, methotrexate, and unfavourable prognostic factors, the recommendation is to add a targeted therapy.

Abatacept has been approved in Europe in intravenous (IV) form since 2007, and is one of the biologics that does not target tumor necrosis factor (TNF). Instead, abatacept acts by selectively modulating the costimulatory signal required for T-cell activation (5). It is indicated, in combination with methotrexate, for the treatment of moderate-to-severe active RA in adult patients who have had an inadequate response to previous treatment with one or more disease-modifying antirheumatic drugs (DMARDs), including methotrexate or anti-TNF agents. A subcutaneous (SC) formulation of abatacept was first introduced in 2014 as a pre-filled syringe, then in 2015 as a pre-filled pen for self-injection by the patient. For many biologics that are available in both IV and SC formulations, including abatacept, the SC form is often preferred by patients due to its greater flexibility of use (6, 7). Non-inferiority clinical studies have demonstrated that the efficacy and tolerability of abatacept SC are comparable with those of abatacept IV and the anti-TNF drug adalimumab (8).

Randomized clinical trials have limited external validity, so observational studies are essential to assess the effectiveness and tolerability of therapies under real-world conditions in a heterogeneous patient population with complex management challenges (9). In this context, treatment persistence is a simple, robust, and relevant assessment tool, because it reflects both the effectiveness and tolerability of therapy (10). Various prospective registries have been established to assess treatment persistence with abatacept IV in patients with RA. The 'Orencia and Rheumatoid Arthritis' (ORA) registry in France (2008–2010), in which almost all patients had biologic therapy failure, showed 2-year persistence rate of 42.5% (11). In addition, the international observational AbataCepT In rOutiNe clinical practice (ACTION) study, conducted in Europe and Canada between 2008 and 2013, showed 2-year persistence rates with abatacept IV of 47.9% for the overall cohort and 44.0% for the French cohort (12, 13).

However, these studies, which were conducted before the introduction of the SC formulation of abatacept, focused exclusively on abatacept IV. In order to specifically assess treatment persistence with abatacept SC in patients with RA, the observational Abatacept SubCutaneOus in Routine clinical practicE (ASCORE) study was implemented across 10 European countries (14). In the overall cohort of 2892 patients, the rate of persistence with abatacept SC at 2 years was 47.3% (95% confidence interval [CI] 45.6–49.2), but in the subgroups of biologic-naive patients and those who have experienced ≥1 or ≥2 previous biologic therapy failures, the 2-year persistence rates were 51.7%, 45.6%, and 43.2%, respectively (14). The aim of the current article is to describe real-world treatment persistence with abatacept SC at 2 years in the French cohort of ASCORE patients, and to put this into perspective with that observed in the other countries participating in ASCORE and in the overall cohort, taking into account differences in health care systems and access to biologic therapies.

Methods

Study methodology and population

ASCORE (NCT02090556) was a 2-year international, prospective, longitudinal, observational study that was conducted in 10 countries (Australia and nine European countries – Austria, France, Germany, Greece, Italy, the Netherlands, Spain, Switzerland and the United Kingdom) (14). The main objective of the study was to assess treatment persistence with abata-

cept SC during routine clinical practice over 2 years in RA patients, overall and stratified by prior biologic use, in each country and in the combined international cohort. The secondary objective was to provide a descriptive analysis of the characteristics of patients treated with abatacept SC in real-world clinical practice.

The study included adults (>18 years) with moderate-to-severe active RA according to the American College of Rheumatology/European League Against Rheumatism (EULAR) 2010 criteria, who were naive to abatacept IV therapy, and within the last 6 months had started treatment with abatacept SC 125 mg/week administered by syringe or pre-filled pen (14). Three patient cohorts were analysed based on previous biologic therapy: 1) naive to biologic therapies; 2) failure with one previous biologic agent; and 3) failure with ≥2 previous biologic agents (14). The only exclusion criterion for the study was concurrent participation in an interventional clinical trial in RA (14).

Abatacept SC therapy had to be initiated by the participating rheumatologist irrespective of whether the patient would be included in the study, and in accordance with the terms of marketing authorisation and standard clinical practice in each country. The rheumatologists participating in the study were randomly selected from independent national databases, and thus constituted a representative sample of specialists in the management of RA in each of the participating countries. To limit patient selection bias, rheumatologists were required to include eligible patients in the study in a consecutive manner.

