Dermatology Practical & Conceptual

Hepatic Safety of IL-17 Inhibitors in Psoriasis and Psoriatic Arthritis: A 12-Month Retrospective Cohort Evaluation Using the FIB-4 Index

Umut Bakay[1], Tugba Izci Duran[1], Ozge Sevil Karstarli Bakay[2], Rahime Ekmekcioglu[2]

1 Denizli State Hospital, Department of Rheumatology, Denizli, Turkey
2 Pamukkale University, Department of Dermatology, Denizli, Turkey

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Corresponding Author: Umut Bakay, MD, Institution: Denizli State Hospital, Department of Rheumatology, Denizli, Turkey.
E-mail: ubakay280220@gmail.com

ABSTRACT

Introduction: Psoriasis (PsO) and psoriatic arthritis (PsA) are chronic immune-mediated diseases frequently associated with metabolic dysfunction–associated steatotic liver disease (MASLD). Interleukin-17 (IL-17) contributes to both psoriatic inflammation and hepatic fibrogenesis. However, long-term real-world data on the hepatic safety of IL-17 inhibitors remain limited.

Objectives: To evaluate longitudinal changes in hepatic fibrosis risk using the Fibrosis-4 (FIB-4) index in PsO and PsA patients treated with IL-17 inhibitors and to assess concurrent trends in skin activity and liver enzymes in a dual-center, retrospective cohort.

Methods: Adults with PsO ± PsA who received secukinumab or ixekizumab for ≥12 months at two tertiary centers were retrospectively analyzed. FIB-4 index, liver enzymes (AST, ALT, GGT), and Psoriasis Area and Severity Index (PASI) were assessed at baseline, 3, 6, and 12 months. Patients with chronic liver disease, hepatotoxic drug exposure, or incomplete follow-up were excluded.

Results: A total of 123 patients (mean age 45.2 ± 11.7 years; 59.3% male; 79.7% with PsA) were included. Median baseline FIB-4 was 1.06 (IQR 0.84–1.32); 17.9% of patients were in the intermediate-high risk category. FIB-4 values and risk distribution remained stable over 12 months (P=0.76). Liver enzyme levels did not change significantly, and no hepatotoxic event occurred. Median PASI improved from 12.3 (IQR 7.9–18.7) to 1.1 (IQR 0.5–2.2) at month 12 (P<0.001), with 68.1% of patients achieving PASI ≤1. There was no correlation between changes in PASI and FIB-4 (ρ= -0.08; P=0.27).

Conclusions: IL-17 inhibitors provided substantial clinical efficacy and stable hepatic fibrosis risk over 12 months, including among patients with intermediate-high baseline FIB-4. These findings support the hepatic safety of IL-17 blockade in psoriatic disease and highlight the importance of routine fibrosis monitoring in metabolic-risk populations.

Introduction

Psoriasis (PsO) and psoriatic arthritis (PsA) are chronic, immune-mediated inflammatory disorders arising from a complex interplay of genetic predisposition, environmental triggers, and dysregulated immune pathways. While PsO predominantly involves cutaneous manifestations and PsA presents with musculoskeletal inflammation, both are increasingly recognized as systemic diseases associated with a wide range of comorbidities, including cardiovascular disease, metabolic syndrome, and hepatic disorders such as metabolic dysfunction-associated steatotic liver disease (MASLD; formerly non-alcoholic fatty liver disease, NAFLD) [1,2]. The prevalence of MASLD in psoriatic disease cohorts is substantially higher than in the general population, reaching 47–59% in some series [3,4]. Because MASLD can progress from simple steatosis to fibrosis, cirrhosis, and hepatocellular carcinoma, its coexistence with PsO/PsA represents a clinically relevant comorbidity that may significantly influence therapeutic strategies and long-term prognosis [5].

The pathophysiological connection between psoriatic disease and MASLD is multifactorial. Chronic systemic inflammation, particularly activation of the IL-23/Th17 axis, plays a pivotal role in driving both cutaneous disease activity and hepatic fibrogenesis [6,7]. Interleukin-17A (IL-17A) promotes hepatic stellate cell activation, induces profibrotic mediators such as transforming growth factor-beta (TGF-β), and enhances extracellular matrix deposition [8,9]. Overexpression of IL-17A has been documented not only in psoriatic skin lesions but also in fibrotic liver tissue, indicating a shared immunopathogenic mechanism [10]. This provides a mechanistic basis for hypothesizing that IL-17 inhibition could attenuate hepatic fibrogenesis while effectively controlling cutaneous and musculoskeletal inflammation.

