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ORIGINAL RESEARCH

Does Prior Exposure Affect Retention? A Real-World, Multicentre Assessment of IL-17 Inhibitor Cycling in Psoriatic Arthritis

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ABSTRACT

***Introduction*:** Interleukin-17 inhibitors (IL-17i) represent a key therapeutic option for psoriatic arthritis (PsA), but real-world evidence regarding the effectiveness of cycling strategies within this class is lacking. This study evaluated the real-world retention of IL-17i in PsA, focusing on whether prior IL-17i exposure affects subsequent IL-17i persistence.

***Methods*:** This multicentre, retrospective, observational study included consecutive patients with PsA treated with an IL-17i across 24 Italian rheumatology centres. The primary outcome was drug retention, analysed using Kaplan–Meier methods, with differences between IL-17i-naïve and IL-17i-experienced patients assessed with the log-rank test. Secondary outcomes included baseline clinical characteristics and predictors of discontinuation.

***Results*:** A total of 868 patients were included (59.3% female, 40.7% male; median age 56 [48–63] years; 89.3% IL-17i-naïve). The overall median IL-17i retention rate was 90.7% [95% CI 88.7–92.8] at 6 months, 77.5% [95% CI 74.6–80.6] at 12 months, 60.9% [95% CI 57.3–64.8] at 24 months, and 52.1% [95% CI 48.1–56.4] at 36 months. Among IL-17i-naïve patients, retention rates were 90.5%, 77.6%, 61.7%, and 53.9% at 6, 12, 24, and 36 months, respectively. Among IL-17i-experienced patients, the corresponding retention rates were 92.2%, 77.0%, 54.0%, and 33.9%. In multivariable Cox regression, male sex and prior IL-17 inhibitor exposure were associated with a lower risk of discontinuation,

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whereas axial involvement, a higher number of previous biologic/targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs), and later calendar year of IL-17i initiation predicted poorer retention.

Conclusions: IL-17i showed high long-term retention in real-world PsA, with no significant difference between naïve and previously exposed patients. These findings support the sustained effectiveness of IL-17i therapy and suggest that cycling within the class may remain a reasonable option for selected cases.

Keywords: Biologic DMARDs; Clinical effectiveness; Cycling; Interleukin-17 inhibitors; Psoriatic arthritis; Real-world evidences; Retention rate; Persistence

Key Summary Points

Why carry out this study?

Interleukin-17 inhibitors (IL-17i) are widely used in psoriatic arthritis, yet real-world evidence on the effectiveness of cycling within this class remains limited.

This study assessed whether prior exposure to an IL-17i affects the real-world retention of a subsequent IL-17i in patients with psoriatic arthritis.

What was learned from the study?

IL-17i showed high long-term retention in real-world psoriatic arthritis, with no statistically significant difference between IL-17i-naïve and IL-17i-experienced patients in survival analysis.

In multivariable analysis, prior IL-17i exposure was associated with lower risk of discontinuation, and factors such as male sex, axial involvement, number of prior biologic disease-modifying anti-rheumatic drugs (bDMARD) lines, and calendar year of prescription were independently associated with treatment persistence, informing treatment decisions.

These findings suggest that cycling within the IL-17i class may represent a viable therapeutic strategy in patients affected by psoriatic arthritis.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory disease lying within the broader concept of psoriatic disease. PsA affects up to 30% of individuals with psoriasis and encompasses a heterogeneous range of clinical domains, including peripheral arthritis, enthesitis, dactylitis, axial involvement, and skin and nail disease [1, 2]. Beyond musculoskeletal and skin domains, patients are frequently affected by cardiovascular, metabolic, neoplastic and psychiatric comorbidities, which significantly impair quality of life, increase mortality, and complicate treatment strategies [3–5].

Over the last two decades, the therapeutic landscape for PsA has expanded remarkably with the development of biologic (b) and targeted synthetic (ts) disease-modifying anti-rheumatic drugs (DMARDs). Tumour necrosis factor inhibitors (TNFi) were the first class of bDMARDs to demonstrate efficacy across all major disease domains and remain the benchmark for patients with PsA requiring biologic therapy [6, 7]. However, a substantial proportion of patients experience an inadequate response or a gradual loss of efficacy over time, ultimately requiring alternative therapeutic strategies [8–10].

In real-world clinical practice, several therapeutic approaches are used after bDMARD discontinuation, including switching to a drug with a different mechanism of action or cycling within the same class, depending on clinical context and prior treatment response.

For TNF inhibitors, multiple studies have investigated these approaches. Overall, treatment responses tend to be lower with subsequent TNFi exposure, although cycling within the class may still be beneficial in selected cases of secondary, rather than primary, loss of efficacy [11–14].

