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ORIGINAL RESEARCH

Interleukin-17A Inhibitors in Patients with Psoriasis and Tuberculosis Infection: A 2-Year Prospective Study on Safety Without Preventive Treatment

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ABSTRACT

Introduction: The necessity for tuberculosis preventive treatment (TPT) and routine T-SPOT.TB monitoring in patients with psoriasis and tuberculosis infection (TBI) undergoing interleukin (IL)-17A inhibitor therapy remains uncertain. This study aims to evaluate the long-term safety of IL-17A inhibitors administered without TPT and analyze changes in T-SPOT.TB among these patients. It also identifies risk factors for TBI in patients with psoriasis.

Methods: This single-center prospective study enrolled adult patients with plaque psoriasis and TBI receiving IL-17A inhibitors. TBI was defined as positive T-SPOT.TB results ($\geq$ 6 spots) without symptoms or evidence of active tuberculosis (ATB). TPT administration was based on contraindications, tuberculosis risk factors, and patient preferences. The primary endpoint was the incidence of ATB over 2 years. Secondary outcomes included T-SPOT.TB changes and TBI risk factors.

Results: Of the 129 patients with psoriasis and TBI enrolled in the study, 97 (75.2%) did not receive TPT, while 32 (24.8%) did. Among them, 109 patients (84.5%) completed the 2-year follow-up. During the 235 person-years of observation, no ATB cases were identified. Median T-SPOT.TB values showed no significant changes from baseline to year 2 in both the non-TPT (20 vs. 17 spots, $p = 0.975$) and TPT groups (55 vs. 58 spots, $p = 0.830$). T-SPOT.TB reversed in 14 patients (12.8%), mostly in the non-TPT group. Moreover, for TBI risk factor analysis, a cohort of 212 patients with psoriasis with negative baseline T-SPOT.TB was evaluated, revealing a TBI prevalence of 37.8%. Logistic regression analysis highlighted age $\geq$ 45 years (odds ratio [OR] 2.44, 95% confidence interval [CI] 1.50–3.99, $p < 0.001$) and body mass index (BMI) < 24.0 kg/m^2 (OR 2.12, 95% CI 1.27–3.54, $p = 0.004$) as independent risk factors for TBI.

Conclusion: IL-17A inhibitors do not appear to reactivate tuberculosis in patients with psoriasis and TBI, potentially reducing the need for routine TBI screening and preventive treatment.

Trial Registration: Chinese Clinical Trial Registry, ChiCTR2100045823.

Chun-Xia He and Chao Wu contributed equally to the study.

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Keywords: Interferon-γ release assay; IGRA; Interleukin-17A; Prophylaxis; Psoriasis; Safety; T-SPOT.TB; Tuberculosis

Key Summary Points

Why carry out this study?

The role for tuberculosis preventive treatment (TPT) and T-SPOT.TB monitoring in patients with psoriasis and tuberculosis infection (TBI) receiving interleukin (IL)-17A inhibitors is controversial.

We aimed to assess the long-term safety of IL-17A inhibitors, without TPT, in this patient population.

What was learned from the study?

Over 2 years, no active tuberculosis (ATB) cases were observed among 129 patients with psoriasis and TBI undergoing IL-17A inhibitor therapy, most of whom did not receive TPT, indicating a minimal risk of tuberculosis reactivation.

For patients with psoriasis without tuberculosis risk factors, the application of IL-17A inhibitors may necessitate only the exclusion of ATB, eliminating the need for TBI screening. Furthermore, even in cases with a positive TBI screening result, TPT may not be obligatory.

The stability of T-SPOT.TB values during the study suggests that routine monitoring might be unnecessary for patients with psoriasis and TBI.

The identification of age $\geq$ 45 years and body mass index $<$ 24.0 kg/m^2 as independent risk factors for TBI offers valuable insights for patient stratification in clinical practice.

INTRODUCTION

Biologics for Psoriasis May Reactivate Tuberculosis: Guidelines Emphasize the Importance of Tuberculosis Screening and Preventive Treatment

Tuberculosis infection (TBI), previously referred to as latent tuberculosis infection, is defined as a persistent immune response to *Mycobacterium tuberculosis* antigens without clinical manifestations of active tuberculosis (ATB). Diagnostic approaches for TBI include the tuberculin skin test and interferon-γ release assays (IGRA), with the latter encompassing methods such as QuantiFERON-TB ([QFT], measuring interferon-γ secretion by white blood cells) and T-SPOT.TB (enumerating interferon-γ-producing T lymphocytes). A confirmed TBI diagnosis requires a positive IGRA test, coupled with the ruling out of ATB through clinical evaluation, chest radiography, and analysis of specimens in symptomatic individuals.

Given the significantly increased risk of tuberculosis reactivation linked to tumor necrosis factor inhibitors [1–4], guidelines recommend tuberculosis screening before initiating biologics in patients with psoriasis [5–7]. For TBI cases, tuberculosis preventive treatment (TPT) is advised, usually consisting of isoniazid, rifampicin, or rifapentine [5–7].

