




Retention rates of adalimumab, etanercept, and infliximab as first- or second-line biotherapies for spondyloarthritis patients in daily practice in Auvergne (France)

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Abstract

Objective: To compare, in real-life settings, the retention rates of initial anti-tumor-necrosis factor (TNF) treatments (etanercept [ETN], adalimumab [ADA] and infliximab [IFX]) used as first-line biotherapy for axial spondyloarthritis (axSpA), and evaluate treatment switches to another anti-TNF inhibitor in the event of treatment failure.

Methods: We analyzed the medical records of all SpA patients (Assessment in Ankylosing Spondylitis International Working Group axial criteria) treated with ETN, IFX or ADA between 2001 and February 2015. Drug retention rates were calculated using the Kaplan-Meier method and compared by means of the Cox extended model. Sub-analyses were performed according to discontinuation reasons.

Results: Of the 249 SpA patients analyzed (135 radiographic cases, 114 non-radiographic), 102 received ETN, 62 ADA, and 85 IFX. In total, 103 discontinued treatment. The retention rates of IFX, ADA and ETN were 67%, 59% and 56% after 3 years; 62%, 42% and 47% after 5 years; 55%, 42% and 24% after 8 years; 53%, 42% and 12% after 10 years, respectively. In multivariate analyses, the predictive factors for retention were: low BASDAI score (hazard ratio [HR]: 1.02 [1.01-1.04]), high C-reactive protein levels (HR: 0.98 [0.97-0.99]), concomitant disease-modifying therapy (HR: 0.4 [0.21-0.75]), and radiographic SpA (HR: 1.5 [1.0-2.52]). In total, 61 patients switched to another anti-TNF therapy. No difference was observed among the three anti-TNF therapies regarding median retention duration, although the retention rate proved higher for treatment switches from one monoclonal antibody to another.

Conclusion: The retention rate in SpA patients proved high, with retention for IFX superior to that of ETN.

KEYWORDS

ankylosing spondylitis, drug treatment

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1 | INTRODUCTION

Using tumor necrosis factor alpha (TNF- α) inhibitors, or anti-TNFs, has considerably improved the treatment of axial spondyloarthritis (axSpA). There are currently five approved anti-TNFs for treating axSpA (infliximab [IFX], adalimumab [ADA], etanercept [ETN], certolizumab, and golimumab). The first three (infliximab, adalimumab, and etanercept) are the most widely used in axSpA. Their efficacy and safety have been demonstrated in extensive randomized controlled trials (RCTs).^{1,2}

Nevertheless, these RCTs were of short duration and included a selected population that differed from patients treated in daily practice. Biotherapy registries have thus been established in many countries in order to better understand long-term clinical efficacy and safety. However, these registries more often address rheumatoid arthritis than axSpA.³⁻¹⁹

While retention rates for anti-TNFs have been investigated using several patient registries, their follow-up duration did not typically exceed 8 years.^{4,5} Young age, male gender and presence of inflammatory syndrome appeared predictive of retention in most, although not all cases.^{4,7,11,12,19} Other debated factors include the anti-TNF type prescribed, presence of other arthritis forms, and using conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) in combination with anti-TNF therapy.^{10,11,14,16} In the event of treatment failure with a single anti-TNF, certain registries have assessed the efficacy of a second anti-TNF, although with little data available on long-term retention.^{6,9,11,17} Only little data are also available on the retention of and response to anti-TNFs in real-life settings, in patients with non-radiographic axSpA (nr-axSpA).^{18,20}

In France, as there is no specific anti-TNF registry, we have implemented an observational study designed to compare the retention rates of anti-TNFs in daily practice and over 15 years in the Auvergne region. The main objective was to compare the retention rates of ADA, ETN and IFX administered as first- and second-line biotherapies for axSpA. The secondary objectives were to evaluate responses at 6 months, compare the retention rates of monoclonal antibody (ADA and IFX) with soluble receptor (ETN) anti-TNFs, identify reasons for treatment discontinuation, determine factors associated with improved retention for the initial anti-TNF, and evaluate retention rates for the second anti-TNF following treatment switch.