Patient enrolment took place between February 2013 and April 2017 for the overall cohort, and between August 2014 and January 2017 for the French cohort. Patients were followed for 30 months following the typical assessment schedule at each institution. It was estimated that patients would be evaluated every 3 months, with ≥1 annual visit conducted as part of the initial hospital prescription. If abatacept SC was discontinued, patients continued to be followed for up to 24 months from the start of treatment.

Data collected and endpoints assessed

The primary endpoint was the rate of treatment persistence with abatacept SC at 2 years (duration of abatacept SC therapy until discontinuation), analysed according to the number of previous biologic therapies. Discontinuation of abatacept SC was defined as switching to abatacept IV, switching to another biologic therapy, discontinuation of abatacept SC for more than 28 days, or permanent discontinuation of abatacept SC. The duration of abatacept SC therapy was calculated as the date of last observed or censored dose minus the date of the first SC injection plus 7 days. For patients lost to follow-up, the date of the last documented abatacept SC dose was considered to be the date of therapy discontinuation. Thus, the patients lost to follow-up at 2 years were considered as having discontinued the drug.

Secondary endpoints included the rate of therapeutic maintenance of abatacept by any route of administration (*i.e.* not considering the switch from SC to IV as treatment discontinuation), and therapeutic response to abatacept SC at 2 years, assessed by line of therapy. Patients who completed the therapy (and were still on abatacept SC therapy at 2 years) were classified as good responders or moderate responders according to their EULAR response based on the activity score (Disease Activity Score-28 [DAS28] with erythrocyte sedimentation rate [ESR] or with C-reactive protein) (15). Furthermore, the proportion of patients with low disease activity or in remission was determined according to the following three definitions: DAS28-ESR ≤3.2, Simple Disease Activity Index (SDAI) ≤11 or Clinical Disease Activity Index (CDAI) ≤10 (16). The therapeutic response was also assessed according to the Boolean remission criteria (17).

Patient demographics and RA characteristics were collected at enrolment and analysed by line of therapy. Adherence to abatacept was assessed using patient-reported data (patient diaries), and calculated as a percentage of the total number of injections performed compared with the total number of injections the patient should receive during the treatment period. A patient with adherence of 80% to 120% was considered to have very good adherence to therapy. Finally, all adverse events (AEs) occurring during the study were collected for tolerability analysis.

Ethics

The study was conducted in accordance with the Declaration of Helsinki and the international guidelines for Good Clinical Practice and Good Epidemiological Practice. Ethics approval was obtained from each participating centre, and all included patients gave their informed consent to participate in the study, in accordance with the local regulations of each country.

Statistical analyses

Statistical analyses were performed with SAS software v. 9.4.

- Sample size

The sample size of the overall cohort was estimated to be at least 2646 patients (1053 biologic-naive patients and 1593 patients with ≥1 previous biologic therapy failure), based on feasibility studies conducted in each country. The French feasibility study estimated enrolment of 510 patients (189 biologic-naive and 321 with ≥1 biologic therapy failure), *i.e.* about 20% of the overall cohort.

Assuming a 2-year treatment persistence rate of 60%, the estimated sample size of the overall cohort would have around 3% precision for the cohort of biologic-naive patients and 2.5% for the cohort with ≥1 biologic therapy failure. For the analyses performed at national level, a sample of at least 150 patients per line of therapy and per country was considered sufficient to estimate the therapeutic maintenance rate at 2 years with acceptable precision (<7.8%), assuming 2-year treatment persistence of 60%.

- Statistical methodology

All patients meeting the enrolment criteria and having received ≥1 dose of abatacept SC were included in the evaluable population. The primary endpoint (treatment persistence at 2 years by line of therapy) was estimated using Kaplan-Meier analysis with 95% CIs. Patient characteristics at enrolment,

therapeutic response at 2 years and incidence of AEs were analysed using descriptive statistics including mean and standard deviation (SD) for continuous variables and number and percentage of patients for categorical variables.

Role of the funding source
The ASCORE study was funded by Bristol-Myers Squibb (BMS). BMS participated in the development of the protocol, operational monitoring of the study, and analysis of the results.

Results

Study population and characteristics at enrolment

In France, 553 patients were enrolled by 121 rheumatologists, and 546 patients (98.7%) were evaluable (Fig. 1). As estimated, the French cohort represented about 20% of the overall study cohort (2956 enrolled and 2892 evaluable patients in the overall cohort).