Biologic agents targeting IL-17A such as secukinumab and ixekizumab are well established as highly effective treatments for moderate-to-severe PsO and active PsA [11,12]. Nevertheless, their net impact on hepatic fibrosis remains under debate. Some observational studies have reported improvements in noninvasive fibrosis indices, including the Fibrosis-4 (FIB-4) index and NAFLD fibrosis score, following IL-17 inhibitor therapy [13,14], whereas others have found no significant change [15,16]. Discrepancies in these findings may reflect differences in study design, patient demographics, baseline fibrosis risk, follow-up duration, and/or the inherent limitations of FIB-4, particularly its age dependence and inability to detect early fibrotic alterations [17,18].

The FIB-4 index, calculated using age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count, is a validated, cost-effective, noninvasive tool for estimating the probability of advanced hepatic fibrosis in various liver diseases [19,20]. Despite its simplicity and widespread use, it has reduced diagnostic accuracy for moderate fibrosis stages compared with imaging modalities such as transient elastography or magnetic resonance elastography (MRE) [21]. However, due to its accessibility, reproducibility, and low cost, FIB-4 remains one of the most practical options for longitudinal fibrosis monitoring, especially in real-world settings where elastography may not be routinely available.

To date, there is a lack of long-term real-world evidence on hepatic outcomes in psoriatic patients receiving biologic therapies, including IL-17 inhibitors. Given the high prevalence of MASLD among psoriatic patients and the expanding use of these agents, robust data on their longitudinal hepatic effects are needed.

This dual-center retrospective cohort study aimed to evaluate longitudinal changes in FIB-4 index over a 12-month period in patients with PsO and PsA treated with IL-17 inhibitors. Secondary objectives were to assess liver enzyme trends, cutaneous disease activity measured by the Psoriasis Area and Severity Index (PASI), and subgroup differences according to baseline fibrosis risk and joint involvement. By integrating dermatological and hepatic endpoints, this study sought to clarify the hepatic safety profile of IL-17 inhibitors and their potential influence on fibrotic progression in psoriatic disease.

Methods

Study Design and Setting

This study was designed as a dual-center retrospective observational cohort conducted at the Rheumatology and Dermatology outpatient clinics of Denizli State Hospital and Pamukkale University Hospital (Denizli, Turkey) between December 2022 and September 2023. The study protocol adhered to the principles of the Declaration of Helsinki and received approval from the Pamukkale University Non-Interventional Clinical Research Ethics Committee (Approval No: E-60116787-020-615482, dated November 27, 2024).

All participants provided written informed consent prior to inclusion in the study. Missing or incomplete data were handled using a complete-case approach, and sensitivity analyses were performed to ensure data robustness.

Study Population

Eligible participants were adult patients (≥18 years) with a confirmed diagnosis of psoriasis (PsO), with or without psoriatic arthritis (PsA), who had been treated with interleukin-17 (IL-17) inhibitor therapy (secukinumab or ixekizumab) for a minimum duration of 12 consecutive months.

The diagnosis of PsO was established by board-certified dermatologists based on clinical and/or histopathological findings. PsA was diagnosed by rheumatologists according to the Classification Criteria for Psoriatic Arthritis (CASPAR), which require the presence of inflammatory articular disease (joint, spine, or entheseal) plus a score of ≥3 points from features including current psoriasis, psoriatic nail dystrophy, negative rheumatoid factor, dactylitis, and radiographic juxta-articular new bone formation. Patient selection and study flow diagram are depicted in Figure 1.