2 | MATERIALS AND METHODS

Our study population consisted of axSpA patients on anti-TNFs meeting the Assessment in Ankylosing Spondylitis International Working Group criteria,²¹ ≥ 18 years old, and included in the local registry of the Clermont-Ferrand University Hospital (CHU) from 2001 to February 2015. The patients were followed up in normal clinical practice by experienced rheumatologists, who established the diagnosis based on clinical, radiographic, and imaging criteria, while ensuring patient follow up. Most patients were seen at consultation in month six in order to re-evaluate their treatment, then every year

thereafter in line with recommended French practice consisting of implementing annual assessments for all anti-TNF patients, on top of their normal independent rheumatology consultations. We selected only cases corresponding to axSpA criteria for analysis.

We collected demographic data (age, gender, weight/size/body mass index [BMI], smoking habits, cardiovascular comorbidities, and axSpA disease duration), as well as data concerning specific rheumatism treatments such as prior therapy and concomitant treatments combined with anti-TNF (non-steroidal anti-inflammatory drugs [NSAIDs], salazopyrin, or methotrexate [MTX]), clinical parameters (pain visual analog scale [VAS], patient activity VAS, arthritis, enthesopathies (Maastricht Ankylosing Spondylitis Enthesitis Score), extra-articular manifestations (Crohn's disease, ulcerative colitis, psoriasis or uveitis), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) scores, in addition to biological parameters (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP] and human leukocyte antigen [HLA]-B27).

The BASDAI and BASFI scores were evaluated at month (M)6, M12 and M24, then once a year. The retention duration for each molecule was calculated from its first administration until discontinuation, as indicated in the registry, or until treatment switch to another anti-TNF. The reasons for treatment discontinuation were classified into two categories: inefficacy or adverse effects. The retention rate for the second anti-TNF was also assessed following treatment switch.

2.1 | Statistical section

Statistical analysis was performed using Stata software, Version 13 (StataCorp, College Station, TX, USA). The tests were two-sided, with a Type I error set at $\alpha = 0.05$. Baseline characteristics were expressed as mean \pm standard deviation (SD) or median (interquartile range) for continuous data (assumption of normality assessed using the Shapiro-Wilk test) and as number of patients and associated percentages for categorical parameters. Comparisons of patient characteristics between treatment groups were carried out using the Chi-squared or Fisher's exact test for categorical variables, and analysis of variance or Kruskal-Wallis tests for quantitative parameters (homoscedasticity verified by Bartlett test). Censored data were estimated by means of the Kaplan-Meier method. The log-rank statistics was employed in univariate analysis in order to investigate the predictive value of certain patient characteristics. Thereafter, a Cox proportional-hazards regression was carried out to confirm the predictive factors in multivariate analysis depending on univariate analysis results and the parameters' clinical relevance. The choice of entry level = 0.05 was described by Hosmer and Lemeshow as too stringent, often excluding essential variables from the model. These authors have thus proposed using a range from 0.15 to 0.25 or even 0.30. Using Monte Carlo simulations, Lee and Koval (1997) demonstrated that the best α varies between 0.05 and 0.40. At the same time, Steyerberg et al (2000) recommended using $\alpha = 0.50$ to include all useful variables for stronger prediction. For our study, we have



considered a Type I error level at 0.15. The proportional-hazard hypothesis was verified using Schoenfeld's test while plotting residuals. The interactions between possible predictive factors were also tested, with results expressed as hazards ratio (HR) and 95% confidence intervals (95% CI).

3 | RESULTS

3.1 | Population characteristics

In total, 249 SpA patients were treated with anti-TNFs between 2001 and 2015. The cohort comprised 157 men and 92 women, with an average age of 42 ± 13 years. Overall, 135 patients exhibited radiographic SpA and 114 non-radiographic SpA (58 with positive magnetic resonance imaging [MRI arm], with 56 meeting the criteria for the Clinical arm).

The mean SpA disease duration was 7 years (1-14) and mean BMI 25.9 ± 7 , with 35.3% of patients smokers. Overall, 22 patients were affected by inflammatory bowel disease, including 19 cases of Crohn's disease, 25 suffering from psoriasis, and 42 with prior uveitis. There were 94 patients (37.8%) with arthritis and 96 (38.6%) with enthesopathic pain. Mean BASDAI score was 56.6 ± 18.7 , VAS 0-100 pain score 62.2 ± 21.0 , and overall SpA activity 63.8 ± 22.8 mm (VAS 0-100 mm). Mean BASFI score was 51.6 ± 20.8 and median CRP value 8.8 mg/L (2.9-23.4). Overall, 157 (63.1%) patients were B27 carriers. The following anti-TNFs were used: ETN (102, 40.9%), IFX (85, 34.1%) and ADA (62, 24.8%). There were 125 patients on NSAIDs, 15 on corticosteroids, and 64 receiving conventional disease-modifying therapy (MTX [$n = 38$] or sulfasalazine [$n = 26$]).