About half of the evaluable patients in the French cohort (281/546; 51.5%) were biologic-naive. Patients who experienced failure of ≥1 previous biologic therapy (n=265; 48.5%) were split evenly between failure of one biologic agent (n=134; 24.5%) and failure of ≥2 biologic agents (n=131; 24.0%). Previous biologic therapy included an anti-TNF agent in 92.5% of patients.

The patient characteristics at enrolment are presented in Table I. The mean age at enrolment was approximately 57 years, and the majority of patients (79%) were female. The three cohorts analysed were broadly comparable in terms of mean age (approximately 57 years), gender distribution, and body weight (mean body mass index 26 kg/m^2, with a majority of patients being overweight or obese).

Compared with biologic-naive patients, those who experienced ≥1 biologic therapy failure had a longer duration of illness: the mean (SD) duration of RA was 7.8 (8.2) years in biologic-naive patients, and 11.9 (9.7) and 16.4 (11.2) years in those who had experienced failure of 1 or ≥2 biologic agents, respectively. Similarly, the proportion of patients with erosions was higher in the cohorts with previous biologic therapy failure than in the biologic-naive cohort: 52.7% (biologic-naive), 63.6% (failure of one biologic) and 76.4% (failure of ≥2 biologics).

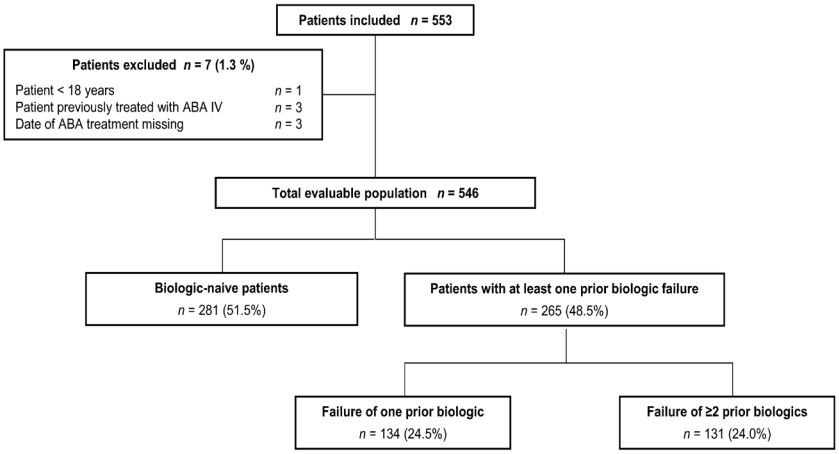

Fig. 1. Patient disposition in the French cohort of the ASCORE study.
ABA: abatacept; IV: intravenous.

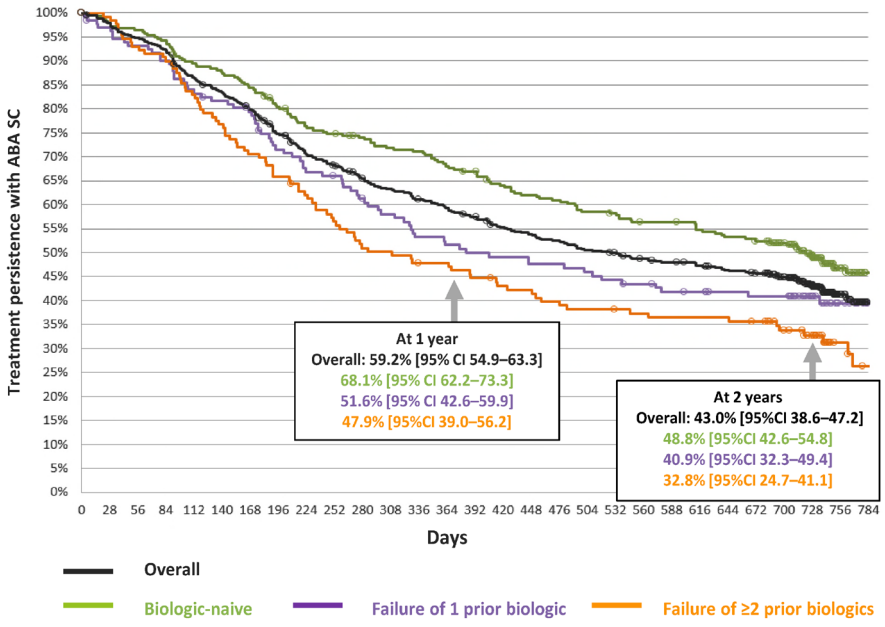

Fig. 2. Treatment persistence with subcutaneous abatacept in the French cohort of the ASCORE study.
ABA: abatacept; CI: confidence interval; SC: subcutaneous.

