

# Clinical Outcomes after Switching from Originator Infliximab to the Biosimilar Ixifi in Patients with Axial Spondyloarthritis: A Single-Center Study from Türkiye

Dilara Bulut Gökten<sup>1</sup>, Rıdvan Mercan<sup>1</sup>

1. Tekirdag Namik Kemal University, Department of Rheumatology

## \* Correspondence:

Dilara Bulut Gökten

Department of Rheumatology, Tekirdag Namik Kemal University

Tekirdag, Türkiye

Email: [dilarabulutgokten@gmail.com](mailto:dilarabulutgokten@gmail.com)

ORCID: 0000-0002-9226-7532

**Running title:** Switching from Originator to Biosimilar

## Abstract

**Background:** Biosimilar infliximab agents are increasingly used in the management of axial spondyloarthritis (axSpA), primarily driven by cost considerations. While clinical outcomes after switching from originator infliximab (INF) to several biosimilars have been reported, real-world data regarding switching to Ixifi remain limited. **Objectives:** To evaluate clinical outcomes, treatment retention and safety following non-medical switching from originator INF to the biosimilar Ixifi in patients with axSpA. **Methods:** This single-center observational cohort study included adult patients with axSpA who were transitioned from originator INF to Ixifi for non-medical reasons. Clinical assessments and laboratory parameters were recorded at baseline and at 3 and 6 months after switching. Disease activity was evaluated using ASDAS, BASDAI and BASFI. Safety outcomes and treatment discontinuation were systematically recorded. **Results:** 72 patients were included. Inflammatory markers, including C-reactive protein and erythrocyte sedimentation rate, remained stable over 6 months ( $p>0.05$  for all), as did ASDAS scores ( $p>0.05$ ). In contrast, BASDAI and BASFI showed modest but statistically significant improvements at month 6 ( $p=0.008$  and  $p=0.002$ , respectively). 2 serious infections (2.8%) and 2 infusion reactions (2.8%) were observed. Treatment discontinuation occurred in 13.9% of

Received: April 2<sup>nd</sup> 2026

Accepted: April 20<sup>th</sup> 2026

Published: May 1<sup>st</sup> 2026

Copyright: © 2026 by the authors.

License: Bulgarian Society for Rheumatology.

This is an open access article distributed under the terms of the Creative Commons Attribution (CC BY) license.

How to cite: Bulut Gökten, D., & Mercan, R. (2026). Clinical Outcomes after Switching from Originator Infliximab to the Biosimilar Ixifi in Patients with Axial Spondyloarthritis: A Single-Center Study from Türkiye. *Rheumatology (Bulgaria)*, 34(1), 4-20. <https://doi.org/10.35465/wx09tq86>



patients, exclusively due to loss of efficacy. The estimated 6-month treatment retention rate was 86.1%. Conclusion: In this real-world cohort, non-medical switching from originator infliximab to Ixifi in axSpA was associated with maintained short-term clinical stability, acceptable treatment retention and a favorable safety profile. However, the absence of a control group limits causal interpretation of these findings. Larger studies with longer follow-up are warranted to confirm long-term outcomes.

**Keywords:** Ankylosing spondylitis; Spondyloarthritis; Infliximab; Biosimilar pharmaceuticals; Drug switching; Treatment outcome

## 1. Introduction

Tumor necrosis factor alpha inhibitors constitute a cornerstone in the management of inflammatory rheumatic diseases by effectively suppressing disease activity and preventing structural and functional damage [1]. Among these agents, originator infliximab (Remicade) has been widely used for over two decades, with robust evidence supporting its efficacy and well-established safety profile across multiple indications [2]. However, the high cost of biologic therapies and the chronic nature of these diseases have imposed a substantial financial burden on healthcare systems, thereby accelerating the adoption of biosimilar agents in routine clinical practice [3].

Biosimilars are biological products that demonstrate a high degree of similarity to their reference product in terms of quality characteristics, pharmacokinetics, efficacy, safety and immunogenicity [4]. For infliximab (INF) biosimilars, randomized controlled trials conducted in patients with rheumatoid arthritis (RA) and other inflammatory conditions have consistently shown comparable clinical efficacy and safety outcomes when compared with the originator molecule [5]. Beyond initial equivalence studies, increasing attention has been directed toward the clinical consequences of switching stable patients from originator INF to biosimilar INF, commonly referred to as non-medical switching [6]. The NOR-SWITCH trial, a large multicenter randomized non-inferiority study including several immune mediated inflammatory diseases, demonstrated that switching from originator INF to the biosimilar CT-P13 was not associated with a higher risk of disease worsening [7]. These findings were further corroborated by the open label extension phase, which showed sustained efficacy and comparable safety following the switch [8]. Large observational cohorts have reported generally stable disease activity following mandatory or voluntary transitions from originator INF to biosimilars,

although slightly increased treatment discontinuation rates have been observed in some studies [9].

