

Supplemental Information

Treatment Persistence and Switching Patterns of Adalimumab Biosimilar ABP 501 in European Patients with Rheumatologic Diseases

Ran Jin,¹ Silvia Kruppert,² Florian Scholz,² Isabelle Bardoulat,³ Khalil Karzazi³, Francois Morand,³ Greg Kricorian¹, David Collier¹, Jonathan Kay⁴

¹Amgen Inc., Thousand Oaks, CA, USA; ²IQVIA Real World Solutions, Frankfurt, Germany;

³IQVIA Real World Solutions, Paris, France, ⁴UMass Chan Medical School, Worcester, MA, USA

Supplemental information 1: Imputation of diagnosis for German LRx data

Supplemental information 2: Imputation of diagnosis for French LRx data

Supplemental Table 1: Drug list for prior medications, concomitant treatments, and drugs patients switched to after discontinuation of ABP 501

Supplemental Table 2. Treatment adherence of patients with RA, PsA, or AS during the first 12 months after initiating ABP 501

Supplemental Table 3. Discontinuation rates and post-ABP 501 switching rates among German and French patients with RA, PsA, or AS during the first 12 months after initiating ABP 501

Supplemental Figure 1. Study design.

Supplemental Figure 2. Kaplan-Meier curve for sensitivity analysis of persistence of ABP 501 (treatment gap ≤ 90 days) among German patients with (A) RA, (B) PsA, and (C) AS and French patients with (D) RA, (E) PsA, and (F) AS.

Supplemental information 1: Imputation of diagnosis for German LRx data

Details of model imputation of disease diagnosis for German LRx data have been described previously (Ran J, et al. *Therap Adv Gastroenterol*. 2024;17:17562848231222332). Briefly, the diagnoses assigned to German IQVIA LRx patients have been generated based on machine learning models developed using the LRx treatment history of the patient as the input. Models were then trained on the German IQVIA Disease Analyzer database, which contains patient prescriptions, treatment, and other medical information from electronic medical records. The results (predicted vs true label in Disease Analyzer) are presented in the figure below.

Confusion matrix for the German machine learning model (all biologics)

	AS	RA	PsA	PsO	IBD	
AS	2,251	255	340	5	56	78%
RA	1,025	8,494	873	22	102	81%
PsA	843	723	1,729	485	51	45%
PsO	138	119	217	4,957	43	91%
IBD	112	52	31	25	4,183	95%
Predicted label (correct predictions in green)						

AS, ankylosing spondylitis; IBD, inflammatory bowel disease; PsA, psoriatic arthritis; PsO, psoriasis; RA, rheumatoid arthritis.

The presented confusion matrix can be interpreted as follows:

- 78% of true AS patients were correctly assigned by the model.
- 81% of true RA patients were correctly assigned by the model.
- 45% of true PsA patients were correctly assigned by the model.
- 91% of true PsO patients were correctly assigned by the model.
- 95% of true IBD patients were correctly assigned by the model.

As shown, a significant number of PsA patients are either mislabeled as RA or AS. This is not surprising since treatment guidelines for PsA significantly overlap with the alternative indications and thus differentiating the diagnosis based on treatment history alone is inherently challenging. However, we do observe patients with multiple diagnoses in each quarter, indicating that physicians may not always differentiate strictly between for example PsO and PsA.

Predictions of PsA/RA/AS grouped together have ~95% accuracy.

Supplemental information 2: Imputation of diagnosis for French LRx data

The diagnoses assigned to French IQVIA LRx patients have been generated based on a mix of rule-based and machine learning approaches. The rule-based approach is the first step, being directly applied in LRx database. For the second step, machine learning models are trained on the French IQVIA electronic medical records (EMR) databases.

First step: rule-based approach

This consists of a 3-stage filter directly applied in LRx database, based on the whole available drug dispensing history of patients. This aims to identify possible diagnoses (treatment indications), by using a scoring model weighing the possible indications at each filter stage completion (=prioritization). Details of the 3-stage filters to identify possible disease diagnosis for French LRx data have been described previously (Ran J, et al. *Therap Adv Gastroenterol.* 2024;17:17562848231222332).