With the introduction of interleukin-17 inhibitors (IL-17i), including secukinumab, ixekizumab, and, more recently, bimekizumab, the therapeutic armamentarium for PsA has expanded. These bDMARDs have demonstrated efficacy and a good safety profile in both randomised controlled trials and real-world settings [15–24]. Despite this, only limited evidence is available about the effectiveness of cycling within the IL-17 inhibitor class.

This study investigated the drug retention of IL-17i in a real-world cohort of patients affected by PsA, with a specific focus on differences between IL-17i-naïve and IL-17i-experienced patients. The primary aim was to assess whether prior exposure to an IL-17i affects the retention of a subsequent agent from the same class, compared with patients initiating their first IL-17i.

Secondary aims were to characterise the clinical features of the treated population and to investigate demographic and clinical factors associated with treatment discontinuation.

METHODS

Study Design and Population

This multicentre, retrospective, observational, longitudinal study was conducted across 24 rheumatology centres in Italy.

All consecutive patients who fulfilled the following inclusion criteria between January 2016 and December 2024 were included in the study, after signing the informed consent. The main inclusion criteria were (a) diagnosis of PsA; (b) age greater than 18 years; (c) current and/or previous treatment with an IL-17i as per clinical indication.

The diagnosis of PsA was based on the rheumatologist expertise, on clinical, laboratory and imaging features, and considering the Classification Criteria for Psoriatic Arthritis (CASPAR) [25].

Axial involvement was identified according to the rheumatologist's clinical judgement and confirmed by targeted MRI assessment when clinically indicated.

This study was designed, conducted and reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

The study protocol was approved by the Area Vasta Emilia Nord (AVEN) Ethics Committee, protocol code 34713, and was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. All study centres accepted the approval of the Area Vasta Emilia Nord Ethics Committee.

Procedures

For all patients who provided consent, demographic and clinical data were retrospectively collected, including disease domains, activity scores, IL-17i exposure status, and the number of prior b/tsDMARD treatment lines.

Drug retention was defined as the time from initiation of IL-17i therapy to permanent discontinuation for any reason, including inefficacy, adverse events, or patient/physician decision. Patients still receiving the drug at their last follow-up visit were considered censored, with retention time calculated up to that date. Temporary treatment interruptions followed by reintroduction were not considered discontinuations, and retention time was calculated until definitive termination of therapy or the last available visit.

Data on previous and concomitant PsA treatments was recorded, including corticosteroids, conventional synthetic DMARDs (csDMARDs), and b/tsDMARDs. Clinical assessments were obtained at baseline (i.e. initiation of IL-17i) and at the time of drug discontinuation, and included tender joint count (68 joints, TJC68), swollen joint count (66 joints, SJC66), and the Disease Activity in Psoriatic Arthritis (DAPSA) composite score. In patients with confirmed axial involvement, the Axial Spondyloarthritis Disease Activity Score (ASDAS) and/or the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) were also collected if available.

Outcomes

The primary outcome of the study was the difference in the retention rate of IL-17i between patients receiving treatment with their first IL-17i and those previously exposed to another agent within the same class.

The secondary outcomes included the description of the characteristics of the study cohort and the clinical predictors of drug discontinuation, based on demographic variables, disease domains, disease activity at baseline, prior lines of therapy, and concomitant treatments.

Data Analysis

All statistical analyses were performed using the R software (version 4.4.2), with a two-sided p value < 0.05 considered statistically significant. The figures were generated with R (version 4.4.2) and GraphPad Prism (version 9.5.1).

For descriptive analyses, categorical variables were reported as absolute numbers and frequencies, and continuous variables were expressed as median and interquartile range (IQR, 25th–75th percentile). Baseline demographic and clinical variables were summarised for the entire cohort and stratified by IL-17i exposure status (naïve vs experienced). Between-group comparisons employed the Wilcoxon rank-sum test for continuous variables and χ^2 tests for categorical variables; Fisher's exact test was applied when expected counts were < 5. Bonferroni adjustments for multiple comparisons were applied, with adjusted P values considered significant if < 0.003 for between-group comparisons.

Kaplan–Meier survival analysis was used to describe drug retention and to compare persistence between IL-17i-naïve and IL-17i-experienced patients, as observed in routine clinical practice. The difference between subgroups was analysed with the log-rank test. The median follow-up duration was estimated using the reverse Kaplan–Meier method. Retention rates at fixed time points (6, 12, 24 and 36 months) were estimated with corresponding 95% CIs calculated by the Greenwood formula.

Among patients previously exposed to an IL-17i, additional analyses evaluated drug survival according to the number of treatment lines separating the current IL-17i from the first IL-17i previously received. Patients were stratified into two categories: those receiving the IL-17i immediately after the first (1-line), and those treated with the second IL-17i after one or more intervening b/tsDMARD (≥ 2 lines).