Managing Psoriasis with Concurrent TBI in China is Challenging, Highlighting the Need for Safer Strategies

In China, about seven million individuals suffer from psoriasis [5]. As a country with a high tuberculosis burden, roughly one-third of these patients may harbor TBI [8]. However, the widespread adoption of TPT is hindered by several factors, including the notable prevalence of drug-resistant tuberculosis [9], the susceptibility of patients to re-exposure and re-infection, and increased risks of adverse drug reactions such as hypersensitivity or liver injury [10]. Therefore, alternative strategies for psoriasis management that do not reactivate tuberculosis are critically needed.

Necessity for TPT in Patients with Psoriasis and TBI Receiving IL-17A Inhibitors Remains a Debated Topic

Preclinical evidence suggests a limited role of interleukin (IL)-17 in the host's immune defense against *M. tuberculosis* [11, 12]. While clinical trials and post-marketing data have not reported ATB cases among patients treated with IL-17A inhibitors [13–15], it should be noted that these studies primarily excluded patients with TBI or only included those who had already undergone TPT. In contrast, a few retrospective studies with limited sample sizes reported no ATB cases among patients with TBI receiving IL-17A inhibitors without TPT [16–18]. This has led to an ongoing debate regarding the necessity of TPT in this context.

Dynamic Monitoring of IGRA in Patients with Psoriasis and TBI is Controversial

Current Chinese guidelines propose semi-annual IGRA monitoring for patients with psoriasis on tumor necrosis factor inhibitors and an annual review for those on other biologics [19], primarily because of concerns about ATB. Many dermatologists in clinical practice strictly follow these guidelines or even conduct more frequent IGRA tests. However, it is important to note that these recommendations are largely based on expert consensus rather than evidence. Few studies have examined IGRA changes in patients with psoriasis and TBI. Additionally, a systematic review and meta-analysis indicated a low positive predictive value of IGRA for TBI progression to ATB (only 4.5%) [20], casting doubt on the clinical utility of frequent IGRA monitoring.

To address these gaps, we conducted a prospective observational study to investigate whether IL-17A inhibitor treatment in patients with psoriasis and TBI, without TPT, increases the risk of developing ATB. We also monitored the changes in T-SPOT.TB levels before and after treatment and explored risk factors contributing to TBI in patients with psoriasis.

METHODS

Study Design and Participants

This prospective, observational study was conducted at Peking Union Medical College Hospital, Beijing, from April 2021 to December 2023. The study enrolled adults diagnosed with plaque psoriasis and concurrent TBI. All participants received IL-17A inhibitors, either secukinumab or ixekizumab. The concurrent administration of TPT was based on tuberculosis risk factors, contraindications to TPT, and patient preferences. The primary endpoint was the incidence of ATB over a 2-year follow-up period.

Eligible participants were (1) aged 18–-75 years, (2) diagnosed with plaque psoriasis, (3) having a disease duration of 6 months or more, (4) with a Psoriasis Area and Severity Index (PASI) score of 10 or higher, or below 10 if traditional treatments had failed, and (5) diagnosed with TBI by infectious disease specialists. A positive T-SPOT.TB test result (Oxford Immunotec; Oxford, UK) was essential for TBI diagnosis, defined as ≥ 6 spots in line with international standards. Participants had neither symptoms nor radiographic evidence of ATB. The study excluded individuals with active malignancy, inflammatory bowel disease, human immunodeficiency virus (HIV) infection, pregnancy, or lactation.

Study Procedure and Outcomes

Baseline assessments included a complete blood cell count, blood biochemistry, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), an infectious panel including hepatitis B, C, HIV, and T-SPOT.TB, along with a chest X-ray. Patients then received either secukinumab (300 mg weekly for 5 weeks, followed by 300 mg monthly subcutaneous injection) or ixekizumab (160 mg at week 0, then 80 mg every other week for 12 weeks, followed by 80 mg monthly subcutaneous injection).

The decision to administer TPT was guided by the presence of contraindications, tuberculosis risk factors, and patient preferences.

Specifically, TPT was not administered to participants who were aged over 65, diagnosed with viral hepatitis, cirrhosis, currently using hepatotoxic drugs, or had a history of drug-induced liver injury. On the other hand, TPT was advised for those with a history of ATB, exposure to pulmonary tuberculosis, chronic renal failure, chronic obstructive pulmonary disease, interstitial lung disease, or those on systemic corticosteroids or immunosuppressants. In instances where these criteria were not met, the preferred approach was to withhold TPT, following a comprehensive consultation with the patient. Infectious disease experts formulated the individualized TPT plans for eligible participants.

Follow-up visits were scheduled at 1, 2, and 3 months, then quarterly over 2 years. During each visit, tuberculosis symptoms and signs were thoroughly examined. Complete blood cell count, biochemistry, ESR, and CRP were conducted biannually. Chest X-rays and T-SPOT.TB were reviewed annually. Adjustments to psoriasis treatment, including combination with other medications or potential reduction in IL-17A inhibitor frequency, were permitted throughout the study.