The between-group differences pertained to extra-articular manifestations that were more common in the IFX and ADA groups as compared to ETN; BASFI score that was lower among ADA-treated patients; acute phase reactants that were more severe in IFX-treated patients, and number of disease-modifying therapies used in combination with IFX (Table 1). Patients on disease-modifying therapy more often presented with arthritis (53% vs 32%; $P = 0.003$), psoriasis (19% vs 182%; $P = 0.17$) or enterocolopathy (19% vs 7%; $P = 0.007$).

3.2 | BASDAI 50 response

Response at M6 was assessed in 178 patients, with the results detailed in Table 2. In total, 87 (48.8%) patients achieved BASDAI 50 response, 35 of whom were on ETN, 22 on ADA, and 30 on IFX, with no between-drug difference observed ($P = 0.63$). The responders tended to be male, younger at the time of diagnosis (30.1 ± 12.7 years vs 37.6 ± 12.4 , $P < 0.001$) or when anti-TNF therapy was initiated (40.2 ± 12.9 years vs 45.9 ± 12.8 , $P = 0.002$), non-smokers ($P = 0.007$), with lower BMI (24.2 ± 4.1 vs 27.8 ± 9.8 , $P = 0.02$) and increased inflammation markers (CRP: 13.5 mg/L [4.2-35.0] vs 4.1 [2.9-12.8], $P < 0.001$ and ESR: 23 [8-40] vs 23 [8-40], $P = 0.004$), and with higher overall SpA activity (69.7 ± 19.0 vs

61.3 ± 23.1 , $P = 0.02$) (Table S1). Response significantly differed between radiographic SpA patients and non-radiographic SpA (60/102 [58.8%] vs 27/76 [35.5%] $P = 0.002$) (Table S1). However, for nr-axSpA patients there was no difference found between those with positive MRI (38% responders) and those only B27 positive (38% vs 32%, $P = 0.58$). On multivariate analyses, the responders were younger (HR: 0.97 [0.94-0.99], $P = 0.020$), non-smokers (HR: 0.42 [0.20-0.90], $P = 0.026$), and with high CRP levels (HR: 1.02 [1.0-1.03], $P = 0.027$).

3.3 | Anti-TNF retention and predictive factors

Median follow up was 26 (9-57) months (12 [6-33] months for the first anti-TNF, 7 [5-18] for the second). In total, 103 patients (34.3%) discontinued their initial anti-TNF treatment. The retention rates of IFX, ADA and ETN were 67%, 59% and 56% after 3 years; 62%, 42% and 47% after 5 years; 55%, 42% and 24% after 8 years; and 53%, 42% and 12% after 10 years, respectively (Figure 1). Retention was longer for IFX compared to ETN (HR: 0.62 [0.39-0.99], $P = 0.049$), although not to ADA (HR: 0.91 [0.56-1.48], $P = 0.70$). There was no difference found between retention rates for ETN and those of both monoclonal antibodies combined ($P = 0.13$).

Treatment retention was superior when the therapy was initiated prior to 2006 compared to those where treatment was initiated after 2011 (HR: 2.53 [1.38-4.65], $P = 0.003$). The patients who discontinued treatment had lower CRP levels (HR: 0.99 [0.97-0.99], $P = 0.01$) and higher BASDAI scores (odds ratio [OR]: 1.02 [1.01-1.04], $P < 0.001$). Patients with radiographic SpA had higher retention rates than those with nr-axSpA (HR: 1.52 [1.03-2.24], $P = 0.04$), as did B27-positive patients (HR: 0.53 [0.30-0.94], $P = 0.03$) in the nr-axSpA group, as well as patients on disease-modifying therapy in combination with the anti-TNF (HR: 0.45 [0.27-0.74], $P = 0.002$). Patients who smoked were more likely to discontinue treatment, although the difference did not reach statistical significance ($P = 0.08$) (Table 2).