In addition to rheumatologic diseases, observational studies in inflammatory bowel disease (IBD) populations have similarly indicated that switching from reference INF to biosimilar is not associated with clinically meaningful deterioration in disease control or increased adverse events [10]. Despite the growing body of evidence supporting INF biosimilars, real-world data evaluating switches to specific biosimilar molecules remain limited. In particular, clinical experience with switching from originator INF to Ixifi, a biosimilar approved based on extrapolation of indications is scarce in the literature [11]. Therefore, additional cohort studies assessing clinical outcomes, treatment persistence and safety following such switches are warranted.

In this context, the present study aims to evaluate the clinical course and treatment outcomes of patients transitioned from originator INF to Ixifi in a real-world rheumatology setting for axial spondyloarthritis patients (axSpA).

## **2. Materials and Methods**

### **Study design and patient selection**

This single-center observational cohort study included adult patients with axSpA who were transitioned from originator infliximab (Remicade) to the biosimilar Ixifi. Patients were eligible for inclusion if they had received at least one infusion of Ixifi following the switch and had available baseline and follow up clinical and laboratory data. Demographic characteristics and disease related variables were recorded at baseline prior to the switch. Patients were consecutively recruited between 2022 and 2026 at the rheumatology outpatient clinic. Individuals with incomplete follow up data or who discontinued treatment immediately after switching were excluded. Given the retrospective design, no imputation methods were applied, and analyses were conducted using available data only.

### **Treatment protocol and switching strategy**

The switch from originator INF to Ixifi was performed for non-medical reasons in accordance with institutional practice [12]. Ixifi was administered using the same dosing regimen and infusion intervals as the originator INF. No changes in concomitant therapies were routinely

mandated at the time of switching. Patients were followed within routine outpatient visits at 3 and 6 months after the switch.

### **Data collection, outcome measures and safety assessment**

Clinical and laboratory parameters were assessed at baseline and during follow up visits at month 3 and month 6. Disease activity was evaluated using the Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) where applicable. Laboratory assessments included inflammatory markers, liver enzymes, renal function parameters, urinalysis findings and hematological indices.

Safety outcomes were evaluated throughout the follow up period. Adverse events were recorded at each visit and classified according to type and severity. Serious adverse events were defined as events requiring hospitalization or leading to treatment discontinuation. Infusion reactions, infections, laboratory abnormalities and cardiovascular events were specifically monitored. Reasons for treatment discontinuation and follow up completion status were documented. Treatment discontinuation due to loss of efficacy was based on the treating physician's clinical judgment, supported by worsening of disease activity parameters, including ASDAS and/or BASDAI scores, as well as persistent or increasing inflammatory markers (CRP, ESR) where available.

### **Statistical analysis**

Continuous variables were assessed for normality and are presented as median and interquartile range (IQR). Comparisons between baseline and follow up measurements were performed using the Wilcoxon signed-rank test. Paired categorical variables were compared using McNemar's test. All statistical analyses were conducted using two-sided tests, and a p value <0.05 was considered statistically significant. Kaplan-Meier analysis was used to estimate treatment retention, and 95% confidence intervals were calculated. Censoring was applied to patients who completed follow-up without discontinuation.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the local ethics committee (approval number: 2025.184.10.19, approval date: 30 October 2025). Due to the retrospective observational design of the study, the use of anonymized data and the absence of any direct patient intervention, the

requirement for written informed consent was waived by the local ethics committee.

3. Results

A total of 72 patients with axSpA who were switched from originator INF to Ixifi were included in the analysis. Baseline demographic and clinical characteristics are summarized in Table (see Table 1).

**Table 1.** Baseline demographic and clinical characteristics of the study population

| Variable                                                    | Value            |
|-------------------------------------------------------------|------------------|
| Age (years), median (IQR)                                   | 49.0 (41.5–57.3) |
| Sex, female, n (%)                                          | 32 (44.4)        |
| Symptom duration (years), median (IQR)                      | 12.0 (10.0–18.0) |
| Age at diagnosis (years), median (IQR)                      | 37.0 (29.0–45.0) |
| Duration of prior infliximab exposure (years), median (IQR) | 4.0 (2.0–5.0)    |
| Ever smoker, n (%)                                          | 40 (55.6)        |
| HLA-B27 positivity, n (%)                                   | 50 (69.4)        |
| <b>Concomitant therapies, n (%)</b>                         |                  |
| On-demand NSAID use                                         | 72 (100)         |
| csDMARDs (sulfasalazine)                                    | 14 (19.4)        |
| Glucocorticoids                                             | 10 (13.9)        |

Values are presented as median (interquartile range, IQR) unless otherwise stated. Categorical variables are expressed as number (percentage). NSAIDs were used on demand. csDMARDs refer to sulfasalazine. IQR, interquartile range; HLA-B27, human leukocyte antigen B27.

Inflammatory markers including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), did not show a statistically significant change over the 6 month follow up period. Disease activity assessed by the ASDAS also remained stable after switching. Functional and disease activity indices demonstrated small but statistically significant improvements over time. Median BASDAI scores decreased from baseline to month 6 ( $p=0.008$ ), and a similar improvement was observed in BASFI scores ( $p=0.002$ ).