The primary outcome of this study was the incidence of ATB over a 2-year follow-up. The diagnosis of ATB was confirmed through a positive *M. tuberculosis* culture or nucleic acid amplification test, or through clinical and radiological evidence, as verified by infectious disease specialists. In cases of confirmed ATB, IL-17A inhibitors were immediately discontinued, and an anti-tuberculosis treatment plan was devised by these specialists.

Secondary outcomes included (1) changes in T-SPOT.TB results from baseline to year 2, (2) completion rates and safety profile of TPT, (3) effectiveness and safety of IL-17A inhibitors, and (4) risk factors for TBI in patients with psoriasis. For the analysis of TBI risk factors, a cohort of patients with psoriasis with negative baseline T-SPOT.TB results from our center was included.

Statistical Analysis

For normally distributed continuous variables, the mean ± standard deviation is presented, and differences between groups were analyzed using a two-tailed *t* test. Non-normally distributed continuous variables are summarized using the median (25th and 75th percentiles), with group differences assessed using the Mann–Whitney *U* test. Categorical variables are expressed as counts (percentages), and intergroup differences were analyzed with the chi-square test or Fisher's exact test. The paired sample *t* test or Wilcoxon signed-rank test was used for changes in laboratory parameters from baseline to year 2. Binary logistic regression was used to analyze risk factors for TBI. Variables showing statistical significance in univariate analysis or considered clinically meaningful were included in the regression equation using an enter method. No imputation was performed for missing data. Statistical analyses were conducted using SPSS 27.0 (SPSS Inc., Chicago, IL, USA), with $p < 0.05$ indicating statistical significance.

All patients provided informed consent for participation in the study. Approval was obtained from the Peking Union Medical College Hospital Ethics Committee (ZS-2850, I-22PJ559). The study was registered at Chinese Clinical Trial Registry (ChiCTR2100045823) and was performed in accordance with the Helsinki Declaration.

RESULTS

Patient Disposition and Baseline Characteristics

From April to December 2021, this study enrolled 129 patients with psoriasis and concurrent TBI. Among these, 97 patients (75.2%) did not receive TPT, whereas 32 (24.8%) did. A total of 109 patients (84.5%) completed the 2-year follow-up, while 20 (15.5%) discontinued for various reasons: 15 (11.6%) were lost to follow-up, 3 (2.3%) withdrew informed consent, and 2 (1.6%) switched to IL-23 inhibitors.

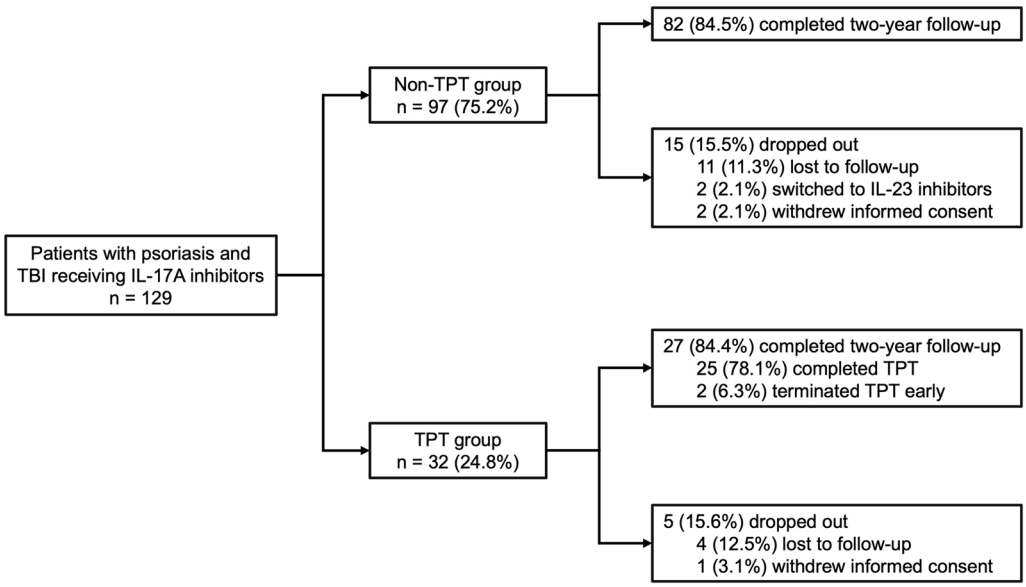

Fig. 1 Participant flow diagram for the study. *IL* interleukin, *TBI* tuberculosis infection, *TPT* tuberculosis preventive treatment

A detailed participant flow diagram is provided in Fig. 1.

At the study's end, the treatment regimens for the 109 patients were as follows: 55 patients (50.5%) received monthly secukinumab 300 mg, 35 (32.1%) were on secukinumab 300 mg every 2–3 months, 14 (12.8%) were administered monthly ixekizumab 80 mg, 5 (4.6%) took bimonthly ixekizumab 80 mg, and 9 (8.3%) were on a combination regimen with acitretin. Notably, 10 patients switched from secukinumab to ixekizumab, and one switched from ixekizumab to secukinumab.