In the multivariate analyses, the predictive factors for retention were low BASDAI score (HR: 1.02 [1.01-1.04], $P < 0.01$), elevated CRP level (HR: 0.98 [0.97-0.99], $P = 0.01$), concomitant use of csDMARDs (HR: 0.4 [0.21-0.75], $P = 0.005$), and radiographic SpA (HR: 1.5 [1.0-2.52], $P = 0.05$).

3.4 | Discontinuation due to either adverse effects or inefficacy

Overall, 23 (9.23%) patients discontinued their anti-TNF therapy due to adverse effects, with similar results obtained among the three anti-TNF groups (Table S2 and Figure S1). No predictive factors for drug discontinuation were identified.

When considering drug discontinuation due to inefficacy, the retention rate was higher for IFX compared to ETN (HR: 0.57 [0.32-0.98], $P = 0.004$), with no difference observed between ADA and ETN (HR: 1.05 [0.61-1.79], $P = 0.87$) (Figure 2). Patients who were older at the time of diagnosis (HR: 1.02 [1.01-1.03], $P = 0.03$), had

**TABLE 1** Comparative analysis according to the first treatment initiated

	Total N = 249	Etanercept N = 102	Adalimumab N = 62	Infliximab N = 85	P value
Male gender, n (%)	157 (63.1)	69 (67.6)	32 (51.6)	56 (65.9)	0.09
Age at diagnosis, years, mean ± SD	33.7 ± 13.5	34.8 ± 13.3	34.0 ± 13.8	32.0 ± 13.4	0.38
Evolution time of SpA	7 [1; 14]	7 [2; 14]	6.5 [1; 15]	6 [1.5; 12.5]	0.48
BMI, mean ± SD	25.9 ± 7.1	25.8 ± 4.4	26.6 ± 11.5	25.6 ± 5.1	0.63
Smoking, n (%)	88 (35.3)	41 (40.2)	19 (30.7)	28 (32.9)	0.39
Criteria, n (%)					
NY	135 (54.2)	55 (53.9)	30 (48.4)	50 (58.8)	0.27
MRI+	58 (23.3)	27 (26.5)	18 (29.0)	13 (15.3)	
B27+	56 (22.5)	20 (19.6)	14 (22.6)	22 (25.9)	
Arthritis, n (%)	94 (37.8)	37 (36.3)	23 (37.1)	34 (40.0)	0.87
Enthesitis, n (%)	96 (38.6)	46 (45.1)	18 (29.0)	32 (37.6)	0.12
Extra-articular events, n (%)	91 (36.5)	26 (25.5)	29 (46.8)	36 (42.4)	0.009
Crohn's disease	19	0	7	12	
Ulcerative colitis	3	0	1	2	
Psoriasis	25	12	5	8	
Uveitis	42	13	15	14	
BASDAI, mean ± SD	56.6 ± 18.7	58.4 ± 18.5	55.3 ± 16.0	55.3 ± 20.9	0.41
VAS axial pain, mean ± SD	62.2 ± 21.0	63.3 ± 20.0	58.9 ± 20.2	63.3 ± 22.4	0.31
VAS global activity (patient), mean ± SD	63.8 ± 22.8	62.4 ± 23.8	63.6 ± 19.5	65.5 ± 24.0	0.55
BASFI, mean ± SD	51.6 ± 20.8	54.2 ± 20.4	44.6 ± 17.8	53.5 ± 22.4	0.01
B27, n (%)	157 (63.1)	63 (61.8)	40 (64.5)	54 (63.5)	0.93
CRP, median [IQR]	8.8 (2.9-23.4)	7.1 (2.9-14.3)	7.3 (2.9-13.2)	18.2 (4.7-45.5)	<0.001
NSAID treatment, n (%)	125 (50.2)	50 (49.0)	34 (54.8)	41 (48.2)	0.83
Corticosteroid treatment, n (%)	15 (6.0)	3 (2.9)	4 (6.5)	8 (9.4)	0.18
Previous disease-modifying treatment, n (%)	64 (25.7)	15 (14.7)	13 (21.0)	36 (42.4)	<0.001
Sulfasalazine	26	9	10	7	
Methotrexate	38	6	3	29	