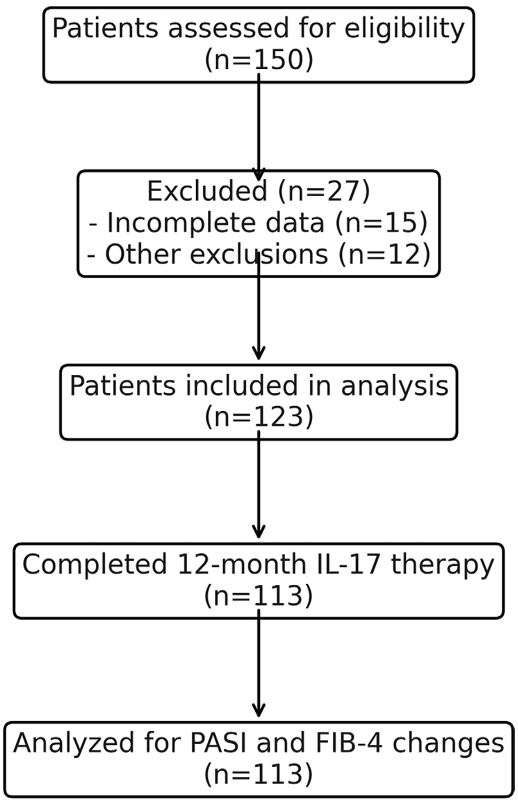

Figure 1. Flow diagram showing patient screening, exclusions, and final cohort included in the analysis.

Inclusion Criteria

- Age ≥18 years
- Confirmed diagnosis of PsO or PsA
- Continuous IL-17 inhibitor therapy for ≥12 months
- Availability of complete laboratory data required for Fibrosis-4 (FIB-4) index calculation at baseline and follow-up visits
- Availability of Psoriasis Area and Severity Index (PASI) scores at baseline and during follow-up

Exclusion Criteria

- History of chronic liver disease (e.g., hepatitis B or C, autoimmune hepatitis, alcoholic liver disease)
- Concomitant use of known hepatotoxic agents (e.g., methotrexate, leflunomide) during the observation period
- Malignancy, organ transplantation, or systemic conditions known to influence liver function
- Incomplete follow-up or missing FIB-4/PASI data preventing valid longitudinal analysis
- Pregnancy or lactation during the study period

Treatment Protocol

Patients with psoriasis (PsO) and psoriatic arthritis (PsA) received IL-17 inhibitor therapy according to the approved dosing regimens for each indication.

Secukinumab

For Psoriasis (PsO): 300 mg subcutaneously at weeks 0, 1, 2, 3, and 4 (loading phase), followed by 300 mg every four weeks thereafter.

For Psoriatic Arthritis (PsA): 150 mg subcutaneously at the same intervals; however, 300 mg doses were administered in patients with extensive skin involvement or inadequate prior biologic response, consistent with label recommendations.

Ixekizumab

For Psoriasis (PsO): 160 mg subcutaneously at baseline, followed by 80 mg every two weeks until week 12, and 80 mg every four weeks thereafter.

For Psoriatic Arthritis (PsA): 160 mg subcutaneously at baseline, then 80 mg every four weeks (without loading phase).

The dosing regimen was selected by the treating physician according to disease phenotype, severity, previous biologic exposure, and comorbidities.

Patients continued therapy uninterrupted for ≥12 months, and treatment adherence was verified from electronic prescription records at both centers.

Outcome Measures

Primary Outcome

- Longitudinal change in liver fibrosis risk, assessed by the FIB-4 index at baseline, 3, 6, and 12 months

Secondary Outcomes

- Change in PASI scores over the same time points
- Trends in liver function tests (AST, ALT, GGT)
- Shifts in fibrosis risk categories according to age-adjusted FIB-4 thresholds

FIB-4 Index Calculation

The FIB-4 index was calculated using the validated formula:

$$\text{FIB-4} = (\text{Age} \times \text{AST}) / (\text{Platelet count} \times \sqrt{\text{ALT}})$$

Risk categories:

- Low risk: FIB-4 <1.3 (<65 years) or <2.0 (≥65 years)
- Intermediate–high risk: FIB-4 ≥1.3 (<65 years) or ≥2.0 (≥65 years)

PASI Assessment

PASI scores were determined by dermatologists trained in standardized scoring methodology at baseline and each follow-up visit (months 3, 6, and 12). Inter-rater reliability was ensured by consensus scoring in cases of uncertainty. For patients with PsA, articular disease activity was recorded but not included in the PASI analysis.