Baseline characteristics of the patients are detailed in Table 1. In summary, the cohort predominantly consisted of men (95 patients, 73.6%), with an average age of 45 years and a body mass index (BMI) of 25.3 kg/m^2. The median duration of psoriasis among the participants was 15 years, and the median PASI score was 15.1. Previous systemic treatments, including acitretin, methotrexate, cyclosporine, and phototherapy, were recorded in 65 patients (50.4%), while 24 (18.6%) had previously used biologics. A history of contact with pulmonary tuberculosis was documented in 4 patients (3.1%). No significant differences were found between TPT and non-TPT groups in demographics, psoriasis severity, and baseline test results, except for higher median T-SPOT.TB values in the TPT group (55 vs. 20 spots, $p = 0.001$).

Primary Outcome

Throughout the study, spanning 235 person-years of follow-up, no ATB cases were identified among the 129 patients.

Secondary Outcomes

Changes and Reversion in T-SPOT.TB Results

At year 2, T-SPOT.TB values showed no significant changes from baseline. In the entire cohort, median T-SPOT.TB values were 27 (10, 70) spots at baseline and 28 (10, 77) spots at year 2 ($p = 0.872$). In the non-TPT group, these values were 20 (9, 58) spots initially and 17 (6, 68) spots after 2 years ($p = 0.975$). For those in the TPT group, median values shifted from 55 (25, 119) spots to 58 (28, 100) spots ($p = 0.830$). Notably, 14 patients (12.8%) experienced T-SPOT.TB reversion (from positive to negative),

Table 1 Baseline characteristics and comparative analysis of patients with psoriasis and TBI

	Total cohort ***n*** **= 129**	**Non-TPT group** ***n*** **= 97**	**TPT group** ***n*** **= 32**	***p*** **value**
Sex, male	95 (73.6%)	72 (74.2%)	23 (71.9%)	0.793
Age, years	45 ± 13	44 ± 13	48 ± 12	0.125
Weight, kg	74 ± 13	74 ± 13	75 ± 12	0.601
Body mass index, kg/m^2	25.3 ± 3.3	25.2 ± 3.4	25.7 ± 2.9	0.447
Psoriasis duration, years	15 (10, 21)	15 (8, 21)	17 (10, 22)	0.772
PASI score (0–72)	15.1 (10.1, 22.5)	15.0 (10.2, 22.5)	17.5 (9.3, 22.2)	0.889
BSA, % (0–100)	15 (10, 25)	15 (10, 30)	19 (10, 21)	0.847
sPGA (0–4)	3 (3, 4)	3 (3, 4)	3 (3, 4)	0.372
Nail involved	52 (40.3%)	39 (40.2%)	13 (40.6%)	0.967
With psoriatic arthritis	7 (5.4%)	3 (3.1%)	4 (12.5%)	0.132
Prior treatments for psoriasis				
Acitretin or phototherapy	59 (45.7%)	43 (44.3%)	16 (50.0%)	0.577
MTX or cyclosporine	6 (4.7%)	3 (3.1%)	3 (9.4%)	0.162
Biologics	24 (18.6%)	20 (20.6%)	4 (12.5%)	0.306
Comorbid diabetes	21 (16.3%)	18 (18.6%)	3 (9.4%)	0.222
Current smoker	33 (25.6%)	27 (27.8%)	6 (18.8%)	0.307
Alcohol consumption	9 (7.0%)	6 (6.2%)	3 (9.4%)	0.689
Pulmonary tuberculosis contact history	4 (3.1%)	1 (1.0%)	3 (9.4%)	0.047
Family history of psoriasis	39 (30.2%)	28 (28.9%)	11 (34.4%)	0.556
ESR, mm/h	8 (4, 12)	8 (3, 13)	7 (4, 12)	0.728
CRP, mg/L	1.46 (0.55, 2.65)	1.37 (0.53, 2.56)	1.90 (0.68, 6.28)	0.300
T-SPOT.TB, spots	27 (10, 70)	20 (9, 58)	55 (25, 119)	0.001
Findings of chest X-ray				
Not clinically significant	100 (77.5%)	79 (81.4%)	21 (65.6%)	0.342
Calcified nodules, lymph nodes or linear opacities	22 (17.0%)	14 (14.4%)	8 (25.0%)	
Pleural thickening or calcification	7 (5.4%)	4 (4.1%)	3 (9.4%)	
Interleukin-17A inhibitors administered				
Secukinumab	113 (87.6%)	89 (91.8%)	24 (75.0%)	0.029
Ixekizumab	16 (12.4%)	8 (8.2%)	8 (25.0%)	

Data are mean ± standard deviation, median (25th and 75th percentiles), or counts (percentages)
BSA body surface area, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *MTX* methotrexate, *PASI* Psoriasis Area and Severity Index, *sPGA* static Physician's Global Assessment, *TBI* tuberculosis infection, *TPT* tuberculosis preventive treatment