Second step: machine learning models to classify rheumatologic patients having RA or AS

The second step consists in the use of automatic machine learning from data available in both LRx and EMR databases, in order to classify patients as having RA or AS (shown in flowchart below). The French EMR database provides systematic ongoing information from physician office-based visits on patients' consultations, diagnoses, and treatment in France. In France, data from panels of primary care physicians and data from specialist panels are available. To develop the machine learning step of the algorithm, only Rheumatologists panel was used, with a national coverage of 5.9% (100 rheumatologists). The main strength of the EMR rheumatologist database is the availability of patients' diagnoses, completed during office-based consultations. First, RA and AS patients are identified through diagnosis from this panel. Their age, gender and cotreatments are also collected (shared information with LRx). Then RA and AS patients of the rheumatologist panel are assigned into two disjoint subsamples: one learning subsample used to develop probabilistic modelling with around 70% of patients and one test subsample to validate predictions of the resulting models. A set of predictive models was built using machine learning technology with the objective of predicting RA or AS for each patient. Performance of competitive machine learning models was evaluated on the test subsample in which the true value of the diagnosis was known. This also allows selection of the best model. Once the best model was identified and validated, this was applied on LRx data in order to identify RA and AS patients among those classified in Rheumatology area.

Machine learning approach (France)

1 Use of EMR** in order to better understand patients' profile per indication

Panel of 100 rheumatologists

Available information via EMR:

- Patient's profile (age, gender...)
- Clinical profile (diagnoses, comorbidities...)
- Treatments prescribed

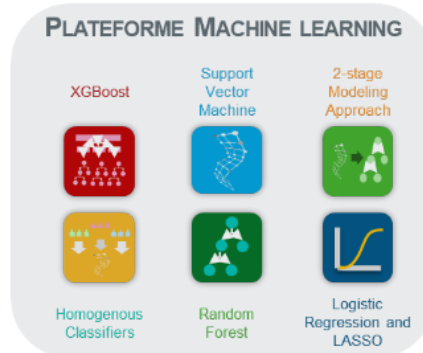
Observing the patient's management at a prescriber level

Patient pathway indicators



2 Type of information and AI modelling

- 1) Use of the following information available in both databases (EMR & LRx): age, gender, co-treatments
- 2) Probabilistic modelling using machine learning technology in order to predict RA or SA for each patient



3 Application of the model to LRx panel by transfer learning

Application of the probabilistic model to LRx patients

EMR: Electronic medical record; AI : Artificial Intelligence; RA: rheumatoid arthritis, SA: spondyloarthritis

Supplemental Table 1: Drug list for prior medications, concomitant treatments, and switching patterns after discontinuation of ABP 501

Glucocorticoids	Immunosuppressive drugs	Targeted therapies				
		ADA biosimilars (excluding ABP 501)	Non-ADA TNFi	Non-TNFi biologics		JAK inhibitors
Parenteral: Bethamethasone Dexamethasone Hydrocortisone Methylprednisolone Prednisolone Triamcinolone acetonide Trimacinalone hexacetonide Oral: Bethamethasone Budesonide Cloprednol Dexamethasone Fludrocortisone Hydrocortisone Methylprednisolone Prednisolone Prednisone Triamcinolone Rectal: Prednisone	Azathioprine Mercaptopurine Mycophenolate mofetil Mycophenolic acid Cyclosporin Tacrolimus	Hulio Imraldi Hyrimoz Idacio	Certolizumab Pegol Etanercept Golimumab Infliximab	IL1 inhibitors: anakinra IL6 inhibitors: sarilumab; tocilizumab IL12/23 inhibitors: ustekinumab IL17 inhibitors: secukinumab; ixekizumab; brodalumab	IL23 inhibitors: tildrakizumab; Risankizumab; guselkumab Integrin antagonists: vedolizumab PDE inhibitors: apremilast Other MOAs: abatacept; rituximab	Baricitinib Tofacitinib Upadacitinib

ADA, adalimumab; IL, interleukin; JAK, Janus kinase; MOA, mechanism of action; PDE, phosphodiesterase; TNFi, tumor necrosis factor inhibitor

Supplemental Table 2. Treatment adherence of patients with RA, PsA, or AS during the first 12 months after initiating ABP 501

	German patients with MPR $\geq 80\%$ of days covered, n/N, %			French patients with MPR $\geq 80\%$ of days covered, n/N, %		
	All patients	Patients naïve to ADA	Patients experienced with ADA	All patients	Patients naïve to ADA	Patients experienced with ADA
RA	1148/2725, 42.1%	677/1701, 39.8%	471/1024, 46.0%	312/827, 37.7%	199/470, 42.3%	113/357, 31.7%
PsA	753/1739, 43.3%	402/952, 42.2%	351/787, 44.6%	76/243, 31.3%	55/169, 32.6%	21/74, 28.4%
AS	958/2275, 42.1%	440/1035, 42.5%	518/1240, 41.8%	338/946, 35.7%	247/572, 43.2%	91/374, 24.3%