Data Quality and Attrition Handling

All laboratory measurements were performed at the institutional biochemistry laboratories of both centers, following standardized protocols. Data verification and harmonization across centers were conducted using a dual-entry audit process. Patients lost to follow-up or discontinuing therapy were documented in the attrition analysis.

Statistical Analysis

Analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA).

Continuous variables are expressed as mean ± standard deviation (SD) for normally distributed data or median (interquartile range, IQR) for non-normal data.

Categorical variables are reported as counts (n) and percentages (%).

Normality of distributions was tested with the Shapiro–Wilk test.

Longitudinal changes in FIB-4 index, PASI scores, and liver enzymes were analyzed using the Friedman test for non-parametric repeated measures, with Holm–Bonferroni-adjusted Wilcoxon signed-rank post-hoc comparisons.

Between-group comparisons (e.g., PsO vs. PsA; low vs. intermediate-high baseline FIB-4) were conducted using the Mann–Whitney U or χ^2/Fisher's exact test, as appropriate.

Correlations between ΔPASI and ΔFIB-4 were explored using Spearman's rank correlation coefficient (ρ).

A two-tailed p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 123 patients with psoriasis (PsO) or psoriatic arthritis (PsA) receiving IL-17 inhibitor therapy were included (Figure 1). The mean age was 43.5 ± 13.5 years, and 59.3% (n=73) were male. Ninety-eight patients (79.7%) had PsO without PsA, and 25 (20.3%) had PsO with PsA. The mean disease duration was 90.8 ± 93.4 months in the PsO without PsA group and 164.0 ± 66.0 months in the PsO with PsA group. Secukinumab was the most frequently prescribed IL-17 inhibitor (83.7%), followed by ixekizumab (16.3%).

Baseline demographic, clinical, and laboratory characteristics stratified by diagnosis are presented in Table 1. There were no statistically significant differences between groups for age, sex, BMI, alcohol intake, PASI score, or Charlson Comorbidity Index (CCI). Methotrexate use was significantly more frequent in patients with PsA (*P*=0.026). CRP levels were higher in the PsA group compared with PsO without PsA (median 7.3 vs. 1.5 mg/L, *P*=0.004), whereas other laboratory parameters did not differ significantly.

Baseline Characteristics by FIB-4 Category

When stratified by baseline FIB-4 category, 17.9% (n=22) of patients were classified as intermediate-high risk. Compared to the low-risk group (n=101), these patients were significantly younger (median 32 vs. 50 years, *P*=0.001), had markedly higher AST (*P*=0.001) and ALT (*P*=0.003) values, and higher CCI scores (*p*=0.001) (Table 2). PASI scores at baseline were lower in the intermediate-high risk group (median 1.2 vs. 11.8, *P*=0.035).

FIB-4 Index Trajectory

At baseline, the median FIB-4 index for the entire cohort was 0.62 (range: 0.19–2.23). Over the 12-month follow-up, median FIB-4 values remained stable (*P*=0.964, Friedman test), and the distribution of risk categories did not significantly change from baseline to month 12 (Table 3, Figure 2).

Subgroup analysis showed no significant differences in FIB-4 trajectories for PsO without PsA (*P*=0.934) or PsO with PsA (*P*=0.475). Similarly, within-group changes were not significant when patients were stratified by baseline fibrosis risk.

Liver Enzyme Trend

Liver enzyme profiles are summarized in Table 1 and Table 2. Median AST remained unchanged (28 U/L at baseline vs. 29 U/L

Table 1. Demographic and clinical characteristics of patients according to diagnosis.

