Original Article
Yonsei Med J 2023 Dec;64(12):697-704
https://doi.org/10.3349/ymj.2023.0151
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

Drug Retention Rate and Factors Associated with Discontinuation of Interleukin-17 Inhibitors in Patients with Axial Spondyloarthritis

Oh Chan Kwon and Min-Chan Park
Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea.

Purpose: To assess the drug retention rate of interleukin-17 inhibitors (IL-17is) over long-term observation in patients with axial spondyloarthritis (axSpA) in whom treatment with tumor necrosis factor inhibitors (TNFis) failed and to determine baseline factors associated with discontinuation of IL-17is.
Materials and Methods: This retrospective cohort study included 68 patients with axSpA started on IL-17is after an inadequate response or intolerance to ≥1 TNFis. Drug retention rates at 1, 2, and 3 years were assessed. Baseline (i.e., at initiation of IL-17is) factors associated with discontinuation of IL-17is were evaluated using multivariable Cox proportional hazard regression analysis.
Results: Over 1933.9 person-months of observation in 68 patients, discontinuation of IL-17is occurred in 27 (39.7%) patients. Twenty (29.4%) patients discontinued IL-17is because of ineffectiveness, and 7 (10.3%) patients discontinued IL-17is because of adverse events. The 1-year, 2-year, and 3-year drug retention rates for IL-17is were 71.9%, 66.5%, and 62.0%, respectively. Current smoking was associated with a higher risk of IL-17is discontinuation [adjusted hazard ratio (HR)=2.256, 95% confidence interval (CI)=1.053–4.831, p=0.036], while previous use of ≥3 TNFis (vs. 1) was significantly associated with a lower risk of IL-17is discontinuation (adjusted HR=0.223, 95% CI=0.051–0.969, p=0.045).
Conclusion: In patients with axSpA in whom TNFis failed, the long-term drug retention rate of IL-17is appears to be acceptable, with a 3-year drug retention rate of approximately 60%. Current smoking was associated with a higher risk of discontinuing IL-17is, whereas previous use of ≥3 TNFis was associated with a lower risk of discontinuing IL-17is.

Key Words: Axial spondyloarthritis, drug retention, interleukin-17 inhibitor

INTRODUCTION

Tumor necrosis factor inhibitors (TNFis) have greatly improved the treatment of axial spondyloarthritis (axSpA) since their introduction as therapeutic agents for axSpA more than two decades ago.[1-5] More recently, interleukin-17 inhibitors (IL-17is) have been approved for the treatment of axSpA, providing another therapeutic option for patients who fail to respond to nonsteroidal anti-inflammatory drugs.[6,7] Although both TNFis and IL-17is are efficacious in controlling inflammation and relieving symptoms of the disease, some patients do not achieve a clinical response to one agent and need to switch to another.[8] Some patients may also discontinue one agent due to an adverse event.[9] Although newer agents [targeted synthetic disease-modifying antirheumatic drugs (DMARDs)] are being added to the arsenal of treatment for axSpA,[6,7] the number of therapeutic agents with different modes of action available for the treatment of axSpA is relatively limited, compared with other inflammatory arthritides, such as rheumatoid arthritis and psoriatic arthritis.[10-12] In South Korea, IL-17is have been approved for use as a second- or later-line biological DMARD (bDMARD) according to national reimbursement policies. If IL-17is fail in this setting, treatment with bDMARD is more

Received: May 9, 2023 **Revised:** August 17, 2023
Accepted: August 21, 2023 **Published online:** November 9, 2023
Corresponding author: Min-Chan Park, MD, PhD, Division of Rheumatology, Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Korea.
E-mail: mcpark@yuhs.ac

•The authors have no potential conflicts of interest to disclose.

limited relative to the use of IL-17is as a first-line bDMARD. Therefore, drug retention rate data on IL-17is as a second- or later-line bDMARD are particularly important for informing physicians on when to choose a therapeutic agent in axSpA.

Drug retention rates for TNFis have been extensively studied. A Danish nationwide study of results from an 8-year surveillance reported 1- and 2-year drug retention rates for TNFis of 74% and 63%, respectively.[13] Similarly, a Norwegian study reported 1- and 2-year drug retention rates of 76% and 65%, respectively.[14] In addition, a Korean study reported a drug retention rate of 75.8% during a median 14 months of follow-up.[15]

Meanwhile, for IL-17is, drug retention rates have mostly been studied in European populations, where IL-17is can be used as a first- or later-line bDMARD. The reported 1-year and 2-year drug retention rates of secukinumab are 55%–72% and 43%–61%, respectively.[16-19] However, data on the drug retention rates of IL-17is when used only as second- or later-line bDMARD (as in the setting of South Korea) are scarce. Although a study from Korea reported a 1-year drug retention rate of 75% for secukinumab,[20] long-term data are limited. Moreover, data on the drug retention rate of ixekizumab, which is a more recently approved IL-17i for the treatment of axSpA, are also lacking.