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, body mass index; CRP, C-reactive protein; IQR, interquartile range; MRI, magnetic resonance imaging; NSAID, non-steroidal anti-inflammatory drugs; NY, New York; SpA, spondyloarthritis; VAS, visual analog scale; bold values : statistically significant.

higher BASDAI scores (HR: 1.02 [1.01-1.04], $P = 0.001$), and exhibited low CRP levels (HR: 0.99 [0.97-0.99], $P = 0.01$) and were more likely to discontinue treatment. Discontinuation was also more common in the event of non-radiographic SpA (HR: 1.98 [1.26-3.10], $P = 0.003$) and in patients not on concomitant disease-modifying therapy (HR: 0.39 [0.21-0.69], $P = 0.01$). In multivariate analyses, the predictive factors for drug retention were: low BASDAI score (HR: 1.03 [1.01-1.04], $P < 0.01$), increased CRP levels (HR: 0.98 [0.96-0.99], $P = 0.007$), concomitant csDMARDs (HR: 0.3 [0.15-0.69], $P = 0.004$), and radiographic SpA (HR: 2.1 [1.2-3.7], $P = 0.007$).

3.5 | Anti-TNF efficacy/tolerance and treatment switches

Of the 80 patients who discontinued treatment due to inefficacy, 61 switched to another anti-TNF. Overall, 22 patients on ETN were

given a monoclonal antibody (MoAb), whereas 39 patients on MoAb were given ETN ($n = 24$) or a different MoAb ($n = 15$). There was no difference observed in median retention duration among the three anti-TNFs administered as second-line treatment ($P = 0.43$). However, in patients whose treatment switch involved ETN (ETN to MoAb or MoAb to ETN), the retention rate was significantly lower than in those taking an MoAb then given another MoAb (HR: 4.52 [1.25-16.26], $P = 0.021$; HR: 4.47 [1.29-15.53], $P = 0.018$, respectively).

4 | DISCUSSION

This retrospective cohort study, based on the local Auvergne region registry and comprising 249 SpA patients, demonstrated that the percentage of patients continuing their initial anti-TNF treatment at

**TABLE 2** Predictive factors for first anti-tumor necrosis factor (TNF) treatment discontinuation

	No treatment discontinuation N = 146	Treatment discontinuation N = 103	HR (95% CI)	P value
Initiation date of anti-TNF treatment				
2002-2005	23 (15.8)	18 (17.5)	Ref	
2006-2010	59 (40.4)	46 (44.7)	1.56 (0.89-2.74)	0.12
2011-2015	64 (43.8)	39 (37.8)	2.53 (1.38-4.65)	0.003
Treatment, n (%)				
Etanercept	58 (39.7)	44 (42.7)	Ref	
Adalimumab	36 (24.7)	26 (25.3)	0.91 (0.56-1.48)	0.70
Infliximab	52 (35.6)	33 (32.0)	0.62 (0.39-0.99)	0.049
Male gender, n (%)	94 (64.4)	63 (61.2)	0.81 (0.54-1.20)	0.29
Age at diagnosis (y), mean ± SD	33.3 ± 13.9	34.3 ± 12.9	1.01 (0.99-1.03)	0.15
Age at first anti-TNF initiation, mean ± SD	42.5 ± 14.2	43.4 ± 12.3	1.01 (0.99-1.04)	0.28
BMI, mean ± SD	25.9 ± 8.2	25.9 ± 4.6	1.00 (0.96-1.05)	0.97
Smoking, n (%)	45 (51.1)	43 (48.9)	1.43 (0.96-2.12)	0.08
Criteria, n (%)				
New York	83 (56.9)	52 (50.5)	Ref	
Non-radiographic	63 (43.2)	51 (49.5)	1.52 (1.03-2.24)	0.04
Arthritis, mean ± SD	53 (36.3)	36 (35.0)	0.79 (0.52-1.18)	0.25
Enthesitis, n (%)	58 (56.9)	44 (43.1)	1.14 (0.76-1.69)	0.51
BASDAI, mean ± SD	52.95 ± 19.7	61.8 ± 16.0	1.02 (1.01-1.04)	<0.001
BASDAI 50 at 6 months	58%	37%	0.34 (0.21-0.54)	<0.001
VAS axial pain, mean ± SD	60.9 ± 20.2	64.2 ± 22.1	2.64 (0.93-7.51)	0.07
VAS global activity (patient), mean ± SD	61.5 ± 23.3	67.7 ± 21.6	2.04 (0.69-6.01)	0.20
BASFI, mean ± SD	49.8 ± 20.4	54.2 ± 21.3	1.01 (0.99-1.02)	0.19
B27	91 (58.0)	66 (42.0)	1.03 (0.69-1.54)	0.90
CRP, mean ± SD	20.5 ± 23.1	18.0 ± 30.5	0.99 (0.97-0.99)	0.01
Disease-modifying treatment, n (%)	44 (68.8)	20 (31.3)	0.45 (0.27-0.74)	0.002