To identify independent factors associated with discontinuation, a multivariable Cox proportional hazards model was fitted, and results reported as hazard ratios (HR) and 95% confidence intervals (CI). Covariates were specified a priori based on clinical plausibility and data availability: sex, age, axial involvement, disease duration at baseline, treatment line, current IL-17i molecule, prior IL-17 exposure, and concomitant csDMARD.

RESULTS

Cohort Characteristics

Clinical and demographic characteristics of the cohort are shown in Table 1. A total of 868 patients were enrolled in the cohort, consisting of 515 (59.3%) women and 353 (40.7%) men. Median age was 56 [48–63] years and median disease duration was 54 [18–112] months. Axial involvement was diagnosed in 329 (37.9%) patients, whereas HLA-B27 was assessed in 426 patients, of whom 29 (6.8%) tested positive.

The most prescribed IL-17i was secukinumab (615, 70.8%), followed by ixekizumab (248, 28.6%) and bimekizumab (5, 0.6%). Most of the patients (642; 74.0%) were bDMARD experienced and median number of previous bDMARD lines was 2 [1–3]. Regarding IL-17i exposure, 775 (89.3%) patients were receiving their first IL-17i (IL-17 naïve), whereas 93 (10.7%) were previously exposed to the same class (IL-17i experienced). Concomitant therapy with csDMARD was recorded in 341 (39.3%) patients, whereas concomitant corticosteroids use was less frequent (129; 14.9%).

At baseline, the cohort showed moderate-to-high median disease activity scores as assessed by DAPSA (21 [14–28]), ASDAS [2.7 (1.8–3.3)], and BASDAI [4.2 (2.4–6.0)] scores.

Table 1 Cohort Characteristics

	Total *n* = 868 (100%)	**IL-17i-naïve** *n* = 775 (89.3%)	**IL-17i exp** *n* = 93 (10.7%)	*p*
Age, years, median [IQR]	56 [48–63]	56 [47–63]	59 [50–67]	0.021
Sex: female, *n* (%)	515 (59.3)	454 (58.6)	61 (65.6)	0.235
Sex: male, *n* (%)	353 (40.7)	321 (41.4)	32 (33.4)	0.235
Axial involvement, *n* (%)	329 (37.9)	274 (35.4)	55 (59.1)	< 0.001
HLA-B27 positive, *n* (%)	29/426 (6.8)	27/389 (6.9)	2/37 (5.4)	> 0.99
Disease duration, months, median [IQR]	54 [18–112]	51 [16–110]	79 [37–118]	0.005
Secukinumab, *n* (%)	615 (70.8)	596 (76.9)	19 (20.4)	< 0.001
Ixekizumab, *n* (%)	248 (28.6)	177 (22.8)	71 (76.3)	< 0.001
Bimekizumab, *n* (%)	5 (0.6)	2 (0.3)	3 (3.2)	0.010
Discontinued, *n* (%)	357 (41.1)	319 (41.2)	38 (40.9)	> 0.99
Previous lines, median [IQR]	2 [1–3]	2 [1–3]	4 [3–5]	< 0.001
1 previous line, *n* (%)	303 (34.9)	287 (37.0)	16 (17.2)	NC
2 previous lines, *n* (%)	174 (20.1)	149 (19.2)	25 (26.9)	NC
≥ 3 previous lines, *n* (%)	165 (19.0)	113 (14.6)	52 (55.9)	NC
Concomitant csDMARD, *n* (%)	341 (39.3)	318 (41.0)	23 (24.7)	0.003
Concomitant steroids, *n* (%)	129 (14.9)	114 (14.7)	15 (16.1)	0.834
DAPSA, median [IQR]	21 [14–28]	21 [13–28]	22 [15–29]	0.037
ASDAS, median [IQR]	2.7 [1.8–3.3]	2.55 [1.7–3.3]	3.1 [2.5–3.4]	0.003
BASDAI, median [IQR]	4.2 [2.4–6.0]	4 [2.2–6.0]	4.5 [4.1–6.8]	0.017

Baseline demographic and clinical characteristics of the overall cohort ($n = 868$) and stratified by IL-17 exposure status (naïve vs experienced). Subgroup comparisons used the Wilcoxon test for continuous variables and the chi-square test for categorical variables; Fisher's exact test was applied when sample count was < 5. *P* values < 0.003 after Bonferroni correction were considered significant

IL-17i interleukin-17 inhibitor, *exp* experienced patients (i.e. patients already exposed to a prior IL-17i), *HLA* human leukocyte antigen, *csDMARD* conventional synthetic disease-modifying anti-rheumatic drug, *DAPSA* Disease Activity in Psoriatic Arthritis, *ASDAS* Axial Spondyloarthritis Disease Activity Score, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *IQR* interquartile range, *NC* not calculated

The subgroup comparison between IL-17i-naïve and IL-17i-experienced patients showed that axial involvement was more frequent in the experienced group (59.1% vs 35.4%). Ixekizumab was more commonly prescribed among IL-17i-experienced patients (76.3% vs 22.8%), whereas secukinumab was predominantly used in IL-17i-naïve group (76.9% vs 20.4%). As expected, IL-17i-experienced patients had a greater median number of previous b/tsDMARD lines (4 [3–5] vs 2 [1–3]). No other significant differences were detected between the two study groups, but a non-significant trend towards shorter retention and higher disease duration and activity scores was observed in the IL-17i-experienced group.