In this study, we aimed to assess the longer-term drug retention rates of IL-17is, including both secukinumab and ixekizumab, in patients with axSpA who have failed to one or more TNFis. We also sought to assess baseline factors associated with drug discontinuation.

MATERIALS AND METHODS

Study population

Patients with axSpA who were started on IL-17is between August 2017 and July 2022 at a tertiary referral hospital in Seoul, South Korea were retrospectively reviewed. All patients met the Assessment of SpondyloArthritis international Society classification criteria for axSpA.[21] Patients followed-up for less than a year were excluded. Since IL-17is are approved for use only as a second- or later-line bDMARD in South Korea, all patients were previously exposed to at least one TNFi before the initiation of IL-17is.

The following covariates at baseline (i.e., the date of initiation of IL-17i) were reviewed as potential covariates that could be associated with discontinuation of IL-17is: age; sex; symptom duration; disease duration; body mass index (BMI); current smoking status; human leukocyte antigen B27 positivity; fulfillment of the radiological criterion of the 1984 modified New York criteria (radiographic axSpA vs. non-radiographic axSpA);[22] ever-presence of peripheral symptoms, uveitis, inflammatory bowel disease, or psoriasis; erythrocyte sedimentation rate (ESR); C-reactive protein (CRP) level; Bath Ankylosing Disease Activity Index (BASDAI);[23] Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP);[24] concomitant use of nonsteroidal anti-inflammatory drugs and conventional synthetic DMARDs (csDMARDs); number of TNFis previously used; and the type of IL-17i initiated (ixekizumab or secukinumab).

This study was approved by the Institutional Review Board (IRB) of Gangnam Severance Hospital (IRB No: 3-2022-0332), and the requirement for informed consent was waived due to the retrospective nature of the study.

Outcome

The outcomes of our study were 1-year, 2-year, and 3-year drug retention rates for IL-17is. Each patient was reviewed for discontinuation of IL-17is from the date of initiation to January 2023. For patients who discontinued IL-17is, the reasons for discontinuation were reviewed. We also assessed the effectiveness of IL-17is by reviewing ESR, CRP, BASDAI, and ASDAS-CRP over time for up to 15 months. ESR and CRP were assessed every 3 months. BASDAI and ASDAS-CRP were assessed at 3 months from the initiation of IL-17is and every 6 months thereafter. Data on patients who discontinued IL-17is were censored at discontinuation. Therefore, the data represent the disease activity indices during exposure to IL-17is.

Statistical analysis

Continuous variables following normal or non-normal distributions are expressed as a mean±standard deviation or median (interquartile range), respectively; while categorical variables are expressed as numbers (%). Kaplan-Meier survival analysis was performed to visualize the drug retention rate of the IL-17is. The log-rank test was used to compare drug retention rates for IL-17is between different groups. Cox proportional hazard regression analyses were conducted to evaluate baseline factors associated with the discontinuation of IL-17is. Initially, univariable analyses using each baseline covariate as an independent variable were conducted. Subsequently, covariates with a $p<0.05$ in the univariable analyses were selected and included in multivariable analysis, which was conducted using the stepwise backward elimination method. Statistical significance was set at $p<0.05$, and all analyses were conducted using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA). Figures were generated using GraphPad Prism (version 7.0; GraphPad Software Inc., San Diego, CA, USA).

RESULTS

Baseline characteristics

A total of 68 patients with axSpA who were started on IL-17is were included. The mean age of the patients was 44.0±13.3 years, and 67.6% of the patients were male. Prior to the initiation of IL-17is, 40 (58.8%), 14 (20.6%), 10 (14.7%), and 4 (5.9%) patients were exposed to one, two, three, and four TNFis, respectively. Ixekizumab and secukinumab were initiated in 15 (22.1%)

https://doi.org/10.3349/ymj.2023.0151

and 53 (77.9%) patients, respectively. The detailed baseline characteristics of the patients are summarized in Table 1.

Drug retention rate

During 1933.9 person-months of observation, IL-17is were discontinued in 27 (39.7%) patients (Table 2). Of these, IL-17is were discontinued in 20 (29.4%) patients because of ineffectiveness (primary failure, n=8; and secondary failure, n=12) and in 7 (10.3%) because of adverse events (infection, n=3; enteritis/colitis, n=2; allergic reaction, n=1; and headache, n=1).