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, body mass index; CRP, C-reactive protein; VAS, visual analog scale; bold values : statistically significant.

1 year was 78%, 72% at 2 years, 62% at 3 years, 52% at 5 years and 38% at 10 years. Median retention duration was 69.7 months. The retention duration of the anti-TNF treatment over the study's early years was consistent with the data from several international registries. To illustrate, according to Czech registry ATTRA, retention was 84% at 1 year, 76% at 2 years and 72% at 3 years.⁴ These figures were lower in the DANBIO registry, with a median drug retention of 4.3 years, with retention rates of 74% and 63% at 1 and 2 years, respectively.^{4,5} In our study, retention rates were higher before 2006 potentially due to later access to other anti-TNFs and because the physicians monitoring the patients probably accepted responses that would today not be judged as satisfactory for continuing treatment. Unlike the Czech and Danish registries, and one Italian multicenter study, the Swedish registry revealed a trend of better retention with ETN compared to IFX. We found IFX retention to be superior to that of ETN (HR: 0.62 [0.39-0.99], $P = 0.049$), with no difference observed between ADA and IFX, along with a lower discontinuation rate for IFX due to inefficacy (HR: 0.57 [0.32-0.99],

$P = 0.004$).^{4,5,11,14} Our study revealed that concomitant or prior use of a csDMARD rendered it possible to further increase the initial anti-TNF's retention duration. Data from the literature prove inconsistent, with a Spanish series and the DANBIO registry revealing no improvement in treatment retention when combining an anti-TNF with disease-modifying therapy, whereas retention improved quite significantly in a similar context in the ARTIS registry in ankylosing SpA and undifferentiated SpA cases.^{5,16,17} In our study, the patients exhibiting extra-spinal symptoms underwent disease-modifying therapy, and the fact that their condition was better managed possibly accounted for their higher treatment retention rates.

Treatment discontinuation was more commonly caused by the treatment's inefficacy than adverse effects (9.23%), with reasons for discontinuation varying depending on the registry considered. In our study, as in the Danish,^{5,11} Italian, and Spanish registries,^{5,11,17} the most common cause for treatment discontinuation proved to be inefficacy. The discontinuation rate for inefficacy and adverse effects was the same in the Swedish and Brazilian registries, whereas the