Survival Analysis

The results of the survival analysis are shown in Table 2 and Figs. 1 and 2.

All patients were included in the survival analysis, accounting for a total of 20,014 patient-months of observation. The median follow-up duration, estimated by the reverse Kaplan–Meier method, was 29.6 months [95% CI 27.2–34.6]. During follow-up, 357 (41.1%) patients discontinued treatment. Among them, 315 (88.2%) discontinued as a result of ineffectiveness, whereas the remaining 42 (11.8%) discontinued because of adverse events. When stratified by sex, female patients showed a significantly higher rate of treatment discontinuation compared to male patients.

The overall median IL-17i retention time was 41.6 months [95% CI 33.8–50.3]. When stratified by prior IL-17i exposure, the median retention was 43.0 months [95% CI 35.4–51.2] in IL-17i-naïve patients and 25.7 months [95% CI 20.5–33.3] in IL-17i-experienced patients (Table 2).

The overall IL-17i retention rate was 90.7% [95% CI 88.7–92.8] at 6 months, 77.5% [95% CI 74.6–80.6] at 12 months, 60.9% [95% CI 57.3–64.8] at 24 months, and 52.1% [95% CI 48.1–56.4] at 36 months (Table 2).

Among IL-17i-naïve patients, retention rates were 90.5%, 77.6%, 61.7%, and 53.9% at 6, 12, 24, and 36 months, respectively. Among IL-17i-experienced patients, the corresponding retention rates were 92.2%, 77.0%, 54.0%, and 33.9% (Table 2).

Although Kaplan–Meier curves suggested a numerically lower persistence among IL-17i-experienced patients, the difference did not reach statistical significance (log-rank $p = 0.13$) (Fig. 1).

Further stratification of IL-17i-experienced patients according to the number of treatment lines separating the current and the first IL-17i is shown in Fig. 2. Among the 93 IL-17i-experienced patients, 56 (60.2%) received their second IL-17i immediately after the first, and 37 (39.8%) received it after one or more courses of other b/tsDMARDs. No significant differences in drug survival were observed across these subgroups (log-rank $p = 0.90$).

Predictors of Discontinuation

A multivariable Cox proportional hazards model was employed to identify variables independently associated with treatment discontinuation and the results are shown in Fig. 3. Data about bimekizumab were excluded from

Table 2 Survival Analysis

IL-17i retention time	Global	IL-17i naïve	IL-17i exp
Median	41.6 [33.8–50.3]	43.0 [35.4–51.2]	25.7 [20.5–33.3]
6 months	90.7 [88.7–92.8]	90.5 [88.4–92.7]	92.2 [86.5–98.4]
12 months	77.5 [74.6–80.6]	77.6 [74.5–80.8]	77.0 [67.9–87.3]
24 months	60.9 [57.3–64.8]	61.7 [57.8–65.8]	54.0 [42.8–68.1]
36 months	52.1 [48.1–56.4]	53.9 [49.7–58.4]	33.9 [22.6–51.0]

IL-17i drug retention in the overall cohort and stratified by prior IL-17i exposure status. The table reports the median retention time (months) and estimated retention rates (%) at 6, 12, 24, 36, and 48 months, with corresponding 95% confidence intervals (CI)

IL-17i interleukin-17 inhibitor, *exp* experienced patients (i.e. patients already exposed to a prior IL-17i), *CI* confidence interval