Table 1. Baseline Characteristics of 68 Patients with axSpA Initiated on IL-17is (n=68)

Characteristics	Value
Age, yr	44.0±13.3
Male, sex	46 (67.6)
Symptom duration, yr	3.4 (1.1–7.8)
Disease duration, yr	5.8 (2.3–10.3)
BMI, kg/m^2	23.0 (21.3–28.5)
Current smoker	20 (29.4)
HLA-B27 positive	58 (85.3)
r-axSpA	61 (89.7)
Syndesmophyte present	17 (25.0)
Peripheral symptoms	47 (69.1)
Uveitis	10 (14.7)
IBD	1 (1.5)
Psoriasis	6 (8.8)
ESR, mm/h	23.5 (5.0–36.8)
CRP, mg/L	1.8 (0.4–10.7)
BASDAI	7.4 (6.1–9.2)
ASDAS-CRP	3.7±0.9
NSAIDs	66 (97.1)
csDMARDs	27 (39.7)
Number of prior TNFis	
1	40 (58.8)
2	14 (20.6)
3	10 (14.7)
4	4 (5.9)
Types of prior TNFis	
Monoclonal antibodies	42 (61.8)
Soluble receptor	6 (8.8)
Monoclonal antibodies and soluble receptor	20 (29.4)
Type of IL-17i started	
Ixekizumab	15 (22.1)
Secukinumab	53 (77.9)

axSpA, axial spondyloarthritis; IL-17is, interleukin-17 inhibitors; IQR, interquartile range; BMI, body mass index; HLA, human leukocyte antigen; r-axSpA, radiographic axial spondyloarthritis; IBD, inflammatory bowel disease; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-reactive protein; NSAIDs, non-steroidal anti-inflammatory drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; TNFis, tumor necrosis factor inhibitors.
Data are presented as mean±standard deviation, median (IQR), or n (%).

Table 2. Discontinuation of IL-17is (n=68)

Variables	Value
Discontinuation of IL-17is	27 (39.7)
Reasons for discontinuation of IL-17is	
Ineffectiveness	20 (29.4)
Primary failure	8 (11.8)
Secondary failure	12 (17.6)
Adverse events	7 (10.3)
Time from initiation to discontinuation of IL-17is, months, median (IQR)	4.2 (2.3–15.9)

IL-17is, interleukin-17 inhibitors; IQR, interquartile range.

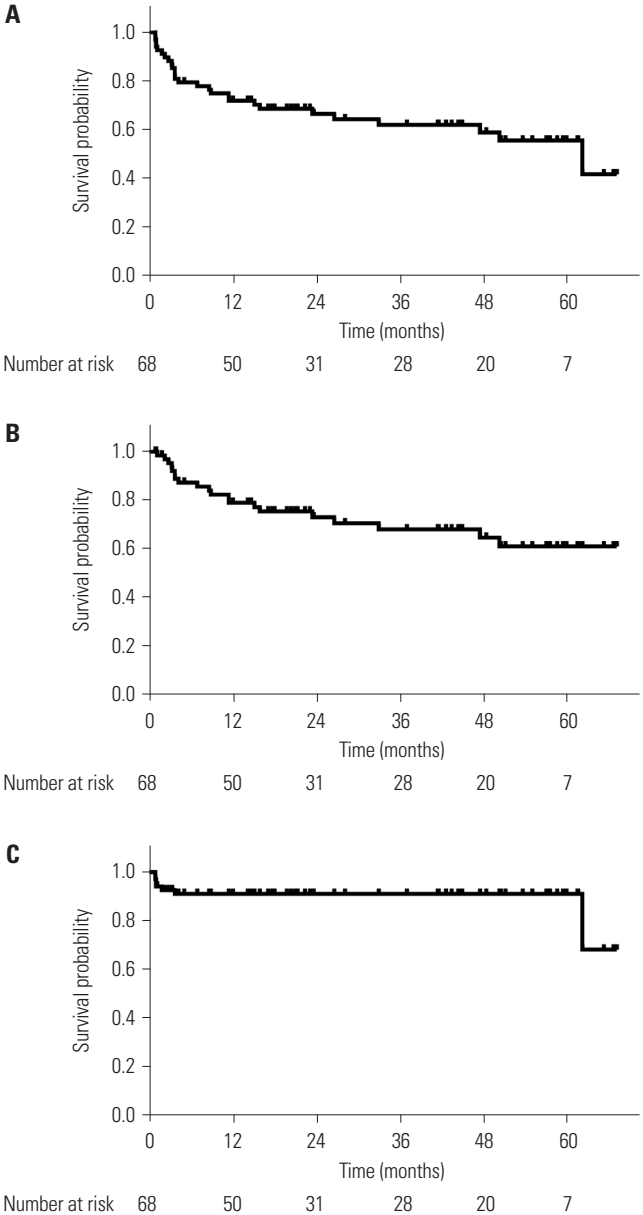

Fig. 1. Drug retention rates of interleukin-17 inhibitors over time. (A) Overall drug retention rates, (B) drug retention rates when drug discontinuation due to ineffectiveness was considered only, and (C) drug retention rates when drug discontinuation due to adverse events was considered only.

For the 27 patients who discontinued IL-17is, the median time from initiation to discontinuation was 4.2 (2.3–15.9) months. The drug retention rate is represented in Fig. 1. The overall 1-year, 2-year, and 3-year drug retention rates were 71.9%, 66.5%, and 62.0%, respectively (Fig. 1A). When drug discontinuation due to ineffectiveness was analyzed separately, the 1-year, 2-year, and 3-year drug retention rates were 79.1%, 73.1%, and 68.1%, respectively (Fig. 1B). When drug discontinuation due to adverse events was analyzed separately, the 1-year, 2-year, and 3-year drug retention rates were all 91.0%, indicating that the majority of the drug discontinuation due to adverse events occurred within 1-year of initiation of IL-17is (Fig. 1C).