The mean (SD) scores for disease activity at abatacept SC initiation were broadly similar regardless of the number of previous biologic therapies: DAS28-ESR at 4.8 (1.3) in all subgroups, CDAI from 24.2 (11.9) to 24.6 (10.7), and SDAI from 25.5 (12.1) to 26.1 (11.3) for the three cohorts.

Fewer than 20% of patients in each group received a loading dose of abatacept IV before starting abatacept SC therapy: 14.6% in the biologic-naive group, and 19.4% and 16.0% in those with 1 or ≥2 biologic therapy failures, respectively.

Treatment persistence rate at 2 years

The 2-year treatment persistence rate was 43.0% (95% CI 38.6–47.2) in the overall French cohort (Fig. 2). This rate was highest in biologic-naive patients (48.8%; 95% CI 42.6–54.8), intermediate in those who had experienced failure of one biologic (40.9%; 95% CI 32.3–49.4), and lowest in those who had experienced failure of ≥2 biologics (32.8%; 95% CI 24.7–41.1).

Two patients switched from abatacept SC to abatacept IV during the study (re-

Table I. Patient characteristics at enrolment in the French cohort of the ASCORE study.

	Biologic-naive (n=281)		Failure of 1 biologic therapy (n=134)		Failure of ≥2 biologic therapies (n=131)	
	n		n		n	
Mean (SD) age, years	281	56.5 (13.7)	134	57.3 (12.3)	131	58.3 (14.2)
Women, n (%)	281	222 (79.0)	134	105 (78.4)	131	103 (78.6)
Mean (SD) weight, kg	281	70.9 (15.7)	134	69.4 (16.9)	131	70.0 (14.8)
Mean (SD) BMI, kg/m^2	279	26.1 (5.4)	133	26.0 (5.5)	120	26.2 (5.1)
Mean (SD) duration of RA, years	281	7.8 (8.2)	134	11.9 (9.7)	131	16.4 (11.2)
Number of previous conventional DMARDs*	281		134		131	
Mean (SD) number		0.6 (0.8)		0.6 (0.8)		0.6 0.8)
1 to 2 therapies, %		37.4		38.8		40.5
≥3 therapies, %		2.8		3.0		3.1
Number of previous anti-TNF therapies			134		131	
Mean (SD) number		N/A		0.9 (0.4)		2.0 (0.7)
1 therapy, %		N/A		85.8		22.1
≥2 therapies, %		N/A		0		77.1
Therapies combined with ABA SC	280		134		131	
ABA SC used as monotherapy, %		3.6		9.7		12.2
Combination with methotrexate, %		74.6		69.4		55.0
Combination with corticosteroids, %		62.1		59.0		57.3
Mean (SD) DAS28-ESR	235	4.8 (1.3)	116	4.8 (1.3)	97	4.8 (1.3)
Mean (SD) DAS28-CRP	251	4.5 (1.2)	123	4.6 (1.1)	116	4.5 (1.2)
Mean (SD) CDAI	258	24.2 (11.9)	118	24.5 (11.0)	117	24.6 (10.7)
Mean (SD) SDAI	250	25.5 (12.1)	118	26.0 (11.5)	114	26.1 (11.3)
RF and anti-CCP status, %	215		95		78	
Double positive		66.0		60.0		66.7
Single positive (one positive/one negative)		20.5		24.2		19.2
Double negative		13.5		15.8		4.1
Presence of radiographic erosion, %	260	52.7	121	63.6	106	76.4
Patients with ≥1 comorbidity, %	281	65.1	134	61.9	131	67.2

*Excluding methotrexate and corticosteroids.
ABA: abatacept; BMI: body mass index; CCP: citrullinated cyclic peptides; CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; DAS28: 28-joint Disease Activity Score; DMARDs: disease-modifying anti-rheumatic drugs ESR: erythrocyte sedimentation rate; N/A: not applicable; RA: rheumatoid arthritis; RF: rheumatoid factor; SC: subcutaneous; SD, standard deviation; SDAI: Simplified Disease Activity Index; TNF: tumour necrosis factor.

corded as therapy discontinuation in the above analysis). A secondary analysis of the treatment persistence rate at 2 years was performed in which switching from SC to IV therapy was not considered as a discontinuation; the 2-year treatment persistence rate of abatacept (regardless of route of administration) was 43.7% (95% CI 39.3–48.0) in the overall cohort, which is comparable with the 43.0% rate observed in the main analysis.