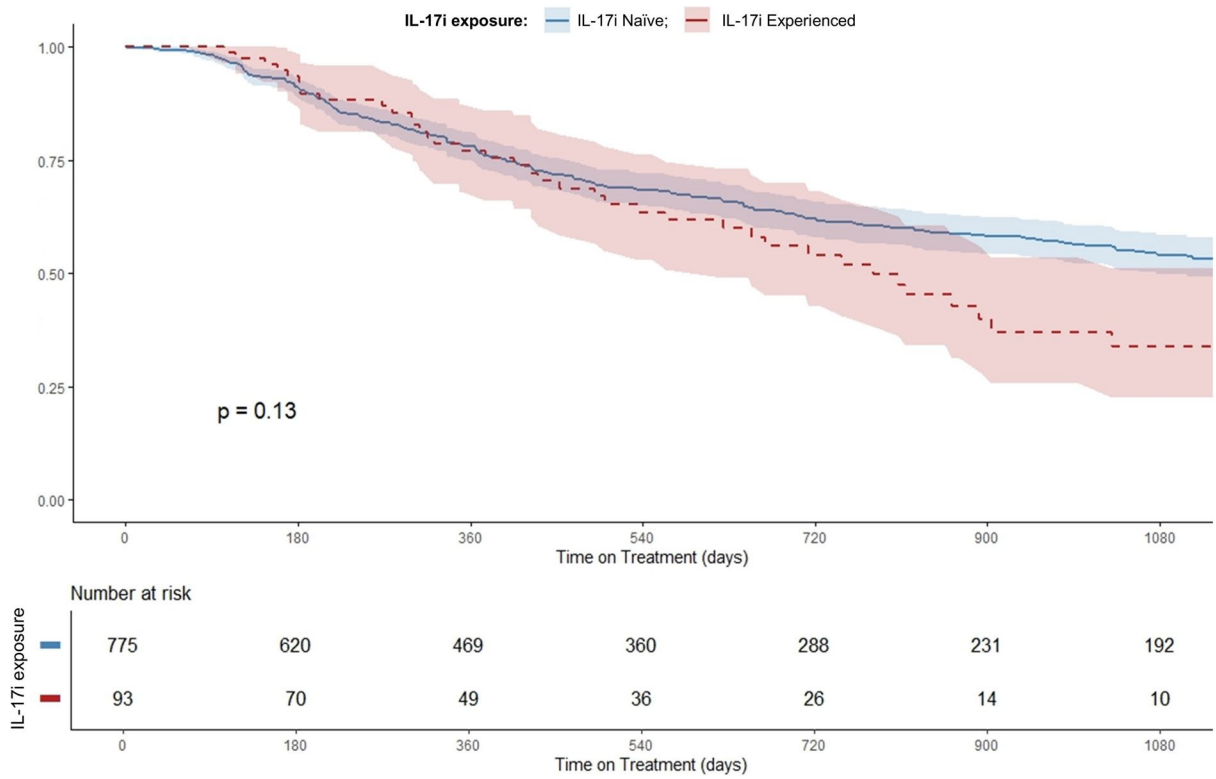

Fig. 1 Kaplan–Meier curves for IL-17i drug retention according to prior IL-17i exposure status. Retention probability is shown for IL-17i-naïve (solid blue line) and IL-17i-experienced (dashed red line) patients, with shaded areas representing 95% confidence intervals. The log-rank test did not demonstrate a statistically significant difference in drug survival between groups ($p = 0.13$). The table below the graph indicates the number of patients at risk at each time point. *IL-17i* interleukin-17 inhibitor

the Cox model because of quasi-separation arising from the small sample size.

Male sex was associated with a reduced risk of treatment discontinuation (HR 0.63, 95% CI 0.50–0.79, $p < 0.001$), whereas axial PsA involvement conferred a higher risk (HR 1.36, 95% CI 1.09–1.70, $p = 0.006$). Age and disease duration showed no significant effect on drug survival.

A higher number of previous b/tsDMARD was correlated with an increased risk of discontinuation (HR 1.17, 95% CI 1.07–1.27, $p < 0.001$), whereas prior IL-17i exposure showed a lower discontinuation risk (HR 0.64, 95% CI 0.42–0.97, $p = 0.034$).

Compared with ixekizumab, treatment with secukinumab was associated with a non-significant trend toward a lower risk of discontinuation (HR 0.76, 95% CI 0.58–1.00, $p = 0.051$). Concomitant csDMARD use did not significantly influence treatment persistence (HR 0.98, 95% CI 0.78–1.23, $p = 0.859$).

Finally, the calendar year of IL-17i initiation showed a significant association with retention, with each additional year reflecting a 14% increase in the hazard of treatment discontinuation.

DISCUSSION

This multicentre real-world study provides one of the largest analyses to date on IL-17i retention in PsA, with specific focus on the impact of prior IL-17i exposure.

Treatment changes are common in PsA as a result of heterogeneous clinical manifestations,