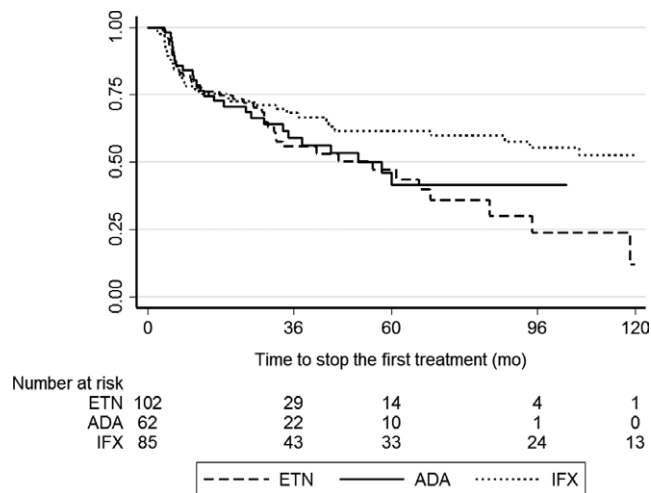


FIGURE 1 Survival curves of the first anti-tumor necrosis factor drug

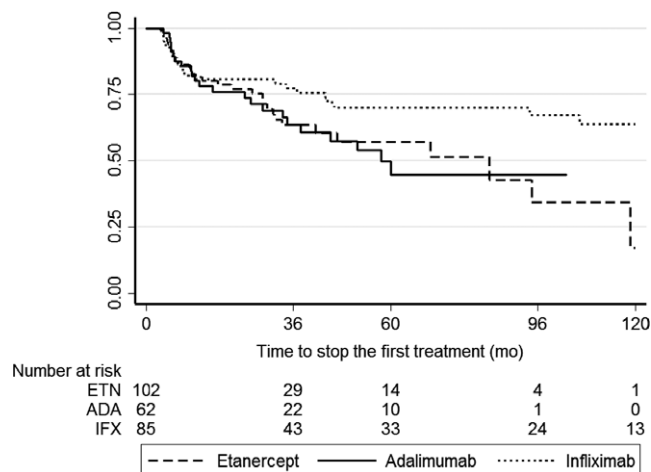


FIGURE 2 Survival curve of first anti-tumor necrosis factor discontinuation due to inefficacy

Czech registry recorded adverse effects as the most common cause of drug discontinuation.^{4,14,15} Although we found our discontinuation rate due to undesirable effects to be relatively low compared to that of other registries, it was nevertheless close to that observed in the NOR-DMARD registry (8.5%).⁸

Retention of the initial anti-TNF treatment was superior in patients exhibiting severe biological inflammatory syndromes, consistent with the data of the Danish and Czech registries, as well as an Italian multicenter study, yet contrasting with the findings of a Swedish and French study.^{4,9,11,12,18} According to the Danish registry, low BASDAI score proved to be a predictive factor for retention in univariate analysis, yet not in the multivariate analyses.⁵ Retention was not as good in patients with non-radiographic SpA compared to those with radiographic SpA, which proved to be contrary to the Lille study's findings.¹⁸

Other results were revealed to differ from those reported in certain registries. These include male gender as a predictive factor for

retention in the ATTRA, DANBIO and SSATG registries.^{4,5,14} SpA disease duration, and smoking.¹⁹ In total, 61 of our patients switched to another anti-TNF therapy, and there was no difference in the median retention duration observed when comparing the three anti-TNFs for second treatment. However, longevity of the second agent was superior when switching from one MoAb to another MoAb, compared to switching from ETN to an MoAb, or from an MoAb to ETN. The Spadaro et al⁶ study revealed no difference in retention rates for the second anti-TNF among patients having switched from IFX to ADA, or ETN to ADA. Furthermore, no clear difference was found between the first and second anti-TNF following treatment switch in the NOR-DMARD and DANBIO registries.^{8,9}

BASDAI 50 response was achieved at M6 by 48.8% of patients, with no difference observed among the three agents, as in line with the data of several therapeutic trials and registries, such as the BRSBR registry.²¹

The predictive factors for good response to an initial anti-TNF therapy were young age at the start of treatment, being a non-smoker, and exhibiting high CRP levels. Our data thus agree those of the DANBIO registry with regard to age and inflammatory syndromes.⁵ High CRP levels were also a predictive response factor in the BSRBR registry,²² whereas smoking was predictive of non-response, as highlighted in the DANBIO registry.¹⁹ Conflicting data were reported concerning the response of radiographic vs non-radiographic SpA patients. Data from the Swiss registry SCQM revealed lower response in non-radiographic SpA patients, although the difference was less significant for patients exhibiting high CRP levels.²³ In the Lille study, no difference was observed between radiographic and non-radiographic SpA cases.¹⁸ Our study found non-radiographic SpA to be a predictive factor of non-response in univariate analysis, yet not in the multivariate analyses.

Our study's principal limitation was its observational nature and retrospective design. In the absence of randomization, patients with different discontinuation risks may have been channeled to a specific treatment, thereby causing selection bias and potentially affecting our analysis. Furthermore, the patient sample size was perhaps too small, especially for subgroup analyses. Our study's strength lies in the fact that it presents the experiences reported by the same team with 10 years of hindsight, which proves to be an unprecedented achievement.

The retention rates of anti-TNFs in axSpA patients proved high, with retention superior in those on IFX than those on ETN. The presence of inflammatory syndrome, moderately increased BASDAI score, and the combined use of csDMARDs were associated with even better retention.

CONFLICT OF INTEREST

No conflict of interest for any of the authors.

ETHICAL APPROVAL

This article does not involve studies with human participants performed by any of the authors. No ethics approval was needed on



account of the retrospective nature of this observational study, which was carried out using data from medical files.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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