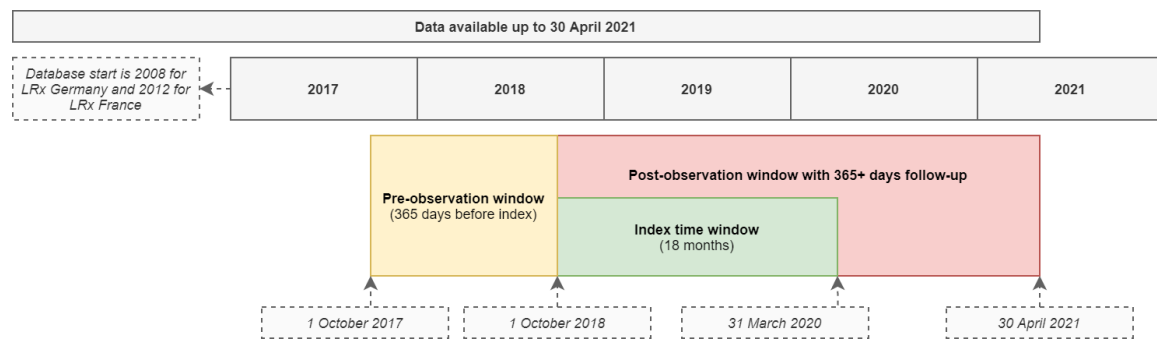
ADA, adalimumab; AS, ankylosing spondylitis; MPR, medical possession ratio; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RP, reference product.

Supplemental Table 3. Discontinuation rates among German and French patients with RA, PsA, or AS during the first 12 months after initiating ABP 501

	German patients									French patients								
	RA			PsA			AS			RA			PsA			AS		
	All patients	Prior exposure to ADA		All patients	Prior exposure to ADA		All patients	Prior exposure to ADA		All patients	Prior exposure to ADA		All patients	Prior exposure to ADA		All patients	Prior exposure to ADA	
		Naïve	Experienced		Naïve	Experienced		Naïve	Experienced		Naïve	Experienced		Naïve	Experienced		Naïve	Experienced
Number of patients in the full cohort	2,725	1,701	1,024	1,739	952	787	2,275	1,035	1,240	827	470	357	243	169	74	946	572	374
Non-persistent patients, n/N, %	1,528/2,725 56.1%	1,033/1,701 60.7%	495/1,024 48.3%	919/1,739 52.8%	555/952 58.3%	364/787 46.3%	1,127/2,275 49.5%	556/1,035 53.7%	571/1,240 46.0%	418/827 50.5%	245/470 52.1%	173/357 48.5%	166/243 68.3%	119/169 70.4%	47/74 63.5%	507/946 53.6%	300/572 52.4%	207/374 54.5%
Discontinued ABP 501	494/1,528 32.3%	388/1,033 37.6%	106/495 21.4%	258/919 28.1%	191/555 34.4%	67/364 18.4%	299/1,127 26.5%	213/556 38.3%	86/571 15.1%	118/418 28.2%	90/245 36.7%	28/173 16.2%	50/166 25.3%	33/119 27.7%	9/47 19.1%	140/507 27.6%	108/300 36.0%	32/207 15.5%
Resumed ABP 501 with a gap of >120 days	216/1,528 14.1%	126/1,033 12.2%	90/495 18.2%	201/919 21.9%	89/555 16.0%	112/364 30.8%	344/1,127 30.5%	135/556 24.3%	209/571 36.6%	75/418 17.9%	44/245 18.0%	31/173 17.9%	20/166 12.0%	12/119 10.1%	8/47 17.0%	94/507 18.5%	50/300 16.7%	44/207 21.3%
Switched to another targeted therapy	818/1,528 53.5%	519/1,033 50.2%	299/495 60.4%	460/919 50.1%	275/555 49.5%	185/364 50.8%	484/1,127 42.9%	208/556 37.4%	276/571 48.3%	225/418 53.8%	111/245 45.3%	114/173 65.9%	104/166 62.7%	74/119 62.2%	30/47 63.8%	273/507 53.8%	142/300 47.3%	131/207 63.3%