	PsO without PSA (n=98)	PsO with PSA (n=25)	p-value
Age, years, mean±SD	42.7±13.6	46.6±13.5	0.455
Female sex n (%)	42 (42.9)	14 (56.0)	0.239
Disease duration, months, mean±SD	90.8±93.4	164.0±66.0	0.777
Alcohol intake, ever n (%)	35 (35.7)	7 (28.0)	0.468
BMI, mean±SD	29.2±4.3	34.2±4.7	0.706
PASI score, mean±SD	13.8±11.4	19.8± 17.4	0.935
Duration of treatment with anti-IL17, months, mean±SD	40.0±21.0	16.6±7.5	0.574
Disease phenotype, n (%)			0.561
PsO without PSA	79 (78.2)	19 (86.4)	
PsO with PSA	22 (21.8)	3 (13.6)	
CCI, median (min-max)	0 (0-3)	1 (0-2)	0.243
CCI subgroups			0.445
0	61 (62.2)	16 (64.0)	
1-2	28 (28.6)	9 (36.0)	
3-4	8 (8.2)	0 (0.0)	
≥5	1 (1.0)	0 (0.0)	
FIB-4 group, n (%)			0.561
Low risk	79 (80.6)	22 (88.0)	
Intermediate-high risk	19 (19.4)	3 (12.0)	
Comorbidities			
Hypertension, n (%)	3 (2.4)	0 (0.0)	1.000
Hyperlipidemia, n (%)	3 (3.1)	2 (8.0)	0.268
Diabetes Mellitus, n (%)	9 (9.2)	5 (20.0)	0.158
Medications			
NSAIDs, n (%)	0 (0.0)	1 (4.0)	0.203
Oral antidiabetics, n (%)	9 (9.2)	6 (24.0)	0.079
Insulin, n (%)	2 (2.0)	0 (0.0)	1.000
Anti-hyperlipidemics, n (%)	6 (6.1)	3 (12.0)	0.386
Methotrexate, n (%)	1 (1.0)	3 (12.0)	**0.026**
Leflunomide, n (%)	0 (0.0)	1 (4.0)	0.203
Laboratory results			
Creatinine, mean±SD	0.77±0.15	0.83±0.41	0.499
AST, median (min-max)	28 (11-144)	14 (13-28)	0.481
ALT, median (min-max)	40 (11-275)	18 (11-40)	**0.855**
ALP, mean±SD	71.2±15.2	99.6±57.5	0.625
GGT, median (min-max)	29 (10-206)	27 (15-47)	0.578
Albumin, median (min-max)	45.5 (30-49)	45.6 (40-48)	0.456
Platelet count, mean±SD	293.1±64.6	311.6±51.5	0.638
ESR, mean±SD	19.7±16.2	20.6±18.1	0.622
CRP, median (min-max)	1.5 (0.14-79.2)	7.3 (5.8-80.2)	**0.004**
FIB-4 index, median (min-max)	0.59 (0.39-2.04)	0.46 (0.34-0.74)	0.352
Lipid profile			
LDL >130 mg/Dl	16 (16.7)	4 (16.7)	1.000
HDL <50 mg /dL	53 (54.6)	14 (58.3)	0.744
Triglyceride >159 mg/dL	35 (35.7)	8 (32.0)	0.728

Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; FIB- 4, fibrosis score- 4; HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; mg/dL, milligrams (mg) per deciliter (dL); NSAIDs, non-steroidal anti-inflammatory drugs; PASI, Psoriasis Area Severity Index; Pso, psoriasis; PsA, psoriatic arthritis; SD, standard deviation.

Note: Intermediate-high risk FIB-4 index was defined as ≥1.3 for patients aged <65 years and ≥2.0 for patients aged ≥65 years.

Table 2. Demographic and clinical characteristics of patients according to FIB-4 index at the initial assessment.