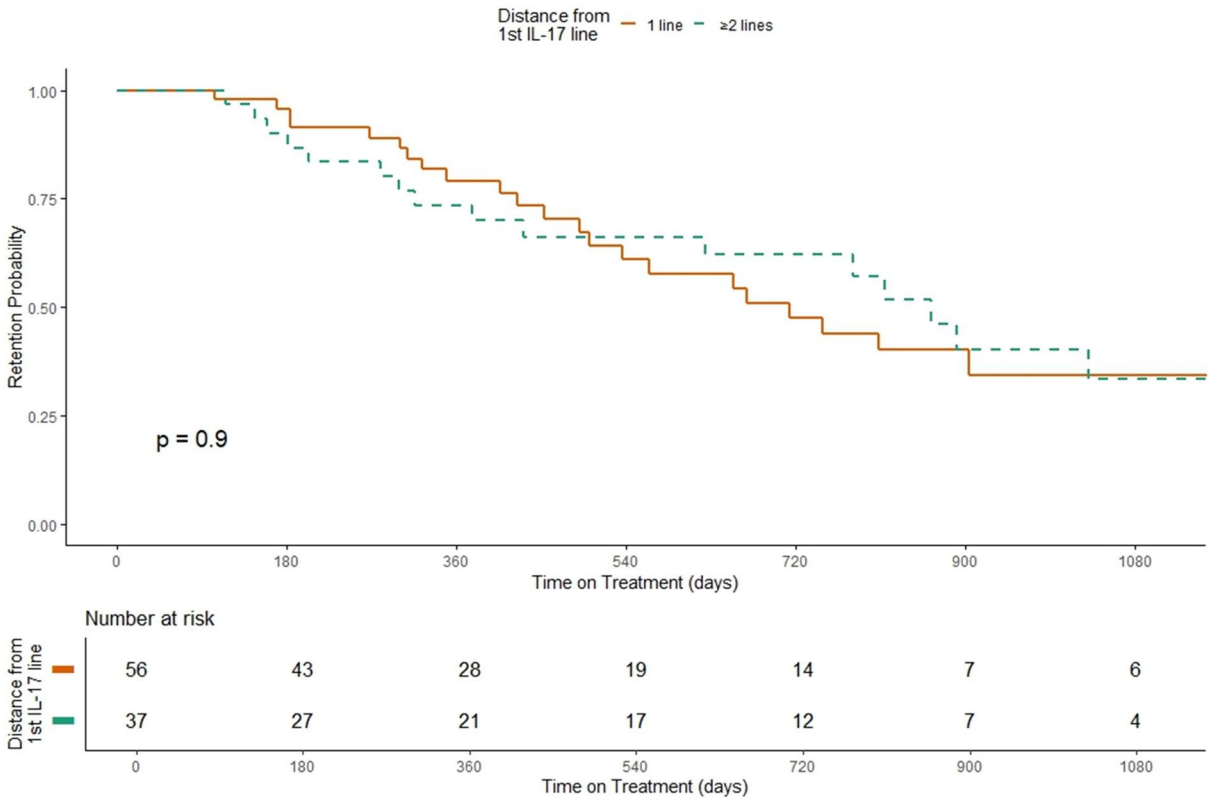

Fig. 2 Kaplan–Meier curves for drug persistence among IL-17i-experienced patients, stratified according to the number of intervening treatment lines between the first and second IL-17i. Patients who initiated a second IL-17i immediately after the first (1 line) are compared with those who received one or more alternative b/tsDMARDs before starting the second IL-17i (≥ 2 lines). No statistically significant differences in drug survival were observed across subgroups (log-rank $p = 0.90$). The table below the graph shows the number of patients at risk at each time point. Curves were plotted without confidence bands for visual clarity. *IL-17i* interleukin-17 inhibitor, *b/tsDMARD* biologic or targeted synthetic disease-modifying anti-rheumatic drug

variable responses across domains, and high rates of therapeutic inefficacy. The choice of the consecutive treatment may be influenced by domain involvement, previous treatments, and comorbidities that may contraindicate specific mechanisms of action. In this context, understanding whether cycling among IL-17i can provide sustained disease control has relevant clinical implications. Moreover, IL-17i are frequently prescribed following TNFi failure, placing these bDMARDs in later treatment lines where the probability of cycling rather than switching increases.

Within this framework, our study offers several insights. Firstly, IL-17i demonstrated favourable long-term persistence, with a median overall retention exceeding 40 months. Secondly, prior IL-17i exposure did not significantly impair subsequent drug survival. Although previously exposed patients exhibited a trend towards shorter retention, the difference compared with IL-17i-naïve patients was not statistically significant. Among IL-17i-experienced patients, we also explored the role of intervening b/tsDMARDs between IL-17i courses. The number of intermediate b/tsDMARDs did not appear to influence subsequent IL-17i retention, though this finding should be interpreted with caution given the limited sample size in this subgroup.