Of the 298 recorded cases of SC abatacept discontinuation at 2 years, almost half (46.6%) were due to lack of efficacy and 18.1% were due to the occurrence of an AE. Other reported reasons for discontinuation included initiation of another biologic therapy (5.4%), patient refusal to continue therapy unrelated to the occurrence of an AE (3.7%), patient lost to follow-up (3.0%), protocol deviations (1.3%), and remissions (0.7%).

After discontinuation of abatacept SC, 41.4% of patients received another biologic therapy, which was an anti-TNF agent in 18.9% of patients and other biologic agents in 22.5%; 11.0% of patients resumed treatment with abatacept SC and 21.6% of patients remained without treatment. The median (range) duration of follow-up after abatacept discontinuation was 439 (1–1078) days.

Information about adherence to treatment was available from 143 patients; adherence was very good in 96.5% of the evaluated patients.

Clinical efficacy at 2 years

Of the 235 patients who were still on abatacept SC at 2 years, 193 completed therapy (82.1%) and therapeutic response was evaluated in 133 patients who completed therapy and had available clinical efficacy data (56.6%) (Table II). The proportion of these patients with a good or moderate EULAR response was 75.0% in biologic-naive patients, and 80.6% and 76.9% in those who had previously experienced failure of 1 or ≥2 biologic therapies, respectively, although the number of patients in these latter two groups was low (n=39 and n=38, respectively).

The proportion of patients with weakly active RA or in DAS28-ESR remission were broadly similar in all three cohorts when this parameter was assessed using the DAS28-ESR score or the proportion of patients in Boolean remission. However, when the proportion of patients with weakly active RA/ in remission was calculated using the CDAI and SDAI, a numerically lower percentage of patients met the criteria in the group who had experienced failure of ≥2 biologic therapies than in the other two cohorts (Table II).

Tolerability

During the follow-up period, 291 patients (53.3%) experienced ≥1 AE; of these, 186 patients (34.1%) experienced ≥1 abatacept-related AE. The incidence rate for abatacept-related AEs in the French cohort was 53 events per 100 patient-years. In patients who had previously received 1 or ≥2 biologics, the incidence rate was 47 and 58 events per 100 patient-years, respectively (Table III).

Similarly, 105 patients (19.2%) experienced ≥1 serious AE (SAE), of which 69 patients (12.6%) experienced ≥1 abatacept-related SAE. The incidence rate for abatacept-related SAEs in the French cohort and in patients who had previously received 1 biologic was 14 events per 100 patient-years. In patients who had previously received ≥2 biologics, the incidence rate was 18 events per 100 patient-years (Table III). Abatacept-related injection site reactions had an incidence rate of 0.88 events per 100 patient-years in the overall cohort.

Serious musculoskeletal disorders, infections, and cardiac disorders occurred in 19 patients (3.5%), 17 patients (3.1%), and 12 patients (2.2%), respectively (Table IV). Among patients who developed serious infections, bronchitis, sepsis, vulvovaginal mycotic infection, and pneumonia occurred in two patients (0.4%) each (Table IV). Serious local injection site reactions were observed in eight patients (1.5%).

Discussion

In the French cohort of the ASCORE study, under actual conditions of clinical use, the 2-year treatment persistence rate with abatacept SC was 43.0% (95% CI 38.6–47.2). Persistence rates were higher in biologic-naive patients (48.8%) than in those who had previously experienced failure of biologic therapies (40.9% after failure of one agent, and 32.8% after failure of two or more agents). The study also showed a favorable therapeutic response at 2 years and a favourable tolerability profile of abatacept SC under real-world conditions, consistent with the results of randomised controlled trials (8), and no new safety signals were identified.

The 2-year persistence rate of 43.0%

Table II. Proportion of patients with a therapeutic response after 2 years of subcutaneous abatacept therapy in the French cohort of the ASCORE study*.