When patients were grouped according to the number of prior TNFis used (1, 2, and ≥3), patients with prior exposure to ≥3 TNFis had a significantly higher drug retention rate than those with prior exposure to one TNFi (p=0.025) (Fig. 2).

Effectiveness

The disease activity indices were well controlled during exposure to IL-17is (Fig. 3). ASDAS-CRP improved from 3.9 (3.3–4.2) at baseline to 2.2 (2.0–2.9) at 3 months (ASDAS-CRP improvement ≥1.1 at 12 weeks). The effect was maintained thereafter (Fig. 3D).

Factors associated with discontinuation of IL-17is

The results of the Cox proportional hazard regression analyses assessing factors associated with the discontinuation of IL-17is are reported in Table 3. In univariable analyses, male sex [unadjusted hazard ratio (HR)=3.359, 95% confidence interval (CI)=1.251–9.018, p=0.016] and current smoking (unadjusted HR=2.307, 95% CI=1.079–4.935, p=0.031) were significantly

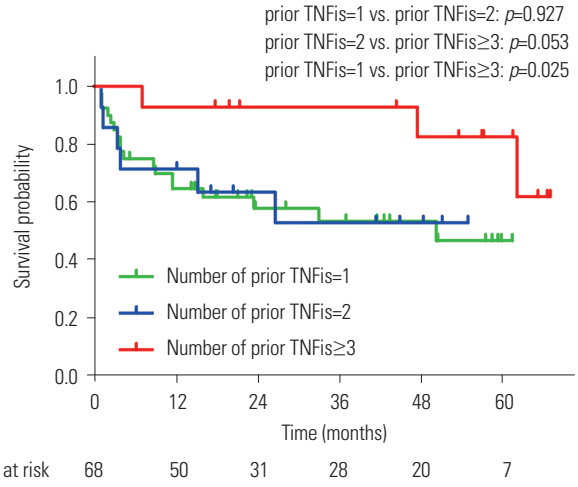

Fig. 2 Comparison of drug retention rates of interleukin-17 inhibitors according to the number of prior tumor necrosis factor inhibitors (TNFis).