The numerical imbalance between IL-17i-naïve and IL-17i-experienced patients

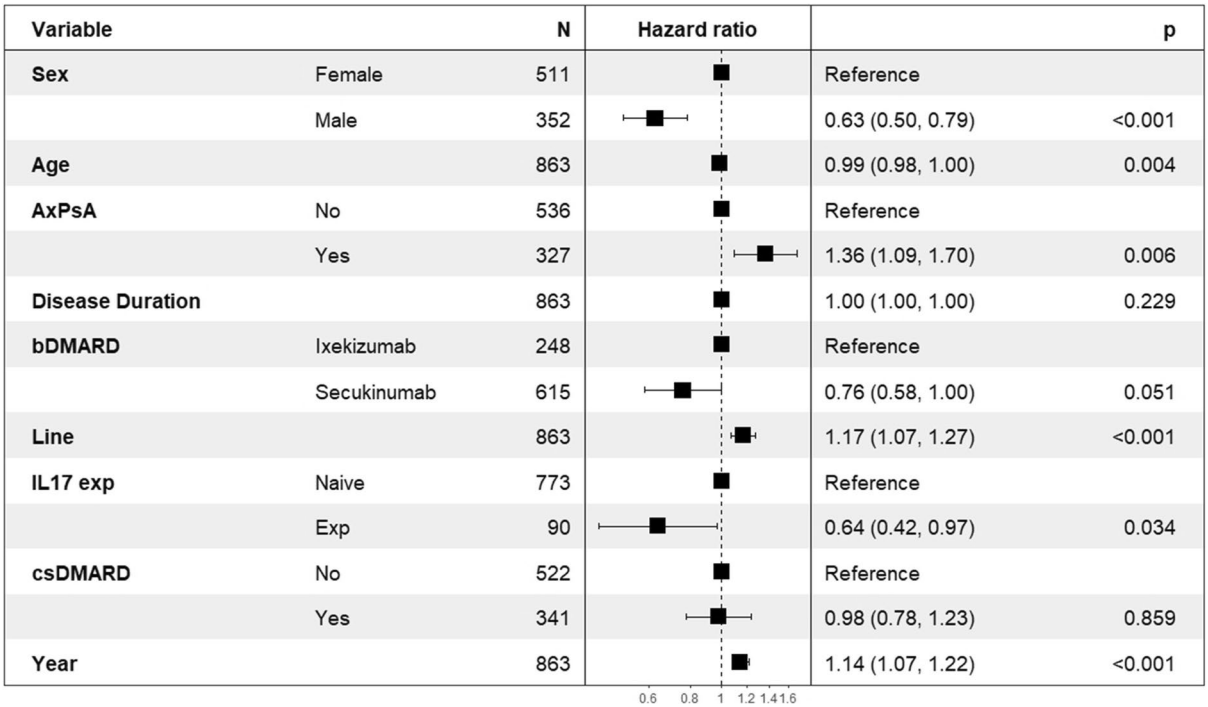

Fig. 3 Forest plot of multivariable Cox proportional hazards regression for predictors of treatment discontinuation. Patients treated with bimekizumab were excluded from the Cox model because of small sample size. *P values* considered significant if < 0.05. *AxPsA* axial involvement in Psoriatic Arthritis, *cs/bDMARD* conventional synthetic/biologic disease-modifying anti-rheumatic drug, *IL-17i* interleukin-17 inhibitor, *exp* experienced patients (i.e. patients already exposed to a prior IL-17i), *Treatment line* number of previous bDMARD lines of treatment, *Year* year of first prescription of the treatment

reflects real-world clinical practice, where receiving more than one IL-17i remains relatively uncommon among the patients affected by PsA. As a consequence, the experienced group represents a clinically selected population with higher disease burden and greater number of prior bDMARDs lines. Our analyses were primarily aimed at exploring drug survival through Kaplan–Meier comparison, fully acknowledging that baseline differences between groups may influence retention estimates. However, this heterogeneity mirrors routine clinical practice, where treatment persistence is inherently shaped by several factors, such as disease burden and therapeutic history. The objective of the present study was to describe what occurs in real-world settings rather than to establish the superiority or inferiority of a specific strategy. Within this context, our findings indicate that, in everyday clinical practice, the use of a second IL-17 inhibitor does not appear to significantly impair drug retention compared with first-time use.

To better explore the impact of baseline characteristics on the probability of discontinuation, we performed a multivariable Cox modelling as a secondary outcome. Consistent with previous literature [26–28], male sex was associated with a lower discontinuation risk, whereas axial involvement predicted poorer persistence, reflecting the well-recognized therapeutic challenges of this disease domain. As expected, a higher number of previous b/tsDMARDs negatively affected treatment persistence.

Interestingly, prior IL-17i exposure was associated with a lower hazard of discontinuation in the Cox model, despite a non-significant opposite trend observed in the Kaplan–Meier comparison. This apparent divergence reflects

the different purposes of the two statistical approaches. The Kaplan–Meier curves describe overall retention patterns between groups as observed in routine care, whereas the Cox model evaluates the independent association between specific variables and the risk of discontinuation after accounting for baseline heterogeneity.

This finding supports the concept that a second IL-17i may still be effective after failure of the first, possibly reflecting molecular differences between available agents. However, it warrants cautious interpretation, as it may also reflect treatment channelling: prior IL-17 exposure could identify patients for whom clinicians considered IL-17 blockade to be particularly appropriate, such as in the case of severe skin involvement and/or axial disease. These scenarios are characterized by a narrower therapeutic armamentarium with a lower propensity to switch, which may result in longer persistence without implying superior drug effectiveness.