	Biologic-naive (N_{compl} = 116)		Failure of 1 biologic therapy (N_{compl} = 39)		Failure of ≥2 biologic therapies (N_{compl} = 38)	
	n_{compl}	%	n_{compl}	%	n_{compl}	%
EULAR response	76		31		26	
Good, %		55.3		54.8		38.5
Good or moderate, %		75.0		80.6		76.9
Low RA activity or in remission						
DAS28-ESR ≤3.2, %	76	63.2	28	64.3	24	62.5
CDAI ≤10, %	98	70.4	35	68.6	33	60.6
SDAI ≤11, %	77	67.5	31	71.0	27	59.3
Boolean remission	81	25.9	31	22.6	27	29.6

*This analysis was made in 193 patients who completed therapy and were continuing the treatment at 2 years (82.1% of the included patients).
N_{compl} = total number of patients who completed therapy and were still treated with abatacept SC at 2 years (total N_{compl} = 193); n_{compl} = number of patients who completed therapy with available clinical efficacy data (total N_{compl} = 133).
CDAI: Clinical Disease Activity Index; DAS28: 28-joint Disease Activity Score; ESR: erythrocyte sedimentation rate; EULAR: European League Against Rheumatism; RA: rheumatoid arthritis; SC: subcutaneous; SDAI: Simplified Disease Activity Index.

Table III. Incidence rates of adverse and serious adverse events (per 100 patient-years) during abatacept (subcutaneous/intravenous) intake in the French cohort of the ASCORE study.

	First-line	Second-line or more	Failure of 1 biologic therapy	Failure of ≥2 biologic therapies	All
AE	107.49	104.23	93.37	116.15	106.09
SAE	23.09	25.46	23.99	27.08	24.11
Related AE	52.85	52.46	47.34	58.43	52.75
Related SAE	12.57	15.96	14.27	17.81	14.03
Injection site reactions	0.77	1.70	1.95	1.43	1.17
Serious injection site reactions	0.26	0.34	0.00	0.71	0.29
Treatment-related injection site reactions	0.51	1.36	1.95	0.71	0.88
Treatment-related serious injection site reactions	0.00	0.34	0.00	0.71	0.15

AE: adverse events; SAE: serious adverse events.

Table IV. Serious adverse events during abatacept (subcutaneous/intravenous) intake in the French cohort of the ASCORE study.

SOC/PT	All (n=546) n (%)	95% CI
Any	105 (19.2)	16.0–22.8
General disorders and administration site conditions	35 (6.4)	4.5–8.8
Musculoskeletal and connective tissue disorders	19 (3.5)	2.1–5.4
Infections and infestations	17 (3.1)	1.8–4.9
Bronchitis	2 (0.4)	0.1–1.3
Sepsis	2 (0.4)	0.1–1.3
Vulvovaginal mycotic infection	2 (0.4)	0.1–1.3
Pneumonia	2 (0.4)	0.1–1.3
Infection	1 (0.2)	0.0–1.0
Lung infection	1 (0.2)	0.0–1.0
Urinary tract infection	1 (0.2)	0.0–1.0
Urosepsis	1 (0.2)	0.0–1.0
Cervicitis human papilloma virus	1 (0.2)	0.0–1.0
Coronavirus	1 (0.2)	0.0–1.0
Diverticulitis	1 (0.2)	0.0–1.0
Erysipelas	1 (0.2)	0.0–1.0
Herpes zoster virus	1 (0.2)	0.0–1.0
Lower respiratory tract infection	1 (0.2)	0.0–1.0