With regard to laboratory safety parameters, liver and renal function tests remained largely stable throughout follow up. A statistically significant change was observed in aspartate aminotransferase levels between baseline and month 6 ( $p=0.004$ ), however, values remained within the normal reference range. Platelet counts also showed a statistically significant difference over time ( $p=0.018$ ). Despite statistical significance, these changes were not considered clinically relevant. No significant changes were observed in hemoglobin levels, white blood cell counts,

creatinine or estimated glomerular filtration rate. The prevalence of hematuria and proteinuria on urinalysis did not differ significantly between baseline and follow-up assessments. Changes in clinical and laboratory parameters are presented in Table 2 (see Table 2).

**Table 2.** Changes in laboratory parameters and disease activity indices from baseline to month 6

| Parameter                                            | Baseline                | Month 3                 | Month 6                 | p value<br>(Baseline<br>vs Month 6) |
|------------------------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------------------|
| <b>Laboratory parameters</b>                         |                         |                         |                         |                                     |
| CRP (mg/L), median (IQR)                             | 4.20<br>(1.23–9.61)     | 3.98<br>(1.42–9.98)     | 2.96<br>(1.15–6.20)     | 0.447                               |
| ALT (U/L), median (IQR)                              | 18.81<br>(15.90–23.55)  | 21.00<br>(16.55–26.25)  | 20.00<br>(15.00–25.00)  | 0.279                               |
| AST (U/L), median (IQR)                              | 18.05<br>(13.97–20.25)  | 19.90<br>(15.28–22.00)  | 19.15<br>(16.85–23.38)  | <b>0.004</b>                        |
| Creatinine (mg/dL), median (IQR)                     | 0.84<br>(0.72–0.98)     | 0.82<br>(0.70–0.97)     | 0.90<br>(0.74–1.01)     | 0.503                               |
| GFR (mL/min), median (IQR)                           | 94.25<br>(80.97–107.29) | 95.80<br>(83.75–108.42) | 93.80<br>(79.75–108.13) | 0.831                               |
| ALP (U/L), median (IQR)                              | 75.00<br>(66.00–93.25)  | 77.50<br>(63.50–95.00)  | 76.50<br>(64.75–92.25)  | 0.986                               |
| GGT (U/L), median (IQR)                              | 23.00<br>(14.00–32.00)  | 22.50<br>(16.00–32.75)  | 26.00<br>(14.75–38.25)  | 0.452                               |
| Hemoglobin (g/dL), median (IQR)                      | 14.05<br>(12.40–14.90)  | 13.53<br>(11.95–14.60)  | 13.85<br>(12.35–14.90)  | 0.844                               |
| WBC ( $\times 10^3/\mu\text{L}$ ), median (IQR)      | 7305<br>(6405–8970)     | 7095<br>(5575–8955)     | 7030<br>(6348–7993)     | 0.213                               |
| Platelet ( $\times 10^3/\mu\text{L}$ ), median (IQR) | 252 (204–288)           | 248.5<br>(209–296.5)    | 256<br>(231.8–293.0)    | <b>0.018</b>                        |
| ESR (mm/h), median (IQR)                             | 11.00<br>(6.00–20.00)   | 14.50<br>(8.00–22.25)   | 13.00<br>(6.00–18.25)   | 0.316                               |
| Hematuria present urinalysis, n (%)                  | 6 (8.3)                 | 6 (8.3)                 | 8 (11.1)                | 0.500                               |
| Proteinuria present urinalysis, n (%)                | 6 (8.3)                 | 6 (8.3)                 | 8 (11.1)                | 0.500                               |
| <b>Clinical and disease activity indices</b>         |                         |                         |                         |                                     |
| ASDAS score, median (IQR)                            | 1.00<br>(0.50–1.60)     | 1.20<br>(0.60–1.52)     | 0.90<br>(0.40–1.40)     | 0.761                               |
| BASDAI, median (IQR)                                 | 3.20<br>(2.77–3.52)     | 3.10<br>(2.50–3.52)     | 3.00<br>(2.49–3.40)     | <b>0.008</b>                        |
| BASFI, median (IQR)                                  | 3.20<br>(2.77–3.73)     | 3.20<br>(2.60–3.70)     | 3.20<br>(2.60–3.42)     | <b>0.002</b>                        |

CRP, C-reactive protein; ASDAS, Ankylosing spondylitis disease activity score; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GFR, glomerular filtration rate; ALP, alkaline phosphatase; GGT, gamma glutamyl transferase; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; IQR, interquartile range. Continuous variables are presented as median (IQR); p values represent comparisons between baseline and month 6 measurements using the Wilcoxon signed-rank test; paired categorical variables were compared using McNemar's test; p values <0.05 were considered statistically significant.