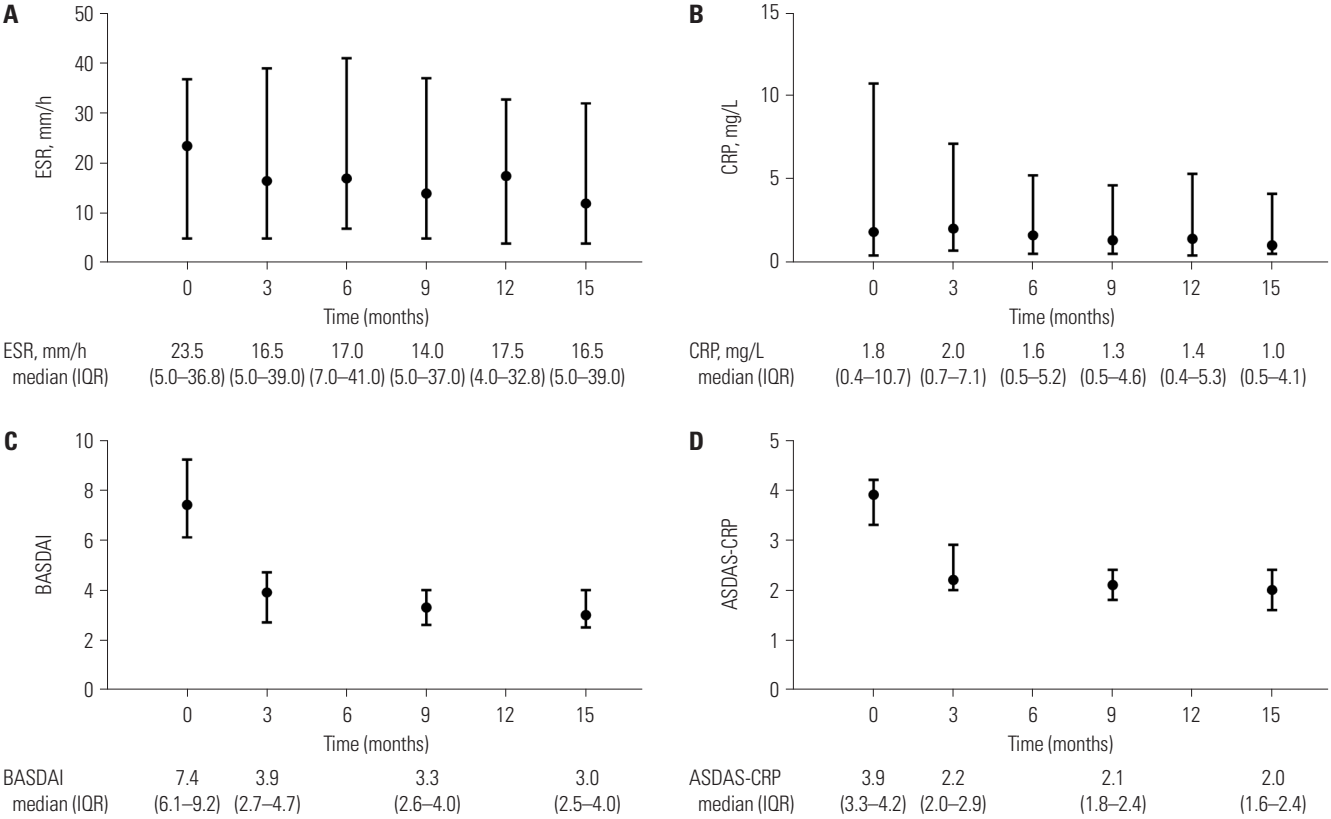

Fig. 3. Disease activity indices over time in patients who maintained interleukin-17 inhibitors. (A) ESR, (B) CRP, (C) BASDAI, and (D) ASDAS-CRP. ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-reactive protein; IQR, interquartile range.

https://doi.org/10.3349/ymj.2023.0151

associated with a higher risk of IL-17is discontinuation, while the number of TNFis previously used was significantly associated with a lower risk of IL-17is discontinuation (≥3 vs. 1, unadjusted HR=0.220, 95% CI=0.051–0.954, p=0.043). In multivariable analysis, male sex was eliminated in step one, while the covariates current smoking and number of TNFis previously used remained in the final model. Current smoking was significantly associated with a higher risk of IL-17is discontinuation (adjusted HR=2.256, 95% CI=1.053–4.831, p=0.036), whereas the number of TNFis previously used was significantly associated with a lower risk of IL-17is discontinuation (≥3 vs. 1, adjusted HR=0.223, 95% CI=0.051–0.969, p=0.045).

DISCUSSION

In this cohort study of patients with axSpA who were initiated on IL-17is after failure of one or more TNFis, the 1-year, 2-year, and 3-year drug retention rates of IL-17is were 71.9%, 66.5%, and 62.0%, respectively. Current smoking was associated with a higher risk of IL-17is discontinuation, while previous use of ≥3 TNFis was associated with a lower risk of IL-17is discontinuation. The effect of IL-17is was well maintained over time.

Our study has clinical significance in that 1) it provides long-term data on the use of IL-17is in a real-world setting of South Korea where IL-17is cannot be used as a first-line bDMARD, which has not been extensively studied and that 2) it provides data on both secukinumab and ixekizumab. The 1-year drug retention rate of IL-17is in our study (71.9%) was similar to that reported in a previous study using the Korean College of Rheumatology Biologics (KOBIO) registry (75%).[20] The KOBIO registry is a Korean nationwide cohort of patients with inflammatory arthritis who are exposed to bDMARDs and/or tsDMARDs.[25] The similar 1-year drug retention rate between our data and the previous nationwide data reflects the external validity of our data. In this study, we advanced the previous knowledge by reporting longer-term drug retention rates (2-year, 66.5%; 3-year, 62.0%) in patients in whom TNFis failed. The drug re-

Table 3. Factors Associated with Discontinuation of IL-17is

	Univariable analysis		Multivariable analysis	
	Unadjusted HR (95% CI)	p value	Adjusted HR (95% CI)	p value
Age	1.010 (0.982–1.039)	0.475		
Male, sex (vs. female, sex)	3.359 (1.251–9.018)	0.016		
Symptom duration	1.029 (0.965–1.097)	0.387		
Disease duration	0.967 (0.898–1.041)	0.374		
BMI	0.995 (0.913–1.083)	0.901		
Current smoker (vs. ex-, nonsmoker)	2.307 (1.079–4.935)	0.031	2.256 (1.053–4.831)	0.036
HLA-B27 positive (vs. negative)	0.979 (0.365–2.622)	0.966		
r-axSpA (vs. nr-axSpA)	1.401 (0.331–5.937)	0.647		
Syndesmophyte present (vs. absent)	0.617 (0.234–1.631)	0.331		
Peripheral symptoms present (vs. absent)	1.430 (0.574–3.562)	0.443		
Uveitis present (vs. absent)	0.827 (0.282–2.432)	0.731		
IBD present (vs. absent)	0.048 (0.000–5545.182)	0.609		
Psoriasis present (vs. absent)	0.784 (0.184–3.335)	0.741		
ESR	0.994 (0.981–1.009)	0.443		
CRP	0.998 (0.981–1.016)	0.838		
BASDAI	0.843 (0.677–1.050)	0.128		
ASDAS-CRP	0.694 (0.426–1.131)	0.143		
NSAIDs used (vs. not used)	0.301 (0.039–2.317)	0.249		
csDMARDs used (vs. not used)	1.027 (0.476–2.218)	0.945		
Number of prior TNFis used				
2 (vs. 1)	0.955 (0.379–2.408)	0.923	0.924 (0.366–2.331)	0.924
≥3 (vs. 1)	0.220 (0.051–0.954)	0.043	0.223 (0.051–0.969)	0.045
Types of prior TNFis				
Soluble receptor (vs. monoclonal antibodies)	1.748 (0.510–5.990)	0.374		
Monoclonal antibodies and soluble receptor (vs. monoclonal antibodies)	0.490 (0.181–1.324)	0.159		
Secukinumab (vs. ixekizumab)	0.828 (0.303–2.257)	0.712		