Table IV. *continued*

SOC/PT	All (n=546) n (%)	95% CI
Pyelonephritis	1 (0.2)	0.0–1.0
Sinusitis	1 (0.2)	0.0–1.0
Cardiac disorders	12 (2.2)	1.2–3.8
Myocardial infarction	3 (0.5)	0.1–1.6
Angina pectoris	2 (0.4)	0.1–1.3
Pericarditis	2 (0.4)	0.1–1.3
Acute coronary syndrome	2 (0.4)	0.1–1.3
Cardiac arrest	1 (0.2)	0.0–1.0
Cardiac failure congestive	1 (0.2)	0.0–1.0
Cardiopulmonary failure	1 (0.2)	0.0–1.0
Arrhythmia	1 (0.2)	0.0–1.0
Atrial fibrillation	1 (0.2)	0.0–1.0
Injury - poisoning and procedural complications	10 (1.8)	0.9–3.3
Respiratory - thoracic and mediastinal disorders	10 (1.8)	0.9–3.3
Lung disorder	3 (0.5)	0.1–1.6
Dyspnea	1 (0.2)	0.0–1.0
Haemoptysis	1 (0.2)	0.0–1.0
Acute respiratory failure	1 (0.2)	0.0–1.0
Asthma	1 (0.2)	0.0–1.0
Chronic obstructive pulmonary disease	1 (0.2)	0.0–1.0
Cough	1 (0.2)	0.0–1.0
Obstructive airways disorder	1 (0.2)	0.0–1.0
Oropharyngeal pain	1 (0.2)	0.0–1.0
Neoplasms benign - malignant and unspecified (including cysts and polyps)	7 (1.3)	0.5–2.6
B-cell lymphoma	1 (0.2)	0.0–1.0
Breast cancer	1 (0.2)	0.0–1.0
Transitional cell carcinoma	1 (0.2)	0.0–1.0
Hepatic cancer	1 (0.2)	0.0–1.0
Neoplasm	1 (0.2)	0.0–1.0
Paget's disease of the nipple	1 (0.2)	0.0–1.0
Pancreatic neoplasm	1 (0.2)	0.0–1.0
Squamous cell carcinoma of skin	1 (0.2)	0.0–1.0
Vascular disorders	5 (0.9)	0.3–2.1
Haematoma	1 (0.2)	0.0–1.0
Peripheral ischaemia	1 (0.2)	0.0–1.0
Aneurysm ruptured	1 (0.2)	0.0–1.0
Deep vein thrombosis	1 (0.2)	0.0–1.0
Lymphoedema	1 (0.2)	0.0–1.0
Blood and lymphatic system disorders	4 (0.7)	0.2–1.9
Cold type haemolytic anaemia	1 (0.2)	0.0–1.0
Hypergammaglobulinaemia	1 (0.2)	0.0–1.0
Iron deficiency anaemia	1 (0.2)	0.0–1.0
Thrombocytopenia	1 (0.2)	0.0–1.0
Thrombocytosis	1 (0.2)	0.0–1.0
Anaemia	1 (0.2)	0.0–1.0
Skin and subcutaneous tissue disorders	4 (0.7)	0.2–1.9
Erythema	1 (0.2)	0.0–1.0
Rash	1 (0.2)	0.0–1.0
Skin lesion	1 (0.2)	0.0–1.0
Eczema	1 (0.2)	0.0–1.0
Gastrointestinal disorders	4 (0.7)	0.2–1.9
Intestinal obstruction	1 (0.2)	0.0–1.0
Colitis ischaemia	1 (0.2)	0.0–1.0
Diarrhoea	1 (0.2)	0.0–1.0
Melaena	1 (0.2)	0.0–1.0
Renal and urinary disorders	3 (0.5)	0.1–1.6
Nervous system disorders	3 (0.5)	0.1–1.6
Pregnancy – puerperium and perinatal conditions	3 (0.5)	0.1–1.6
Eye disorders	2 (0.4)	0.1–1.3
Psychiatric disorders	2 (0.4)	0.1–1.3
Ear and labyrinth disorders	1 (0.2)	0.0–1.0
Investigations	1 (0.2)	0.0–1.0
Reproductive system and breast disorders	1 (0.2)	0.0–1.0
Surgical and medical procedures	1 (0.2)	0.0–1.0
Product issues	1 (0.2)	0.0–1.0

CI: confidence interval; PT: preferred term; SOC: system organ class.

with abatacept SC in the French cohort (n=546) was comparable with that of the overall ASCORE study cohort (n=2892 in 10 countries), which was 47.3% (95% CI 45.6–49.2) (14). As observed in the French cohort, the 2-year treatment persistence rate in the international ASCORE cohort was higher in biologic-naive patients (51.7%) than in those who had experienced failure of previous biologic therapies (45.6% after failure of one agent, and 43.2% after failure of two or more agents) (14).

In the international ASCORE cohort, the highest 2-year persistence rate with abatacept SC was found in Italy (54.8%) and the lowest in the Netherlands (34.9%) (18). With a maintenance rate of 43.0%, the results of the French cohort are midway between these two extremes and are in line with several other countries in the study, such as Germany (47.6%) and the United Kingdom (45.1%).

The development of new targeted therapies means that the management of RA is constantly evolving, requiring updated real-world data to optimise therapeutic strategies. In France, real-world data on abatacept persistence rates are limited and outdated; treatment was initiated more than 10 years ago (between 2008–2010) in the ORA registry and between 2010 and 2013 in the ACTION observational study (11-13). These two studies, which focused exclusively on the IV formulation of abatacept, showed a 2-year persistence rate of 42.5% in ORA (n=610) (11) and 44% in ACTION (n=455) (13), similar to that observed in our analysis with abatacept SC in the French ASCORE cohort. The comparable persistence rates between patients receiving the IV and SC formulations of abatacept are consistent with the results of the ACQUIRE study, which showed a similar number of patients continuing treatment with both formulations, as well as non-inferior results in terms of efficacy and tolerability (19).