During the follow up period, adverse events were infrequent. 2 patients (2.8%) experienced an infection classified as a serious adverse event, which led to treatment discontinuation. 2 infusion reactions (2.8%) were observed. No cases of transaminase elevation, hematological abnormalities or cardiovascular adverse events were recorded. Overall, 10 patients (13.9%) discontinued Ixifi during follow up, all due to loss of efficacy, occurring at a mean duration of 4.2 months. Among the 10 patients who discontinued treatment, discontinuations occurred predominantly within the first 3 months after switching (n=6), with fewer events at months 4 and 6. Although baseline clinical and laboratory parameters varied among these patients, no clear distinguishing pattern was identified. Given the limited number of discontinuations, detailed subgroup analysis was not feasible. No discontinuations related to patient preference, access issues, or remission were observed. A total of 62 patients (86.1%) completed the 6 month follow up period (see Table 3).

**Table 3.** Adverse events, safety outcomes, and reasons for treatment discontinuation

| Adverse events and safety outcomes                         |         |                          |                                        |
|------------------------------------------------------------|---------|--------------------------|----------------------------------------|
| Adverse event type                                         | n (%)   | Serious adverse event, n | Related to drug discontinuation, n (%) |
| Infection (upper respiratory / pneumonia / other)          | 2 (2.8) | 2                        | 2 (2.8)                                |
| Transaminase elevation                                     | 0 (0.0) | 0                        | 0 (0.0)                                |
| Hematological (anemia, leukopenia, thrombocytopenia)       | 0 (0.0) | 0                        | 0 (0.0)                                |
| Infusion reaction                                          | 2 (2.8) | 0                        | 0 (0.0)                                |
| Hypertension / heart failure exacerbation                  | 0 (0.0) | 0                        | 0 (0.0)                                |
| Reasons for treatment discontinuation and follow up status |         |                          |                                        |
| Reason                                                     | n (%)   | Mean duration (months)   |                                        |

|                                    |              |     |
|------------------------------------|--------------|-----|
| Loss of efficacy                   | 8<br>(11.1)  | 4.2 |
| Patient preference / access issues | 0 (0.0)      | —   |
| Discontinuation due to remission   | 0 (0.0)      | —   |
| Total discontinuations             | 10<br>(13.9) | 4.2 |
| Completed 6 months, n (%)          | 62<br>(86.1) | —   |

Adverse events are presented as number (percentage). Pneumonia was classified as a serious adverse event. 2 adverse events led to treatment discontinuation. Treatment discontinuation was exclusively driven by insufficient clinical or laboratory response, occurring at a mean of 4.2 months. No patient discontinued therapy due to remission.

Kaplan-Meier analysis demonstrated an estimated 6-month treatment retention rate of 86.1%, with most discontinuations occurring within the first 3 months after switching (see Figure 1).