IL-17is, interleukin-17 inhibitors; HR, hazard ratio; CI, confidence interval; BMI, body mass index; HLA, human leukocyte antigen; r-axSpA, radiographic axial spondyloarthritis; nr-axSpA, non-radiographic axial spondyloarthritis; IBD, inflammatory bowel disease; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-reactive protein; NSAIDs, nonsteroidal anti-inflammatory drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; TNFis, tumor necrosis factor inhibitors.

tention rate of IL-17is observed in our study was similar to that of secukinumab reported in European populations (1-year, 55%–72%; 2-year, 43%–61%).[16-19] Considering that all patients in our study received IL-17is as a second- or later-line bDMARD, whereas in the European studies a proportion of patients (8.0%–30.8%) received secukinumab as a first-line bDMARD,[16-19] the similar drug retention rate observed in our study is encouraging. Moreover, the drug retention rate of IL-17is in our study was also similar to that of TNFis used as first-line bDMARD (1-year, 74%–76%; 2-year, 63%–65%),[13,14] suggesting that IL-17is could be a good therapeutic option even as a later-line bDMARD. Regarding the type of IL-17is, we found no significant difference in the risk of IL-17is discontinuation between secukinumab and ixekizumab (unadjusted HR=0.828, 95% CI=0.303–2.257, *p*=0.712).

Compared with ex- and nonsmokers, current smokers had a more than two-fold higher risk (adjusted HR=2.256) of discontinuing IL-17is. This is in line with a previous study reporting a lower response to secukinumab in patients with ankylosing spondylitis who are smokers.[26] Smoking is also known to be associated with a higher disease activity, functional disability, and radiographic progression rate in axSpA.[27-29] These adverse impacts of smoking on the disease may have led to the higher discontinuation rate of IL-17is.

Previous studies have reported that the drug retention rate of secukinumab is lower (i.e., higher discontinuation rate) when used as a second- or later-line bDMARD than when it is used as a first-line bDMARD.[16-18] Since IL-17is are approved for use only as second- or later-line bDMARD in Korea, all patients included were previously exposed to at least one TNFi. Interestingly, when patients who were previously exposed to one TNFi were used as a reference, patients who were previously exposed to ≥3 TNFis had a lower risk (adjusted HR=0.223, 95% CI=0.051–0.969, *p*=0.045) of discontinuing IL-17is. This differs from the results of previous studies that used bDMARD-naïve patients as the reference: higher discontinuation rate of IL-17is when used as a second- or later-line bDMARD than when used as a first-line bDMARD (i.e., bDMARD-naïve).[16-18] It is possible that in patients in whom treatment with multiple TNFis has failed, the key cytokine that plays the pathogenic role could be IL-17A rather than TNF-α. This may be the reason for the lower risk of IL-17is discontinuation in patients who previously received ≥3 TNFis. Another point to consider is that the number of bDMARDs with different modes of action available in axSpA is limited. Therefore, if a patient has failed treatment with multiple TNFis prior to IL-17i initiation, the patient will more likely tend to maintain IL-17i irrespective of effectiveness, as there are few treatment options left. However, during exposure to IL-17is, we observed that ESR, CRP, BASDAI, and ASDAS-CRP were well controlled over time (Fig. 3). This suggests that for patients receiving IL-17is, the IL-17is were maintained because the disease was well controlled rather than due to concern for the limited number of treatment options left.

Obesity has been suggested as a factor associated with a favorable drug retention rate of secukinumab.[17,19] Obesity promotes the expansion of IL-17-producing T cells in peripheral tissues.[30] Moreover, compared with nonobese individuals, obese individuals have higher serum levels of IL-17.[31] Together, these suggest IL-17 as a key pathogenic cytokine in obese patients, possibly explaining the lower risk of discontinuation of secukinumab in obese patients observed in previous studies.[17,19] However, in our study, BMI was not associated with the risk of IL-17is discontinuation (unadjusted HR=0.995, 95% CI=0.913–1.083, *p*=0.901). When interpreting our data, it should be considered that in the previous studies that reported the association between obesity and lower risk of discontinuation of secukinumab, the cut-off BMI for obesity was 30 kg/m^2.[17,19] In our study population, the median BMI was 23.0 (21.3–28.5) kg/m^2, which is relatively low, and a BMI in this range was not associated with a lower risk of drug retention of IL-17is.