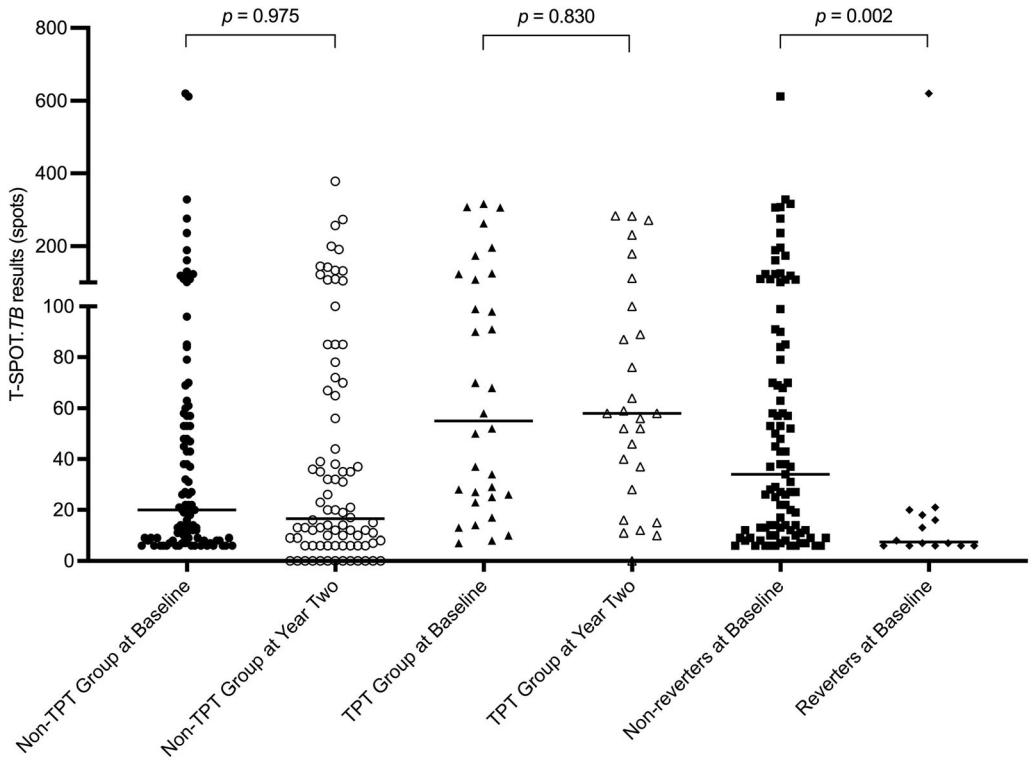

Fig. 2 T-SPOT.TB test results at baseline and year 2 in various subgroups of the study. *TPT* tuberculosis preventive treatment

predominantly in the non-TPT group (13 out of 14 cases). This suggests a higher tendency for reversion in the non-TPT group (15.9%) compared to the TPT group (3.7%, $p = 0.181$). Patients who experienced reversion had significantly lower baseline T-SPOT.TB values (8 [6, 19] spots) compared to those who did not revert (34 [12, 85] spots, $p = 0.002$). Further details are shown in Fig. 2.

Completion Rate and Adverse Reactions of TPT

The preventive regimens in TPT group varied: 20 patients (62.5%) received 9 months of isoniazid, 9 (28.1%) took 3 months of isoniazid plus rifapentine, and 3 (9.4%) underwent 6 months of isoniazid plus rifampicin. Within this group, 25 out of 32 patients (78.1%) completed the full course of TPT, while 2 patients (6.3%) terminated TPT early at their request, and 5 (15.6%) dropped out. Adverse reactions were minimal. Notably, only two patients (6.3%) reported mild elevation in alanine transaminase levels, and there were no hypersensitivity reactions, serious adverse events, or withdrawals due to adverse reactions.

Effectiveness and Safety of IL-17A Inhibitors

At year 2, the PASI 75, 90, and 100 response rates in the entire cohort were 76.9%, 46.3%, and 25.0%, respectively. There were no significant differences in response rates between the non-TPT and TPT groups at any time point, as shown in Fig. 3.

Adverse reactions to IL-17A inhibitors occurred in 17 cases (13.2%) of the entire cohort. These included injection site reactions (10 cases, 7.8%), exacerbated dermatitis, eczema, or urticaria (4 cases, 3.1%), vulvovaginal candidiasis (2 cases, 1.6%), and new-onset palmoplantar pustulosis (1 case, 0.8%). The laboratory test results at year 2 showed no significant changes in complete blood cell count,