	Low risk FIB-4 index (n=101)	Intermediate-high risk FIB-4 index (n=22)	p-value
Age, years, median (min-max)	50 (30-55)	32 (25-61)	**<0.001**
Female sex n (%)	48 (47.5)	8 (36.4)	0.341
Disease duration, months, median (min-max)	132 (12-252)	12 (12-120)	0.224
Alcohol intake, ever n (%)	37 (36.6)	5 (22.7)	0.213
BMI, mean±SD	29.6±16.1	28.7±4.8	0.409
PASI score, median (min-max)	11.8 (6.6-40)	1.2 (1.2-25.2)	0.035
Duration of treatment with anti-IL17, months, median (min-max)	45 (8-64)	12 (12-36)	0.587
Disease phenotype, n (%)			0.561
PsO without PSA	79 (78.2)	19 (86.4)	
PsO with PSA	22 (21.8)	3 (13.6)	
CCI, median (min-max)	1 (0-2)	0 (0-3)	**<0.001**
CCI subgroups			**0.003**
0	70 (69.3)	7 (31.8)	
1-2	26 (25.7)	11 (50.0)	
3-4	5 (5.0)	3 (37.5)	
≥5	0 (0.0)	1 (4.5)	
Comorbidities			
Hypertension, n (%)	2 (2.0)	1 (4.5)	0.449
Hyperlipidemia, n (%)	5 (5.0)	0 (0.0)	0.584
Diabetes Mellitus, n (%)	11 (10.9)	3 (13.6)	0.715
Medications			
NSAIDs, n (%)	1 (1.0)	0 (0.0)	1.000
Oral antidiabetics, n (%)	12 (11.9)	3 (13.6)	0.731
Insulin, n (%)	2 (2.0)	0 (0.0)	1.000
Anti-hyperlipidemics, n (%)	8 (7.9)	1 (4.5)	1.000
Methotrexate, n (%)	2 (2.0)	2 (9.1)	0.146
Leflunomide, n (%)	1 (1.0)	0 (0.0)	1.000
Laboratory results			
Creatinine, median (min-max)	0.73 (0.51-1.41)	0.89 (0.89-0.94)	0.097
AST, mean±SD	19.4±7.3	109.0±58.0	**<0.001**
ALT, mean±SD	28.2±20.0	125.0±130.2	**0.003**
ALP, median (min-max)	70 (53-166)	71 (66-91)	0.982
GGT, median (min-max)	27 (10-206)	29 (14-40)	0.138
Albumin, median (min-max)	45.5 (30-49)	46.1 (44-49)	0.438
Platelet count, mean±SD	325.8±44.4	235.3±31.5	0.743
ESR, mean±SD	24.7±16.8	9.0±3.0	0.426
CRP, median (min-max)	5.8 (01.-80.2)	39.4 (0.3-79.2)	0.971
FIB-4 index, mean±SD	0.47±0.13	1.74±0.35	**0.028**
Lipid profile			
LDL >130 mg/dL	17 (17.2)	3 (14.3)	1.000
HDL <50 mg /dL	58 (58.0)	9 (42.9)	0.204
Triglyceride >159 mg/dL	35 (34.7)	8 (36.4)	0.879

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; FIB- 4, fibrosis score- 4; HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; mg/dL, milligrams (mg) per deciliter (dL); NSAIDs, non-steroidal anti-inflammatory drugs; PASI, Psoriasis Area Severity Index; PsO, psoriasis; PsA, psoriatic arthritis; SD, standard Deviation. Note: Intermediate-high risk FIB-4 index was defined as ≥1.3 for patients aged <65 years and ≥2.0 for patients aged ≥65 years.

Table 3. PASI and FIB-4 index changes during treatment in patients with Pso with and without PSA.

		month 0 (n=123)	month 3 (n=123)	month 6 (n=123)	month 12 (n=113)	p-value
FIB-4 Index group	Low Risk	101 (82.1)	110 (89.4)	112 (91.1)	105 (85.4)	
	Intermediate-High Risk	22 (17.9)	13 (10.6)	11 (8.9)	8 (6.5)	
FIB-4 Index, median (min-max)		0.62 (0.19-2.23)	0.62 (0.19-3.64)	0.62 (0.15-2.52)	0.67 (0.17-2.12)	0.964
PASI		8.8 (0-48)	0 (0-15.5)	0 (0-8)	0 (0-18)	<0.001

P-values are based on Friedman test for repeated measures.

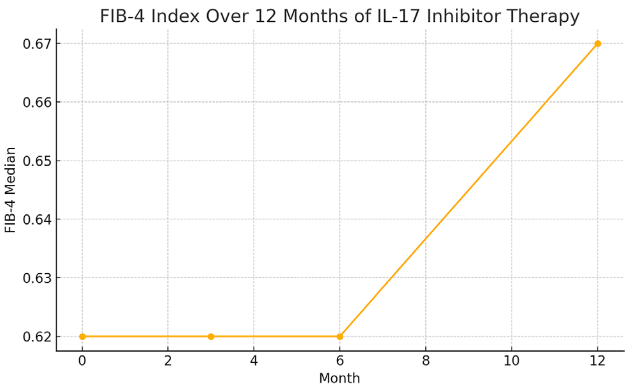

Figure 2. FIB-4 index changes during 12 months of IL-17 inhibitor therapy. Mean FIB-4 index values at baseline, 6 months, and 12 months, demonstrating stable hepatic fibrosis risk during follow-up (p = 0.964). Error bars indicate standard error of the mean.