ADA, adalimumab; AS, ankylosing spondylitis; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

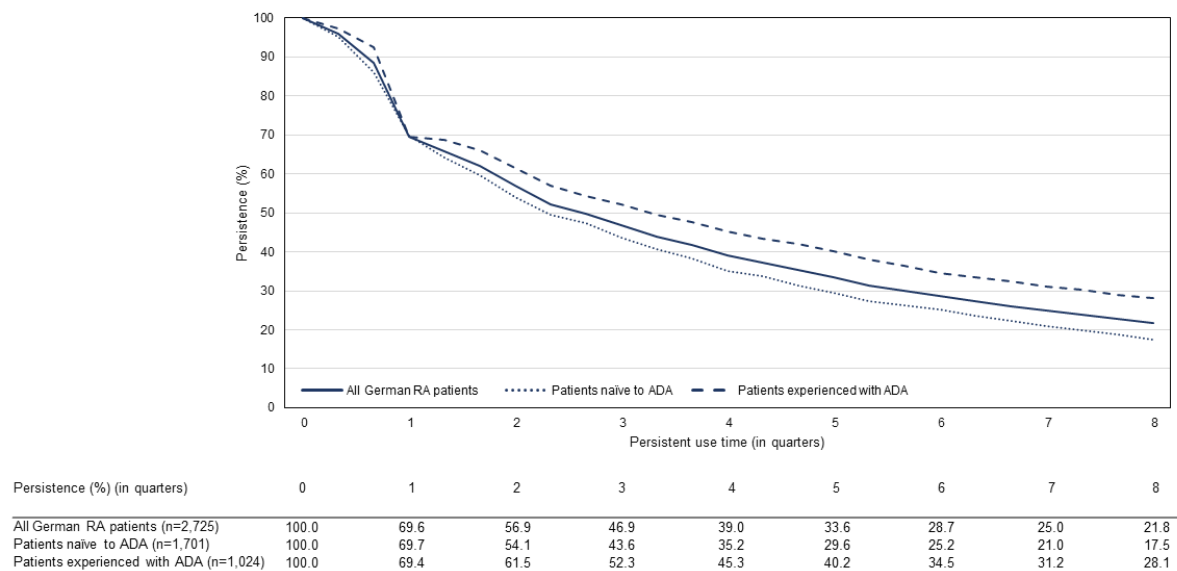
Supplemental Figure 1. Study design.



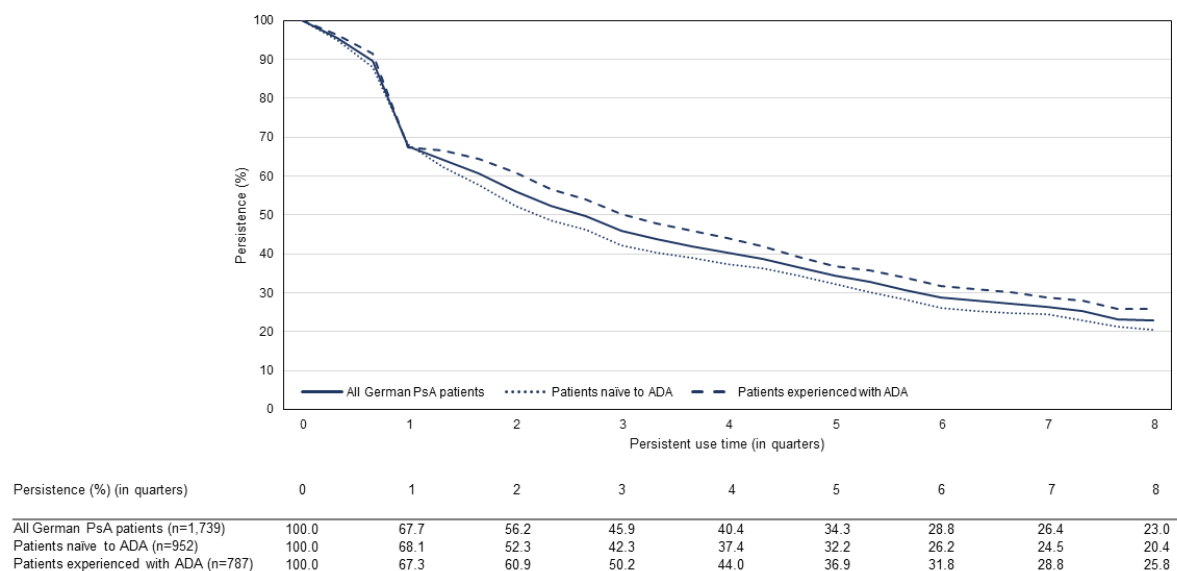
LRx, longitudinal prescription data.