More recent French data on abatacept persistence come from an observational study conducted by the French-RIC Network (2008–2016), which reported a persistence rate of 52% at 2 years in 517 patients treated with abatacept IV

between 2008 and 2014, or either the SC or IV routes from 2014 (20). A retrospective study conducted between 2005 and 2018 at a single centre in France reported a 2-year persistence rate of 48.5% among the 72 patients receiving IV abatacept (21).

The ASCORE study (patient enrolment from 2013–2017) provides updated real-world data for abatacept use in 10 European countries (including France), taking into account a more competitive therapeutic environment and more recent treatment regimens available for RA (14). It is also the first study to assess treatment persistence specifically with the SC formulation of abatacept. The retention rates reported for SC abatacept in ASCORE (overall: 47%; French cohort: 43%) are similar to the abatacept rate reported in the French ORA registry study (39%), and lower than the rates reported for other biologics in patients with RA in routine clinical practice (63% for tocilizumab and 69% for rituximab) (11). Interestingly, in a recent large observational study based on French data from the National Health Data System (Système National des Données de Santé), treatment persistence at 1 year with SC formulations of anti-TNF agents was between 51.8% and 56.6% in biologic-naive patients (22), comparable or even lower than the level observed with abatacept SC at 1 year in ASCORE (59.2% for the overall French cohort, and 68.1% for biologic-naive patients).

The current data also confirm the real-world effectiveness of SC abatacept in patients with RA. In the overall ASCORE study population, the response to abatacept (in terms of CDAI and SDAI) tended to be better in patients who were seropositive for both rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) than in patients who were RF and ACPA negative (double-negative) (14). The differences between RF/ACPA double-positive and double-negative patients tended to be more marked in the group who were receiving abatacept as their first biologic compared with the biologic-experienced cohort (14). A separate analysis is being undertaken examining factors that are predictive of response in patients who received abatacept in the ASCORE study in France and the ACTION study in Germany, Austria and Switzerland, and results are expected shortly. In ASCORE, the patients who were seropositive for both RF and ACPA also had a better 2-year persistence rate than patients who were RF/ACPA double-negative (14, 23).

Although biologic DMARDs targeting B or T cells are effective against RA, they are associated with increased risks of serious/opportunistic infections. Furthermore, patients with RA tend to carry an increased risk of infection compared with other individuals (24). In the current study, abatacept-related SAEs occurred in 69 patients (12.6%) and serious infections were observed in only 17 patients (3.1%), regardless of relatedness to abatacept. The reported safety data are similar to that of the overall ASCORE study (7.8% of patients reported abatacept-related SAEs) (14) and that reported in previous observational studies (12). Notably, the low incidence of serious infections provides additional evidence to support the strong tolerability profile of abatacept.

The limitations of our study are related to its observational nature and the lack of a comparator group. The ASCORE study defined abatacept discontinuation as stopping treatment for 28 days or more, but data show that many RA patients who stop treatment resume the same regimen 3–6 months later (25). Indeed, 11.0% of patients in our study resumed treatment with abatacept SC after meeting the criteria for discontinuation. Therefore, our findings are likely to underestimate the true rate of persistence with abatacept SC. In addition, the French cohorts of patients who had previously experienced biologic therapy failure included ≤134 patients each (*i.e.* below the target sample size of 150 patients); therefore, results in these cohorts should be interpreted with caution. In addition, our estimates for sample size were based on an assumed 2-year treatment persistence rate of 60%, but the actual rate was 43%; as such, our findings should be confirmed in a larger cohort of patients. Lastly, given the rapid evolution of practices and recommendations in RA, the observations of this study conducted in 2014–2017 may not reflect current real-world clinical practice in France.

In conclusion, the data from the French cohort of the ASCORE study confirm the therapeutic value of abatacept SC under real-world conditions in patients with RA. Treatment persistence with abatacept SC in France was comparable to persistence in other countries in ASCORE, and equivalent to that of the IV form. In real-world clinical practice, treatment persistence with abatacept SC had better effectiveness when used as a first-line biologic therapy than in later lines of biologic therapy.

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Competing interests

R.-M. Flipo is a member of the BMS national board and of the scientific committee of the ASCORE study; is a member of the advisory boards of AbbVie, Pfizer, MSD, and Roche Chugai; has received consulting fees from AbbVie, BMS Laboratories, MSD, and Pfizer; and has received honoraria from AbbVie, BMS Laboratories, Celltrion, Galapagos, Lilly, MSD, Pfizer, and Roche Chugai.

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