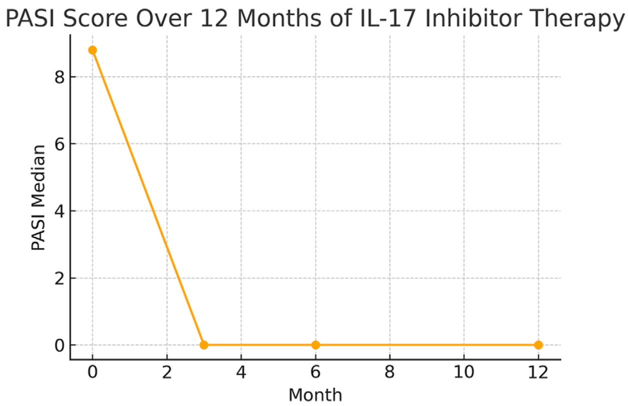

Figure 3. PASI score changes during 12 months of IL-17 inhibitor therapy. Mean PASI scores at baseline, 6 months, and 12 months, showing sustained clinical improvement over time. Error bars indicate standard error of the mean.

at month 12). ALT showed a non-significant decrease (40 to 18 U/L), and GGT levels were stable (29 to 27 U/L). No statistically significant change was observed over time, and no patient experienced grade ≥2 transaminase elevations or discontinued therapy due to hepatotoxicity.

PASI Score Improvement

The baseline median PASI score was 8.8 (range: 0–48). There was a marked and statistically significant improvement over time ($\chi^2(3)$ = 247.1, *P*=0.001), with median PASI scores of 0 at month 3 (range: 0–15.5), month 6 (range: 0–8), and month 12 (range: 0–18) (Table 3, Figure 3). The improvement pattern was consistent across PsO without PsA and PsO with PsA subgroups.

Correlation Between Skin and Hepatic Outcomes

No significant correlation was observed between changes in PASI and changes in FIB-4 index from baseline to month 12 in either diagnostic subgroup.

Attrition and Data Completeness

The patient selection process and attrition details are shown in Figure 1. Of the 123 enrolled patients, 113 (91.9%) completed the 12-month follow-up with complete FIB-4 and PASI data. Loss to follow-up occurred due to treatment discontinuation (n=5), transfer to other centers (n=3), or missing follow-up data (n=2). No withdrawal was related to hepatic adverse events.

Discussion

In this 12-month real-world observational cohort of patients with psoriasis and psoriatic arthritis treated with IL-17 inhibitors, we observed substantial and sustained improvement in skin disease activity, while hepatic fibrosis risk remained stable as assessed by the FIB-4 index. Liver enzyme profiles did not show clinically meaningful longitudinal changes, and no hepatotoxic events were recorded during follow-up. By integrating dermatologic response metrics with pragmatic fibrosis surveillance over a full year, our findings support the hepatic safety of IL-17 blockade in routine practice, including among patients with elevated baseline fibrosis risk. Notably, baseline CRP was higher in patients with PsA, and the intermediate–high FIB-4 group exhibited higher transaminases and comorbidity burden, suggesting that systemic inflammation and multimorbidity may influence hepatic vulnerability and warrant closer metabolic-risk management.

Comparison with Previous Literature

Our results are consistent with observational data indicating that IL-17 inhibitors do not worsen noninvasive fibrosis markers in psoriatic disease [13,14,29]. While Takamura et al. reported modest reductions in FIB-4 and NAFLD fibrosis scores after IL-17 blockade in higher-risk cohorts [12], the absence of measurable improvement in our study may relate to the relatively small intermediate–high risk subgroup (17.9%), stable metabolic status during follow-up, and the limited time horizon for detecting fibrosis regression, which often requires ≥2–3 years in MASLD [22,30]. In parallel, longer-term biologic studies in psoriasis have also reported stability rather than consistent improvement in fibrosis indices. For example, Mortato et al. (2025) observed stable FIB-4 values over three years among patients treated with guselkumab, with disease duration emerging as a modifier of hepatic outcomes [14]. Collectively, these findings suggest that cytokine-targeted control of psoriatic inflammation, whether through IL-17 or IL-23 pathways, is unlikely to accelerate fibrosis, whereas meaningful improvements in fibrosis risk may depend on concurrent metabolic interventions. This interpretation is supported by systematic reviews showing that hepatic fibrosis indices do not uniformly improve despite reductions in systemic inflammation during biologic therapy [23,31].