Supplemental Figure 2. Kaplan-Meier curve for sensitivity analysis of persistence of ABP 501 (treatment gap ≤ 90 days) among German patients with (A) RA, (B) PsA, and (C) AS and French patients with (D) RA, (E) PsA, and (F) AS.

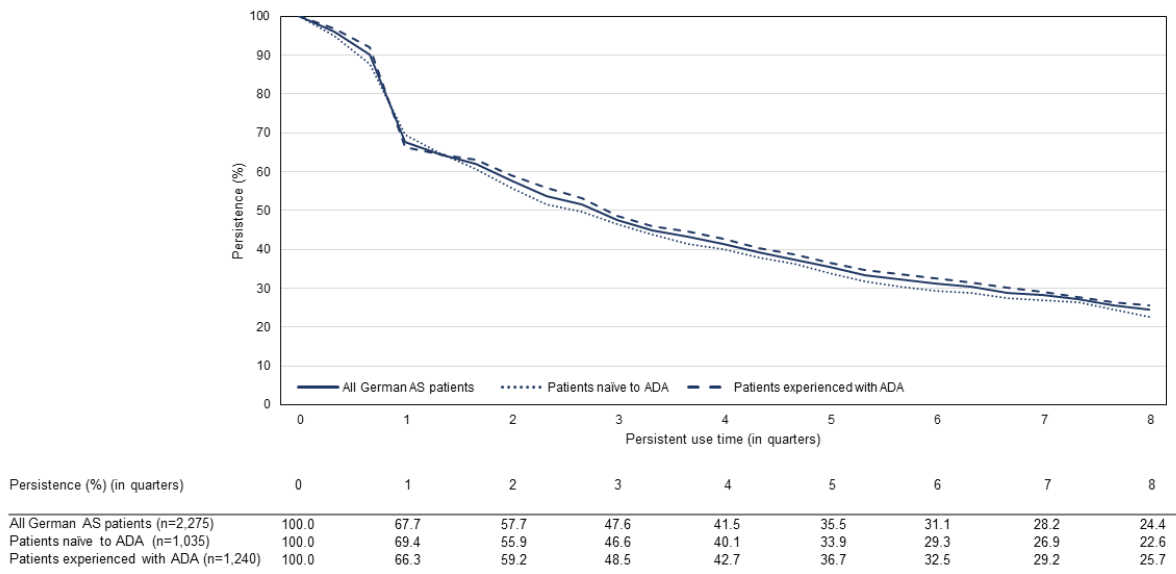
A.



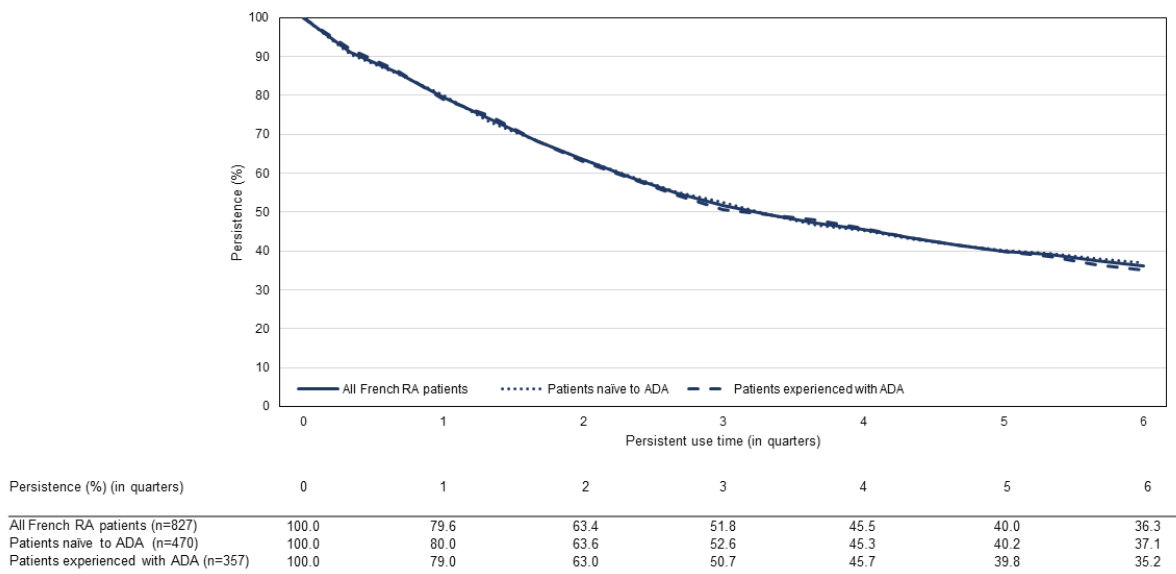
B.