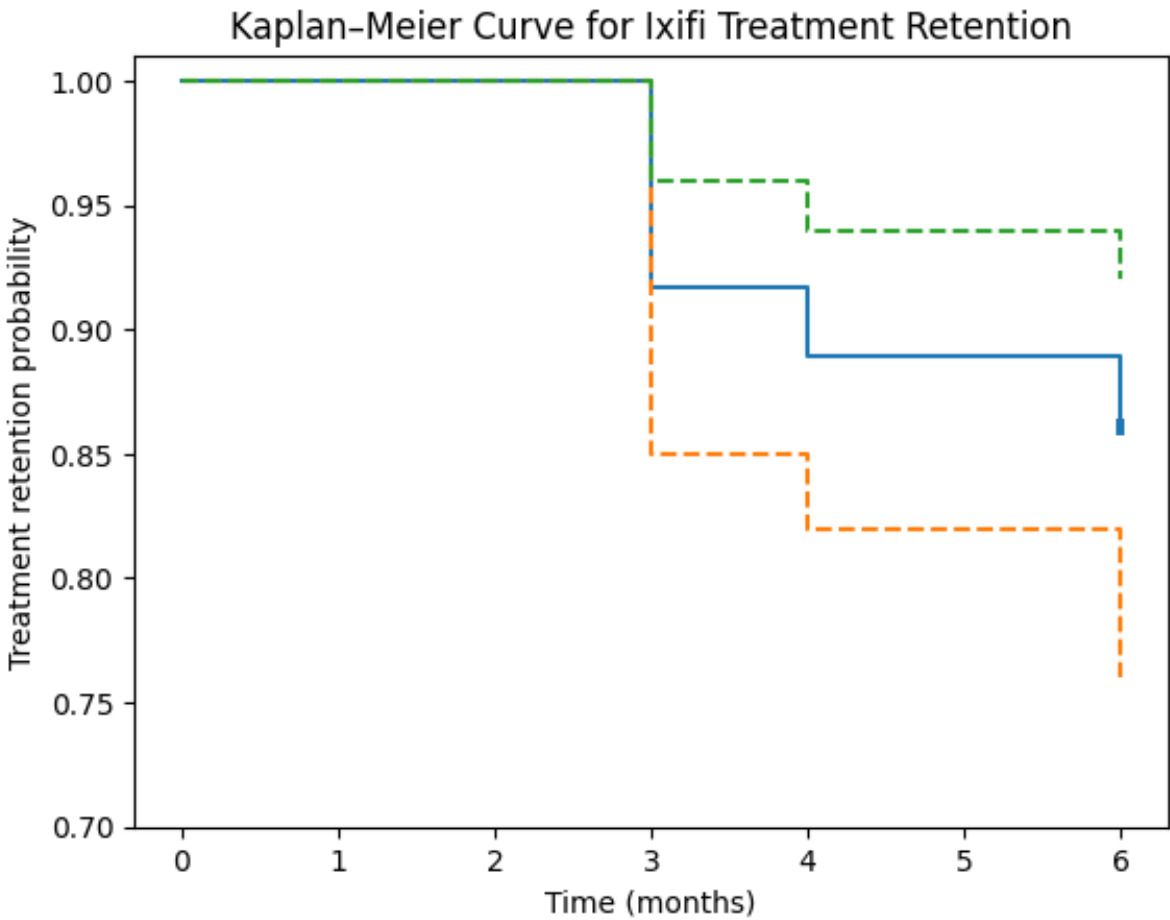


**Figure 1.** Kaplan-Meier curve showing treatment retention after switching from originator INF to Ixifi. The estimated 6-month treatment retention rate was 86.1% (95% CI: 76–92%). Tick marks indicate censored observations. The number of patients at risk at each time point is shown below the x-axis.

## 4. Discussion

To our knowledge, there are no previously published cohort studies from Türkiye evaluating clinical outcomes after switching from originator INF to the biosimilar Ixifi. Previous Turkish data have mainly focused on transitions to other INF biosimilars or utilization patterns of INF products [13]. These gaps highlight the novelty and regional contribution of the present analysis.

Randomized evidence from the NOR-SWITCH trial demonstrated that switching from originator INF to CT-P13 was not inferior to continued originator treatment across several indications, although the study was not powered for non-inferiority within each individual disease subgroup [7]. The subsequent extension study supported maintained effectiveness and a comparable safety profile in patients who switched, reinforcing the overall feasibility of switching strategies in stable patients [8]. While current study lacked a parallel originator continuation arm, the absence of meaningful deterioration in inflammatory markers and ASDAS after switching is directionally consistent with these randomized findings [7, 8].

Within SpA specifically, controlled and observational data have generally suggested that switching from reference INF to biosimilars does not lead to clinically relevant loss of disease control. In AxSpA, the PLANETAS extension reported comparable efficacy and safety after switching from reference INF to CT-P13 [14]. Moreover, registry-based evidence from DANBIO, which included patients with axSpA among other inflammatory arthritides, found no negative impact on disease activity after a nationwide switch, although treatment retention appeared slightly lower compared with a historic originator cohort [9, 15]. This study's observed retention and the timing of discontinuations, predominantly early after switching, fit the pattern described in real-world studies, where early stops may cluster around the switch period [15].

A notable observation in the current cohort was the modest but statistically significant improvement in BASDAI and BASFI at month 6, despite stable ASDAS and inflammatory markers. This discrepancy highlights the well-recognized divergence between patient-reported outcomes and objective measures of inflammation. While BASDAI and BASFI primarily capture subjective domains such as pain, fatigue and functional limitation, ASDAS incorporates an objective inflammatory parameter (CRP) [16], providing a more inflammation-driven assessment of disease activity. In this context, the observed improvements in patient-reported outcomes may reflect factors beyond true biological changes in inflammation, including

variability in symptom perception and expectancy-related effects. Although the nocebo effect has been widely discussed in the setting of biosimilar switching, a converse placebo or positive expectancy effect may also occur, particularly when patients perceive the switch as clinically acceptable or beneficial [17,18]. Such effects may preferentially influence subjective outcomes, including symptom perception and functional status, without corresponding changes in objective inflammatory markers [19]. Therefore, the observed improvements in BASDAI and BASFI should be interpreted with caution and may not necessarily reflect a true biological improvement in disease activity. Although BASFI showed a statistically significant improvement over time, the median values remained unchanged between baseline and month 6. This apparent discrepancy may be explained by the distribution of individual patient changes, where small but consistent improvements across a subset of patients can lead to statistical significance without a shift in the median value [20].

From a safety standpoint, adverse events were infrequent in the present cohort. In contrast, the French nationwide ReFLECT cohort reported at least one adverse event in more than half of patients, while serious adverse events occurred in approximately 10–14% across rheumatic indications, including axSpA [21]. Similarly, in a prospective cohort of patients with IBD undergoing a non-medical switch to the INF biosimilar GP-1111, allergic and paradoxical reactions were observed and led to treatment discontinuation in a subset of patients, although no new or unexpected safety signals were identified [22]. Differences in adverse event frequency across studies are likely attributable to variations in sample size, underlying disease populations and duration of follow up rather than to biosimilar specific safety concerns. Consistent with these observations, a narrative review by Abidin et al. summarizing randomized and observational studies on switching from reference INF to biosimilars across multiple inflammatory diseases reported maintained disease control and an acceptable safety profile without new safety concerns [23].

Although statistically significant changes were observed in AST and platelet levels over time, these variations remained within normal laboratory reference ranges and were not accompanied by clinical symptoms or other laboratory abnormalities suggestive of hepatotoxicity or hematological dysfunction. Therefore, these findings were considered unlikely to be clinically meaningful. However, it should be acknowledged that subtle trends, even within the normal range, may become more relevant over longer follow-up periods [24]. Accordingly, these parameters may warrant closer monitoring in future studies with extended observation periods [25].