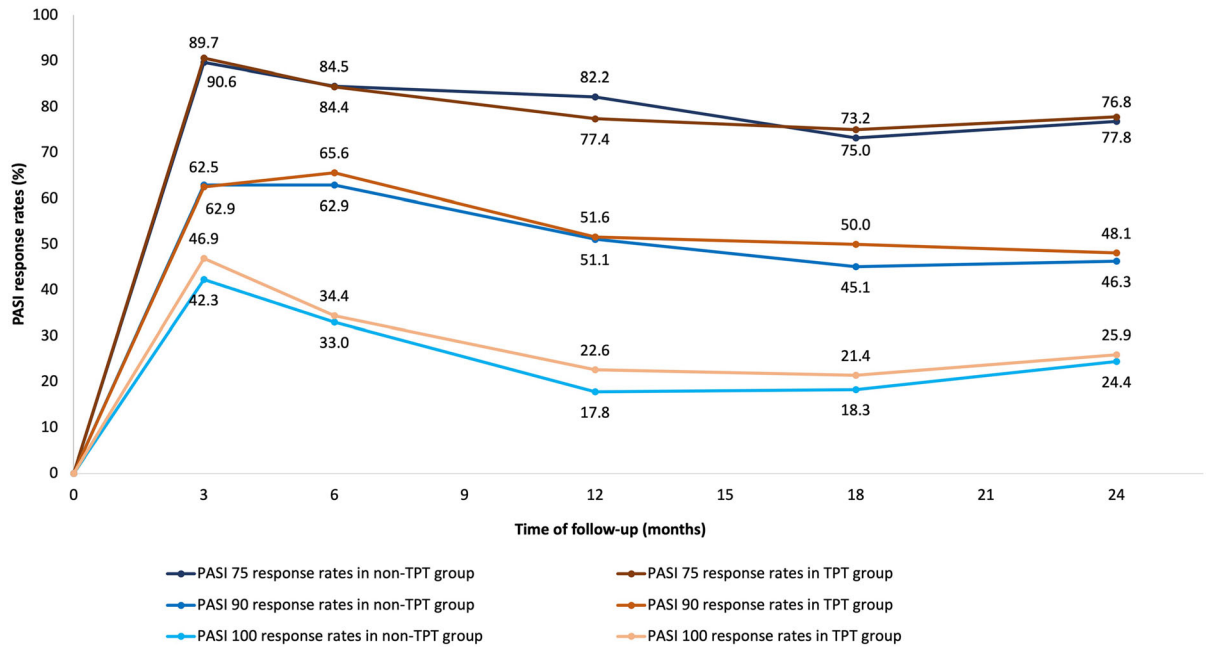

Fig. 3 The PASI response rates between the non-TPT and TPT groups at different time points. *PASI* Psoriasis Area and Severity Index, *TPT* tuberculosis preventive treatment

liver and kidney function, blood lipids, ESR, and CRP from baseline.

Risk Factors for TBI in Patients with Psoriasis

From April to December 2021, in addition to enrolling 129 patients with psoriasis and TBI, our center also included 212 individuals diagnosed with plaque psoriasis for biologic therapy, all of whom exhibited negative T-SPOT.TB results at baseline. The prevalence of TBI among these patients was 37.8%. Baseline characteristics comparing patients with psoriasis with and without TBI are detailed in Table 2. Logistic regression analysis identified age $\geq$ 45 years and BMI $< 24.0\ kg/m^2$ as independent risk factors for TBI in this population. Patients aged 45 or older had a 2.44-fold increased likelihood of TBI compared to younger patients (95% confidence interval [CI] 1.50–3.99, $p < 0.001$). Similarly, BMI $< 24.0\ kg/m^2$ was associated with a 2.12-fold increase in TBI risk compared to a higher BMI (95% CI 1.27–3.54, $p = 0.004$). Gender, PASI score, smoking, and diabetes were not significant risk factors. Additional details can be found in Fig. 4.

In the cohort of 212 patients without TBI, 177 (83.5%) completed a 2-year follow-up, during which 7 individuals (3.3%) converted to a positive T-SPOT.TB status.

DISCUSSION

This study represents the first prospective cohort study focused on assessing the safety of IL-17A inhibitors, without TPT, in patients with psoriasis and TBI. During the 2-year treatment period with IL-17A inhibitors, in which most patients did not undergo TPT, there were no instances of ATB reported in our cohort. A population-based multicenter prospective study conducted in rural China observed an ATB incidence rate of 0.87 (95% CI 0.68–1.07) per 100 person-years in QFT-positive individuals [21]. On the basis of this data, around two ATB cases might have been anticipated in our non-TPT group. Had IL-17A inhibitors been capable of reactivating tuberculosis, we would have expected to observe more ATB cases. The absence of ATB cases in our study suggests that IL-17A inhibitors do not heighten the risk of

Table 2 Comparison of baseline characteristics between patients with psoriasis with and without TBI