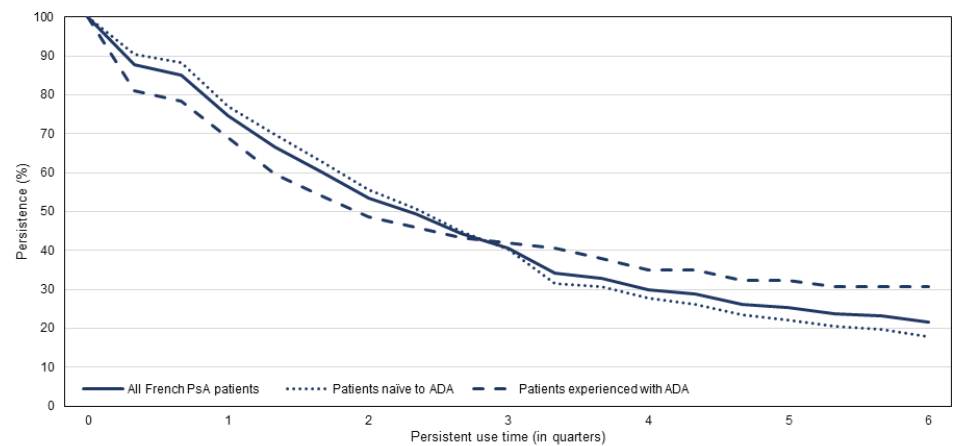
C.



D.

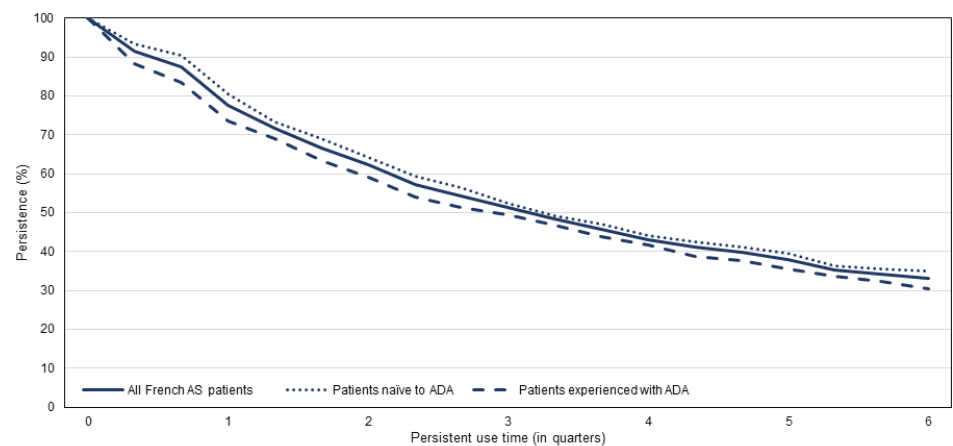


E.



Persistence (%) (in quarters)	0	1	2	3	4	5	6
All French PsA patients (n=243)	100.0	74.5	53.5	40.7	30.0	25.2	21.7
Patients naive to ADA (n=169)	100.0	76.9	55.6	40.2	27.8	22.0	17.8
Patients experienced with ADA (n=74)	100.0	68.9	48.6	41.9	35.1	32.3	30.7

F.



Persistence (%) (in quarters)	0	1	2	3	4	5	6
All French AS patients (n=946)	100.0	77.7	62.3	51.2	43.1	38.0	33.1
Patients naive to ADA (n=572)	100.0	80.4	64.3	52.3	44.1	39.6	34.9
Patients experienced with ADA (n=374)	100.0	73.5	59.1	49.5	41.7	35.6	30.5

ADA, adalimumab; AS, ankylosing spondylitis; PsA, psoriatic arthritis; RA, rheumatoid arthritis.