When the situation in Türkiye is considered, real-world data on biologic switching and the use of INF biosimilars in axSpA have increasingly become available. Data from the TURKBIO registry have shown that the INF biosimilar CT-P13 is associated with acceptable long-term effectiveness, treatment retention and a favorable safety profile in axSpA [26]. In addition, national real-world analyses from Türkiye have evaluated treatment patterns with CT-P13, a descriptive study based on Turkish Ministry of Health claims reported higher discontinuation and switching rates among patients initiating CT-P13 compared with those starting on reference INF, suggesting differences in real-world utilization patterns between the biosimilar and the originator [13].

This study has limitations. The observational single-center design and the absence of a control group preclude causal inference and do not allow clear attribution of the observed outcomes to the switching strategy. The apparent stability in disease activity may partly reflect the natural course of the disease or regression to the mean, rather than a true effect of switching. Therefore, the findings should be interpreted with caution and considered descriptive rather than confirmatory. Follow-up was limited to 6 months, which may be insufficient to fully capture long-term treatment effectiveness, safety outcomes and durability of response in a chronic disease. In particular, this relatively short observation period may not adequately reflect the impact of immunogenicity, including the development of anti-drug antibodies (ADAs), which can occur over time. Additionally, certain adverse events, especially those related to cumulative exposure or delayed immunological mechanisms, may not be fully captured within this timeframe. Therefore, the present findings should be interpreted as reflecting short-term clinical stability and long-term outcomes after switching remain to be confirmed.

Additional important limitation is the lack of immunogenicity assessment, including INF trough levels and ADA measurements. This is particularly relevant given that treatment discontinuation in this cohort was exclusively attributed to loss of efficacy. In the absence of pharmacokinetic and immunogenicity data, it is not possible to distinguish between true pharmacodynamic failure and secondary loss of response. The development of ADAs has been associated with reduced drug levels and diminished clinical response in patients. This limitation is especially important for INF, as immunogenicity is known to play a central role in treatment response and persistence. Therefore, the lack of these data limits the interpretation of treatment discontinuation and prevents a more precise understanding of the underlying mechanisms.

Although this study provides real-world evidence on switching from originator INF, it was not designed or powered to formally assess non-inferiority. The relatively modest sample size and the absence of a parallel control group limit the ability to detect small differences in clinical outcomes or safety signals. The findings should be interpreted as descriptive and hypothesis-generating rather than confirmatory. In addition, treatment discontinuation due to loss of efficacy was not based on predefined standardized criteria but rather on physician judgment supported by clinical and laboratory parameters, which may introduce variability in outcome assessment. Future adequately powered, controlled studies with integrated immunogenicity monitoring are needed to assess non-inferiority between originator and biosimilar INF in axSpA, as well as to better define predictors of treatment failure following switching. The exclusion of patients with incomplete follow-up or those who discontinued treatment immediately after switching may introduce selection bias. This approach may have led to an overestimation of treatment retention rates and a potential underestimation of early adverse outcomes, particularly those occurring shortly after the switch.

Despite these limitations, current data contribute real-world evidence on switching from originator INF to Ixifi in axSpA which is a setting where molecule specific experience is still scarce. Taken together with prior randomized and registry data on INF switching, this study's findings may estimate that switching to Ixifi can be performed with maintained short term clinical stability, a favorable safety profile, and acceptable treatment persistence. Larger multicenter studies with longer follow up and immunogenicity monitoring are warranted to further clarify predictors of discontinuation and long-term outcomes after switching to Ixifi in axSpA.

## 5. Conclusions

In this cohort of patients with axSpA, switching from originator INF to the biosimilar Ixifi was associated with maintained short term clinical stability, acceptable treatment retention and a favorable safety profile. No clinically meaningful deterioration in disease activity or new safety concerns were observed over 6 months of follow up. These findings suggest that non-medical switching to Ixifi may be feasible in axSpA in the short term, however, larger studies with longer follow up are required to better define long term outcomes.

## Declarations

### Author Contributions

Conceptualization: D.B.G. and R.M.; Methodology: D.B.G and R.M.; Formal analysis: D.B.G.; Investigation: D.B.G.; Writing – original draft: D.B.G.; Writing – review & editing: all authors.

### Funding

This research received no external funding.

### Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of [Tekirdag Namik Kemal University] (approval number:2025.184.10.19, approval date: 30 October 2025)

### Informed Consent Statement

Due to the retrospective observational design of the study, the use of anonymized data and the absence of any direct patient intervention, the requirement for written informed consent was waived by the local ethics committee.

### Data Availability Statement

The data presented in this study are available on reasonable request from the corresponding author.

### Conflicts of Interest

The authors declare no conflict of interest.