Our study has some limitations. First, this was a retrospective study with a relatively small sample size. Second, although we observed a significant association between current smoking and a higher risk of IL-17is discontinuation, we lacked data regarding the quantity of smoking, and we were unable to assess the association between the amount of smoking and risk of IL-17is discontinuation. Third, as IL-17is are approved only as a second- or later-line bDMARD in South Korea, there were no patients who used IL-17is as a first-line bDMARD in our study. Due to this unique condition, we were unable to directly compare the drug retention rate of IL-17is when used as a first-line and later-line bDMARD. Despite these limitations, our study is noteworthy in that it provides comprehensive real-world data on the long-term use of IL-17is in patients with axSpA who failed to TNFis, on which there is currently very limited data.

In conclusion, in patients with axSpA initiated on IL-17is (secukinumab or ixekizumab) after an inadequate response or intolerance to ≥1 TNFis, the 1-year, 2-year, and 3-year drug retention rates of IL-17is were 71.9%, 66.5%, and 62.0%, respectively. The effect of IL-17is was maintained over time in patients who retained IL-17is. Current smoking was associated with a higher risk of discontinuing IL-17is, whereas previous use of ≥3 TNFis was associated with a lower risk of discontinuing IL-17is. These data provide valuable information that can be considered when using IL-17is in patients with axSpA in treatment with TNFis has failed.

ACKNOWLEDGEMENTS

This study was supported by a research fund from the Rheumatology Research Foundation (RRF-2022-02).

AUTHOR CONTRIBUTIONS

Conceptualization: Oh Chan Kwon and Min-Chan Park. Data cura-

https://doi.org/10.3349/ymj.2023.0151

tion: Oh Chan Kwon and Min-Chan Park. Formal analysis: Oh Chan Kwon and Min-Chan Park. Funding acquisition: Oh Chan Kwon. Investigation: Oh Chan Kwon and Min-Chan Park. Methodology: Oh Chan Kwon and Min-Chan Park. Project administration: Oh Chan Kwon and Min-Chan Park. Resources: Oh Chan Kwon and Min-Chan Park. Software: Oh Chan Kwon and Min-Chan Park. Supervision: Min-Chan Park. Validation: Oh Chan Kwon and Min-Chan Park. Visualization: Oh Chan Kwon and Min-Chan Park. Writing—original draft: Oh Chan Kwon. Writing—review & editing: Oh Chan Kwon and Min-Chan Park. Approval of final manuscript: all authors.

ORCID iDs

Oh Chan Kwon https://orcid.org/0000-0001-7962-3697
Min-Chan Park https://orcid.org/0000-0003-1189-7637