	With TBI *n* = 129	Without TBI *n* = 212	OR	95% CI	*p* value
Sex, male	95 (73.1%)	150 (70.8%)	1.16	0.71–1.89	0.565
Age, years	45 ± 13	40 ± 12	1.03	1.01–1.05	0.001
Weight, kg	74 ± 13	78 ± 15	0.98	0.97–1.00	0.054
Body mass index, kg/m^2	25.3 ± 3.3	26.4 ± 3.8	0.92	0.86–0.98	0.009
Psoriasis duration, years	15 (10, 21)	12 (8, 21)	1.017	0.995–1.040	0.130
PASI score (0–72)	15.1 (10.1, 22.5)	14.0 (9.9, 22.6)	0.999	0.979–1.019	0.933
BSA, % (0–100)	15 (10, 25)	15 (10, 30)			0.827
sPGA (0–4)	3 (3, 4)	3 (3, 4)			0.498
Nail involved	52 (40.3%)	100 (47.2%)			0.216
Prior treatments for psoriasis					
Acitretin or phototherapy	59 (45.7%)	90 (42.5%)			0.553
MTX or cyclosporine	6 (4.7%)	18 (8.5%)			0.179
Biologics	24 (18.6%)	47 (22.2%)			0.432
Comorbid diabetes	21 (16.3%)	36 (17.0%)	0.951	0.527–1.713	0.866
Current smoker	33 (25.6%)	61 (28.8%)	0.851	0.519–1.396	0.523
Alcohol consumption	9 (7.0%)	17 (8.0%)	0.860	0.372–1.991	0.725
Family history of psoriasis	39 (30.2%)	69 (32.5%)			0.656
ESR, mm/h	8 (4, 12)	6 (3, 14)			0.864
CRP, mg/L	1.46 (0.55, 2.65)	1.68 (0.75, 3.37)			0.137

Data are mean ± standard deviation, median (25th and 75th percentiles), or counts (percentages)
BSA body surface area, *CI* confidence interval, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *MTX* methotrexate, *OR* odds ratio, *PASI* Psoriasis Area and Severity Index, *sPGA* static Physician's Global Assessment, *TBI* tuberculosis infection

ATB, echoing the results from both preclinical and retrospective studies. Segueni et al. found minimal changes in the transcriptomic levels of *Il17* and *Il23a* in *M. tuberculosis*-infected mice, indicating a limited role for IL-17 pathways in controlling tuberculosis infection [11]. Shu et al. and Xiao et al. observed no ATB cases among patients with psoriasis and TBI treated with secukinumab without TPT over median follow-up of 52 weeks and 23 months, respectively [17, 18]. Our study, with a larger sample size and longer follow-up duration, strengthens these consistent findings.

We advocate for a personalized approach to TBI screening and TPT administration among patients with psoriasis before initiating IL-17A inhibitors: (1) TBI screening is recommended for individuals with tuberculosis risk factors such as HIV infection, active malignancy, those undergoing chemotherapy or transplantation, or with renal failure. Patients with TBI under these conditions should receive TPT. (2) For patients without these risk factors, a comprehensive imaging assessment, clinical symptom evaluation, and ruling out of ATB are suggested, potentially foregoing the need for IGRA

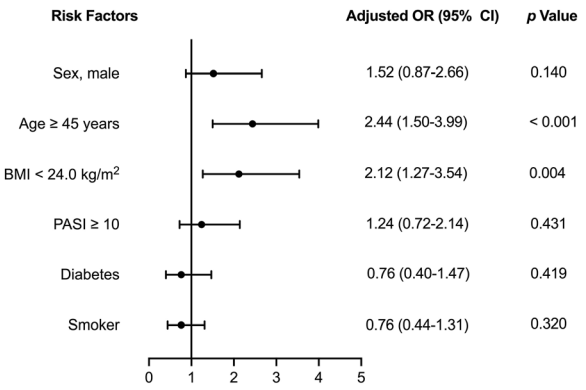

Fig. 4 Identified risk factors for TBI in patients with psoriasis. *BMI* body mass index, *CI* confidence interval, *OR* odds ratio, *PASI* Psoriasis Area and Severity Index, *TBI* tuberculosis infection

screening. This strategy aims to alleviate the economic impact on patients and limit their exposure to anti-tuberculosis medications.

In our study, no severe adverse reactions associated with TPT were reported, though the completion rate was only 78.1%. Considering that non-standardized prophylaxis might increase the risk of drug-resistant tuberculosis and diminish protective efficacy, it is crucial to prioritize patient education and enhance adherence to TPT regimens.

Our findings demonstrate that T-SPOT.TB levels remained stable throughout IL-17A inhibitor therapy in patients with psoriasis, regardless of whether they underwent TPT or not. Intriguingly, the non-TPT group exhibited a higher reversion rate of T-SPOT.TB (15.9% vs. 3.7% in the TPT group). This reversion predominantly occurred in patients with significantly lower initial T-SPOT.TB levels, suggesting a spontaneous tendency towards reversion, particularly when levels are marginally above the threshold. Meta-analyses and randomized trials have consistently reported QFT reversion rates of approximately 20% in individuals with TBI, regardless of TPT use [22, 23]. Additionally, QFT dynamics appear to be poorly correlated with the risk of ATB development [22]. A recent propensity score-matched study found no significant differences in QFT values before and after secukinumab treatment in patients with psoriasis and TBI for both the TPT and non-TPT groups [17]. Given these findings, continuous IGRA monitoring may not be essential for patients with psoriasis and TBI on IL-17A inhibitor therapy. Identifying ATB may be more effectively achieved by focusing on clinical symptoms, inflammatory markers, and radiologic assessments, rather than relying on regular IGRA tests.