Biological Considerations

IL-17A is implicated in hepatic stellate cell activation, collagen deposition, and profibrotic cytokine release [6-9]. Experimental models have shown that IL-17 inhibition can downregulate TGF-β signaling and attenuate stellate cell activation [24,32]. However, MASLD progression is multifactorial, involving metabolic dysfunction, insulin resistance, lipotoxicity, and systemic inflammation [17,18,33]. The elevated CRP levels observed in PsA patients and the higher liver enzyme levels in the intermediate-high FIB-4 group suggest that systemic inflammatory load and comorbidity burden may contribute to hepatic vulnerability, but IL-17 blockade alone may address only part of this pathogenic spectrum. The absence of correlation between PASI and FIB-4 changes in our study likely reflects the age-dependence and limited sensitivity of FIB-4 for detecting early fibrotic changes, the short follow-up duration, and the influence of metabolic rather than inflammatory drivers on hepatic fibrosis progression.

Clinical and Guideline Context

The stability of FIB-4 scores in our study supports that IL-17 inhibitors are hepatically safe for PsO and PsA, including those with baseline intermediate-high fibrosis risk, provided that structured monitoring is in place. According to the 2024 EULAR PsA management recommendations and the 2023 AAD–NPF psoriasis guidelines, regular liver function and fibrosis risk assessments are advised in patients with metabolic comorbidities [26,27,34]. Our findings reinforce these recommendations, emphasizing that clinical improvement in psoriatic disease should not lead to complacency in hepatic surveillance. Furthermore, biological therapies can effectively improve skin and joint disease without increasing hepatic risk, and early intervention may reduce long-term fibrosis progression. Lifestyle modification, weight reduction, and metabolic optimization remain cornerstone strategies for reversing fibrosis [28,35], and biological therapy should be incorporated into a multidisciplinary management approach addressing both dermatological and metabolic comorbidities.

Strengths and Limitations

The strengths of this study include its real-world design, inclusion of both PsO and PsA patients, and the integration of hepatic and dermatologic endpoints with high follow-up retention. Limitations include its retrospective dual-center nature, modest intermediate-high FIB-4 subgroup size, lack of advanced imaging modalities such as transient elastography or MRE, and the relatively short 12-month follow-up compared with longer-term biologic studies (e.g., EGIPT trial with 3-year duration). The use of FIB-4, while practical, may have limited sensitivity in detecting early or minimal fibrotic changes.

Future Perspectives

Future research should focus on multicenter prospective trials with ≥3-year follow-up, stratified recruitment of high-risk MASLD patients, and the use of advanced fibrosis tools such as MRE, ELF, and PRO-C3. Combined strategies incorporating IL-17 blockade with structured metabolic interventions (e.g., dietary modification, physical activity, insulin-sensitizing therapies) could clarify whether synergistic benefits on hepatic outcomes can be achieved. Integration of multi-biomarker panels and imaging modalities may further enhance early risk detection and individualized fibrosis monitoring in psoriatic patients treated with biologic therapy.

Conclusion

IL-17 inhibitors demonstrated a favorable hepatic safety profile and strong clinical efficacy in both psoriasis (PsO) and psoriatic arthritis (PsA) patients, including those with intermediate-high baseline fibrosis risk. Throughout 12 months of therapy, no hepatotoxicity or fibrosis progression was observed, while significant improvements in cutaneous disease activity were maintained. These results highlight that targeted IL-17 blockade can be safely employed in psoriatic patients with coexisting metabolic or hepatic risk factors when appropriate monitoring is performed.

Future studies should focus on prospective, multicenter designs with longer follow-up durations, incorporating advanced fibrosis assessment techniques (e.g., MRE, ELF, PRO-C3) and structured metabolic interventions to better elucidate the long-term hepatic outcomes of biological therapy in psoriatic disease.

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