REFERENCES

1. van der Heijde D, Dijkmans B, Geusens P, Sieper J, DeWoody K, Williamson P, et al. Efficacy and safety of infliximab in patients with ankylosing spondylitis: results of a randomized, placebo-controlled trial (ASSERT). Arthritis Rheum 2005;52:582-91.
2. Davis JC Jr, Van Der Heijde D, Braun J, Dougados M, Cush J, Clegg DO, et al. Recombinant human tumor necrosis factor receptor (etanercept) for treating ankylosing spondylitis: a randomized, controlled trial. Arthritis Rheum 2003;48:3230-6.
3. van der Heijde D, Kivitz A, Schiff MH, Sieper J, Dijkmans BA, Braun J, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheum 2006;54:2136-46.
4. Inman RD, Davis JC Jr, Heijde Dv, Diekman L, Sieper J, Kim SI, et al. Efficacy and safety of golimumab in patients with ankylosing spondylitis: results of a randomized, double-blind, placebo-controlled, phase III trial. Arthritis Rheum 2008;58:3402-12.
5. Landewé R, Braun J, Deodhar A, Dougados M, Maksymowych WP, Mease PJ, et al. Efficacy of certolizumab pegol on signs and symptoms of axial spondyloarthritis including ankylosing spondylitis: 24-week results of a double-blind randomised placebo-controlled phase 3 study. Ann Rheum Dis 2014;73:39-47.
6. Ward MM, Deodhar A, Gensler LS, Dubreuil M, Yu D, Khan MA, et al. 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. Arthritis Rheumatol 2019;71:1599-613.
7. Ramiro S, Nikiphorou E, Sepriano A, Ortolan A, Webers C, Baraliakos X, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis 2023;82:19-34.
8. Navarro-Compán V, Sepriano A, El-Zorkany B, van der Heijde D. Axial spondyloarthritis. Ann Rheum Dis 2021;80:1511-21.
9. Kwon OC, Park JH, Park MC. Factors affecting drug survival of an alternative TNF inhibitor and secukinumab in patients with ankylosing spondylitis switching from the first TNF inhibitor. Ther Adv Musculoskelet Dis 2021;13:1759720X211009021.
10. Fraenkel L, Bathon JM, England BR, St Clair EW, Arayssi T, Carandang K, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol 2021;73:1108-23.
11. Smolen JS, Landewé RBM, Bergstra SA, Kerschbaumer A, Sepriano A, Aletaha D, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. Ann Rheum Dis 2023;82:3-18.
12. Gossec L, Baraliakos X, Kerschbaumer A, de Wit M, McInnes I, Dougados M, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis 2020;79:700-12.
13. Glintborg B, Ostergaard M, Krogh NS, Dreyer L, Kristensen HL, Hetland ML. Predictors of treatment response and drug continuation in 842 patients with ankylosing spondylitis treated with anti-tumour necrosis factor: results from 8 years' surveillance in the Danish nationwide DANBIO registry. Ann Rheum Dis 2010;69:2002-8.
14. Lie E, van der Heijde D, Uhlig T, Mikkelsen K, Rødevand E, Koldingsnes W, et al. Effectiveness of switching between TNF inhibitors in ankylosing spondylitis: data from the NOR-DMARD register. Ann Rheum Dis 2011;70:157-63.
15. Kim HA, Lee SK, Oh S, Park EH, Park YB, Shin K. Comparison of retention rates between tumor necrosis factor-α inhibitors in patients with ankylosing spondylitis: data from the Korean College of Rheumatology Biologics Registry. Front Med (Lausanne) 2021;8:689609.
16. Michelsen B, Lindström U, Codreanu C, Ciurea A, Zavada J, Loft AG, et al. Drug retention, inactive disease and response rates in 1860 patients with axial spondyloarthritis initiating secukinumab treatment: routine care data from 13 registries in the EuroSpA collaboration. RMD Open 2020;6:e001280.
17. Alonso S, Villa I, Fernández S, Martín JL, Charca L, Pino M, et al. Multicenter study of secukinumab survival and safety in spondyloarthritis and psoriatic arthritis: secukinumab in cantabria and ASTURias study. Front Med (Lausanne) 2021;8:679009.
18. Moreno-Ramos MJ, Sanchez-Piedra C, Martínez-González O, Rodríguez-Lozano C, Pérez-Garcia C, Freire M, et al. Real-world effectiveness and treatment retention of secukinumab in patients with psoriatic arthritis and axial spondyloarthritis: a descriptive observational analysis of the Spanish BIOBADASER registry. Rheumatol Ther 2022;9:1031-47.
19. Armağan B, Kılıç L, Farisoğulları B, Yardımcı GK, Bilgin E, Bölek EÇ, et al. Drug retention rate and predictive factors of drug survival for secukinumab in radiographic axial spondyloarthritis. Rheumatol Int 2023;43:147-56.
20. Min HK, Kim HR, Lee SH, Hong YS, Kim MY, Park SH, et al. Retention rate and effectiveness of secukinumab vs TNF inhibitor in ankylosing spondylitis patients with prior TNF inhibitor exposure. Rheumatology (Oxford) 2021;60:5743-52.
21. Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al. The development of assessment of spondyloarthritis international society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 2009;68:777-83.
22. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361-8.
23. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the bath ankylosing spondylitis disease activity index. J Rheumatol 1994;21:2286-91.
24. Lukas C, Landewé R, Sieper J, Dougados M, Davis J, Braun J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:18-24.
25. Kim J, Koh JH, Choi SJ, Jeon CH, Kwok SK, Kim SK, et al. KOBIO, the first web-based Korean biologics registry operated with a unified platform among distinct disease entities. J Rheum Dis 2021;

28:176-82.
26. Chimenti MS, Fonti GL, Conigliaro P, Sunzini F, Scrivo R, Navarini L, et al. One-year effectiveness, retention rate, and safety of secukinumab in ankylosing spondylitis and psoriatic arthritis: a real-life multicenter study. Expert Opin Biol Ther 2020;20:813-21.
27. Zhao S, Challoner B, Khattak M, Moots RJ, Goodson NJ. Increasing smoking intensity is associated with increased disease activity in axial spondyloarthritis. Rheumatol Int 2017;37:239-44.
28. Zhang H, Wan W, Liu J, Dai S, Zou Y, Qian Q, et al. Smoking quantity determines disease activity and function in Chinese patients with ankylosing spondylitis. Clin Rheumatol 2018;37:1605-16.
29. Poddubnyy D, Haibel H, Listing J, Märker-Hermann E, Zeidler H, Braun J, et al. Baseline radiographic damage, elevated acute-phase reactant levels, and cigarette smoking status predict spinal radiographic progression in early axial spondylarthritis. Arthritis Rheum 2012;64:1388-98.
30. Queiro R, Lorenzo A, Tejón P, Coto P, Pardo E. Obesity in psoriatic arthritis: comparative prevalence and associated factors. Medicine (Baltimore) 2019;98:e16400.
31. Pantano I, Iacono D, Favalli EG, Scalise G, Costa L, Caso F, et al. Secukinumab efficacy in patients with PsA is not dependent on patients' body mass index. Ann Rheum Dis 2022;81:e42.

https://doi.org/10.3349/ymj.2023.0151