A population-based, multicenter, prospective study in rural China reported QFT positivity rates ranging from 13% to 20% [24]. In contrast, our research revealed a higher T-SPOT.TB positivity rate of 37.8% among patients with psoriasis undergoing biologic therapy. This discrepancy could partially be explained by the differing demographics of the study populations. The population-based study showed increased QFT positivity with age and higher rates in males. Children and adolescents, representing 17% of their participants with a mere 3% QFT positivity rate, and male participants comprising 46% of their sample, contrast with our study's all-adult participants, averaging 45 years old, predominantly male (73.6%). Our results align with Sun et al.'s single-center retrospective study, which enrolled 93 patients with moderate to severe psoriasis treated with biologics, reporting an average age of 45 years, 76.3% male participants, and a baseline QFT positivity rate of 32.0% [8].

In our study, we observed a cumulative T-SPOT.TB conversion rate of 3.3% over 2 years in patients with psoriasis. This finding aligns with previous studies. For instance, a retrospective study from Taiwan reported a 1.3% QFT conversion rate among patients with psoriasis undergoing nearly a year of IL-17A inhibitor treatment [25]. Furthermore, a population-based prospective study in rural China recorded an approximate annual TBI rate of 1.5%, determined by consistent positive results after QFT conversion [26].

This study revealed that patients with psoriasis aged 45 years or older had a 2.44 times greater risk of TBI. Furthermore, BMI lower than 24.0 kg/m^2 was associated with a 2.12 times increased risk of TBI. Factors such as gender, diabetes, smoking, and PASI score were not correlated with an elevated TBI risk. Contrasting with findings from an Italian study, which

identified male gender (OR 1.30, 95% CI 1.04–1.62, $p = 0.02$) and age over 55 (OR 2.93, 95% CI 2.18–3.93, $p < 0.001$) as independent TBI risk factors in patients with psoriasis [27], our research is the first to highlight BMI under 24.0 kg/m^2 as a potential independent risk factor, suggesting higher susceptibility to TBI among patients of normal or lower weight.

In our cohort, post 2 years of IL-17A inhibitor therapy, the PASI 75, 90, and 100 response rates were 76.9%, 46.3%, and 25.0%, respectively, which are modest compared to previously reported studies [28, 29]. This discrepancy may be attributed to (1) a reduction in IL-17A inhibitor frequency by some participants over time; (2) the study's 15.5% dropout rate without imputation for missing data; and (3) many patients had prior systemic and biologic treatments, which could influence response rates. The adverse reactions to IL-17A inhibitors aligned with existing literature, mainly consisting of injection site reactions, exacerbated dermatitis or eczema, and vulvovaginal candidiasis [30–33].

Our study has several limitations that merit attention. Primarily, its observational, open-label design, although informative, lacks the robustness of randomized, double-blind trials. Additionally, we did not explore the potential role of contact with pulmonary tuberculosis as a risk factor for TBI, as a result of the minimal number of such cases. Importantly, this research was specifically aimed at individuals with moderate-to-severe plaque psoriasis eligible for biologic therapy, excluding those with coexisting conditions like malignancies, HIV infection, or inflammatory bowel diseases. This delineation may restrict the extrapolation of our findings to a wider patient demographic. Moreover, the absence of ATB cases within our cohort should be interpreted with caution—it tentatively suggests that IL-17A inhibitors do not markedly raise the risk of tuberculosis reactivation. This tentative conclusion, juxtaposed with a relatively small sample size and limited follow-up period, and considering the low incidence of ATB in TBI individuals (a cumulative 5-year incidence rate of 2.4% [34]), underscores our findings as preliminary. It emphasizes the need for further, more comprehensive studies involving larger, randomized trials to validate our observations and clarify the implications of IL-17A inhibitor therapy in this patient population.

CONCLUSION

Our investigation delineates that the administration of IL-17A inhibitors to patients with psoriasis and TBI, in the absence of TPT, did not lead to any cases of ATB over a span of 2 years. This finding indicates a minimal risk of tuberculosis reactivation with IL-17A inhibitor therapy. The observed stability or reversion in T-SPOT.TB levels further suggests that regular monitoring of T-SPOT.TB may not be essential. Additionally, the surveillance for ATB should emphasize the evaluation of clinical symptoms, inflammatory markers, and radiographic findings rather than the dynamic changes in T-SPOT.TB. It is crucial to highlight that middle-aged and elderly patients with psoriasis, particularly those with normal or reduced BMI, represent a demographic at elevated risk for TBI and warrant particular attention.

These findings necessitate a reconsideration of the initial assessment protocols for patients with psoriasis being considered for IL-17A inhibitor treatment. It appears that merely ruling out ATB, especially in the absence of risk factors for tuberculosis, may be adequate, thereby diminishing the necessity for routine TBI screening or TPT. Such a shift in perspective could potentially alter clinical practice, ensuring that treatment strategies are more closely tailored to the unique risk profiles of individual patients.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Chun-Xia He, Chao Wu, Li Zhang and Hong-Zhong Jin declare that they have no competing interests.

Ethics Approval. Approval was obtained from the Peking Union Medical College Hospital Ethics Committee (ZS-2850, I-22PJ559). The study was conducted in accordance with the Helsinki Declaration. All patients provided informed consent for participation in the study.

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