## References

1. Gerriets, V., A. Goyal, and K. Khaddour, Tumor necrosis factor inhibitors. StatPearls Publishing; 2023
2. Braun, J., J. Brandt, J. Listing, et al., Treatment of active ankylosing spondylitis with infliximab: a randomised controlled multicentre trial. *Lancet*. 2002;359(9313):1187-93. doi: 10.1016/s0140-6736(02)08215-6.
3. Hillhouse, E., K. Mathurin, J. Bibeau, et al., The Economic Impact of Originator-to-Biosimilar Non-medical Switching in the Real-World Setting: A Systematic Literature Review. *Adv Ther*. 2022;39(1):455-487. doi: 10.1007/s12325-021-01951-z.

4. Castañeda-Hernández, G., R. González-Ramírez, J. Kay, et al., Biosimilars in rheumatology: what the clinician should know. *RMD Open*. 2015;1(1):e000010. doi: 10.1136/rmdopen-2014-000010.
5. Choe, J.Y., N. Prodanovic, J. Niebrzydowski, et al., A randomised, double-blind, phase III study comparing SB2, an infliximab biosimilar, to the infliximab reference product Remicade in patients with moderate to severe rheumatoid arthritis despite methotrexate therapy. *Ann Rheum Dis*. 2017;76(1):58-64. doi:10.1136/annrheumdis-2015-207764.
6. Dolinar, R., C.G. Kohn, F. Lavernia, et al., The non-medical switching of prescription medications. *Postgrad Med*. 2019;131(5):335-341. doi: 10.1080/00325481.2019.1618195.
7. Jørgensen, K.K., I.C. Olsen, G.L. Goll, et al., Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. *Lancet*. 2017;389(10086):2304-2316. doi: 10.1016/S0140-6736(17)30068-5.
8. Goll, G.L., K.K. Jørgensen, J. Sexton, et al., Long-term efficacy and safety of biosimilar infliximab (CT-P13) after switching from originator infliximab: open-label extension of the NOR-SWITCH trial. *J Intern Med*. 2019;285(6):653-669. doi: 10.1111/joim.12880.
9. Glintborg, B., I.J. Sørensen, A.G. Loft, et al., A nationwide non-medical switch from originator infliximab to biosimilar CT-P13 in 802 patients with inflammatory arthritis: 1-year clinical outcomes from the DANBIO registry. *Ann Rheum Dis*. 2017;76(8):1426-1431. doi: 10.1136/annrheumdis-2016-210742.
10. Chaparro, M., A. Garre, M.F. Guerra Veloz, et al., Effectiveness and Safety of the Switch from Remicade® to CT-P13 in Patients with Inflammatory Bowel Disease. *J Crohns Colitis*. 2019;13(11):1380-1386. doi: 10.1093/ecco-jcc/ijz070.
11. Hussein, R.G. and M.Q. Al-Atrakji, Impact of Infliximab Biosimilar (Ixifi®) Trough Levels on Disease Activity and Inflammatory Markers in Iraqi Rheumatoid Arthritis Patients. *Al-Rafidain Journal of Medical Sciences*, 2024;7(1):36-40. [https://doi.org/10.54133/ajms.v7i1\(Special\).906](https://doi.org/10.54133/ajms.v7i1(Special).906).
12. Jankowska, M., K. Dessureault, J. MacDougall, et al., Impact of Nonmedical Switches From Reference Infliximab to Biosimilars on Disease Control Within a Rheumatology Practice. *J Pharm Technol*. 2025;41(2):83-89. doi: 10.1177/87551225241308475.
13. Yazici, Y., L. Xie, A. Ogbomo, et al., A descriptive analysis of real-world treatment patterns of innovator (Remicade) and biosimilar infliximab in an infliximab-naïve Turkish population. *Biologics*. 2018;12:97-106. doi: 10.2147/BTT.S172241.
14. Park, W., D.H. Yoo, P. Miranda, et al., Efficacy and safety of switching from reference infliximab to CT-P13 compared with maintenance of CT-P13 in ankylosing spondylitis: 102-week data from the PLANETAS extension study. *Ann Rheum Dis*. 2017;76(2):346-354. doi: 10.1136/annrheumdis-2015-208783.
15. Scherlinger, M., V. Germain, C. Labadie, et al., Switching from originator infliximab to biosimilar CT-P13 in real-life: The weight of patient acceptance. *Joint Bone Spine*. 2018;85(5):561-567. doi: 10.1016/j.jbspin.2017.10.003.
16. Machado, P., V. Navarro-Compán, R. Landewé, et al., Calculating the ankylosing spondylitis disease activity score if the conventional c-reactive protein level is below the limit of detection or if high-sensitivity c-reactive protein is used: an analysis in the DESIR cohort. *Arthritis Rheumatol*. 2015;67(2):408-13. doi: 10.1002/art.38921.