Finally, including the calendar year of IL-17i initiation in the Cox model demonstrated an independent association with discontinuation, with more recent years corresponding to a higher hazard of treatment discontinuation. This finding is consistent with previous literature [12, 29] and likely reflects temporal trends in prescribing behaviour, with increasing availability of additional treatment molecules and evolving clinical practice in the context of tight control and treat-to-target strategies.

To our knowledge, this is the first study comparing retention between IL-17i-naïve and IL-17i-experienced patients with PsA. However, our findings regarding overall IL-17i persistence align well with recently published evidence. A real-world study conducted in Spain [30] reported IL-17i retention rates of 88.4% and 81.0% at 6 and 12 months, respectively. The authors further observed slightly higher persistence of ixekizumab compared with secukinumab, although no formal statistical comparison was performed.

Regarding secukinumab, a recent study reported 24-month retention rates comparable to ours [28], although another one showed higher persistence at 48 months [21]. Regarding ixekizumab, a recent study demonstrated a 38-month cumulative retention rate of 43.8%, which was slightly lower than that observed in our cohort [31]. Nevertheless, our study did not perform a direct comparative analysis of secukinumab and ixekizumab persistence because of the marked imbalance between the two treatment groups, and separate estimates for each drug are therefore not available. Greater inconsistency among studies exists regarding the factors influencing treatment discontinuation, highlighting the need for further research to clarify this aspect.

The major strengths of this study include its large, multicentre real-world design, the substantial sample size, and the long-term follow-up. Nevertheless, several limitations should be acknowledged. The retrospective nature of the study implies inherent selection and information biases. Consequently, reasons for discontinuation were not uniformly available, preventing stratified analyses by inefficacy or adverse events, and precluding an evaluation of whether the cause of discontinuation of the first IL-17i influenced the persistence of a subsequent agent within the class. Moreover, objective measures of skin involvement were not systematically collected, limiting the ability to evaluate the impact of psoriasis severity on treatment retention. In addition, we could not systematically assess changes in concomitant csDMARD therapy over time, which may have affected drug retention. Regarding axial involvement in PsA, its identification relied on local clinical assessment and imaging confirmation, without a predefined diagnostic algorithm or centralised imaging review, which may have introduced intercentre variability. Moreover, intercentre variability in treatment decisions and follow-up schedules may have influenced retention estimates. Finally, the relatively small number of patients exposed to bimekizumab precluded its inclusion in multivariable analyses, and residual confounding by unmeasured variables cannot be excluded.

CONCLUSIONS

In this large real-world cohort of patients with PsA, IL-17i demonstrated favourable long-term

retention, with no significant difference between IL-17i-naïve and IL-17i-experienced patients. Male sex, the number of prior b/tsDMARDs, the presence of axial involvement, and the specific IL-17i agent were identified as factors potentially influencing drug survival. Overall, these findings support the sustained effectiveness of IL-17i therapy in PsA and suggest that cycling within the class may represent a reasonable therapeutic option for selected patients with previous IL-17i exposure. Nevertheless, further studies are warranted to better define the clinical contexts in which this approach could be most appropriate.

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Data Availability. The individual participant data that underlie the results reported in this article will be made available upon reasonable request to the corresponding author. Requests for data sharing outside the European Union will be evaluated in accordance with the EU General Data Protection Regulation (Regulation [EU] 2016/679, GDPR) and applicable Italian privacy laws, to ensure appropriate safeguards for international data transfer.

Declarations

Conflict of Interest. Valentino Paci reports speaking and/or consulting fees from AbbVie, Eli Lilly and Johnson & Johnson. Alarico Ariani reports honoraria as a speaker and/or an advisory board member of Abbvie, Amgen, Bristol-Myers Squibb, Stava EG, Johnson and Johnson, Lilly, Novartis, and UCB Pharma. Federica Lumetti has received honoraria as an advisory board member of Amgen. Michele Maria Luchetti Gentiloni reports research support from AbbVie, speaking and/or consulting fees from AbbVie, Amgen, Eli Lilly, Johnson & Johnson, Novartis and Pfizer. Gabriele Amati reports consulting fees from Novartis. Gianluca Moroncini reports speaking and/or consulting fees from AbbVie, Johnson & Johnson, Novartis and Pfizer. Eleonora Celletti, Olga Addimanda, Alberto Lo Gullo, Camilla Mazzanti, Myriam Di

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Ethical Approval. The study protocol was approved by the Area Vasta Emilia Nord (AVEN) Ethics Committee, protocol code 34713, and was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. All study centres accepted the approval of the Area Vasta Emilia Nord Ethics Committee.

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