17. Rezk, M.F. and B. Pieper, To See or NOsee: The Debate on the Nocebo Effect and Optimizing the Use of Biosimilars. *Adv Ther.* 2018;35(6):749-753. doi: 10.1007/s12325-018-0719-8.
18. Odinet, J.S., C.E. Day, J.L. Cruz, et al., The Biosimilar Nocebo Effect? A Systematic Review of Double-Blinded Versus Open-Label Studies. *J Manag Care Spec Pharm.* 2018;24(10):952-959. doi: 10.18553/jmcp.2018.24.10.952.
19. Wei, J.C., L.J. Zhang, and J.X. Huang, Placebo responses in ankylosing spondylitis patients worldwide: variations and possible explanations. *Expert Rev Clin Immunol.* 2020;16(5):447-450. doi: 10.1080/1744666X.2020.1748500.
20. Guyatt, G.H., D. Osoba, A.W. Wu, et al., Methods to explain the clinical significance of health status measures. *Mayo Clin Proc.* 2002;77(4):371-83. doi: 10.4065/77.4.371.
21. Marotte, H., A. Cantagrel, F. Coury, et al., Real-World Effectiveness and Safety of Infliximab Biosimilar CT-P13 for Rheumatic Diseases: A National Observational Cohort Study (ReFLECT). *Adv Ther.* 2025;42(9):4659-4680. doi: 10.1007/s12325-025-03304-6.
22. Pápista, M., T. Resál, P. Bacsur, et al., Efficacy, Safety, and Cost-Effectiveness of the Infliximab Biosimilar GP-1111 in Patients with Inflammatory Bowel Disease Who Underwent a Nonmedical Switch: A Prospective Cohort Study. *Biologics.* 2025;19:731-743. doi: 10.2147/BTT.S559503.
23. Abidin, A.Z., C.L. Snoswell, L. Shafiee Hanjani, et al., Infliximab switching from reference product to biosimilar: a review of evidence regarding the clinical efficacy, safety profile and immunogenicity. *Journal of Pharmacy Practice and Research.* 2021;51(5):358-373. doi:10.1002/jppr.1754.
24. French, J.B., M. Bonacini, M. Ghabril, et al., Hepatotoxicity Associated with the Use of Anti-TNF- $\alpha$  Agents. *Drug Saf.* 2016;39(3):199-208. doi: 10.1007/s40264-015-0366-9.
25. Toussiro, E. and D. Wendling, The use of TNF-alpha blocking agents in rheumatoid arthritis: an overview. *Expert Opin Pharmacother.* 2004;5(3):581-94. doi: 10.1517/14656566.5.3.581.
26. Uslu, S., S. Güle, G. Sen, et al., Efficacy and Safety of CT-P13 as First- and Second-Line Treatment in Patients with Ankylosing Spondylitis. *Journal of Clinical Medicine.* 2024;13(23):7266. doi:10.3390/jcm13237266.

## Клинични резултати след преминаване от оригинален инфликсимаб към биоподобен Ixifi при пациенти с аксиален спондилоартрит: едноцентрово проучване от Турция

### Резюме

**Въведение:** Биоподобните агенти инфликсимаб се използват все по-често при лечението на аксиален спондилоартрит (axSpA), главно поради съображения за цена. Въпреки че са докладвани клинични резултати след преминаване от оригинален инфликсимаб (INF) към няколко биоподобни лекарства, данните от реалния свят относно преминаването към Ixifi остават ограничени. **Цели:** Целта е да се оценят клиничните резултати, задържането на лечението и безопасността след немедицинско преминаване от оригинален INF към биоподобен Ixifi при пациенти с axSpA. **Методи:** Това едноцентрово обсервационно кохортно проучване включва възрастни пациенти с axSpA, които са преминали от оригинален INF към Ixifi по немедицински причини. Клиничните оценки и лабораторните параметри са записани в началото и на 3 и 6 месеца след преминаването. Активността на заболяването е оценена с помощта на ASDAS, BASDAI и BASFI. Резултатите от безопасността и прекратяването на лечението са систематично записани. **Резултати:** Включени са 72 пациенти. Възпалителните маркери, включително С-реактивен протеин и скорост на утаяване на еритроцитите, останаха стабилни в продължение на 6 месеца ( $p > 0,05$  за всички), както и ASDAS резултатите ( $p > 0,05$ ). За разлика от тях, BASDAI и BASFI показаха умерени, но статистически значими подобрения на 6-ия месец (съответно  $p = 0,008$  и  $p = 0,002$ ). Наблюдавани са 2 сериозни инфекции (2,8%) и 2 инфузионни реакции (2,8%). Прекратяване на лечението е наблюдавано при 13,9% от пациентите, изключително поради загуба на ефикасност. Очакваният 6-месечен процент на задържане на лечението е 86,1%. **Заклучение:** В тази реална кохорта, немедикаментозното преминаване от оригинален инфликсимаб към Ixifi при axSpA е свързано с поддържана краткосрочна клинична стабилност, приемливо задържане на лечението и благоприятен профил на безопасност. Липсата на контролна група обаче ограничава причинно-следствената интерпретация на тези резултати. Необходими са по-големи проучвания с по-дълго проследяване, за да се потвърдят дългосрочните резултати.

**Ключови думи:** Анкилозиращ спондилит; Спондилоартрит; Инфликсимаб; Биоподобни фармацевтични продукти; Смяна на лекарството; Резултат от лечението