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ORIGINAL RESEARCH

A Propensity Score-Matched Study on the Changes of TB Status and TB-IGRA Values in Patients with Psoriasis with Latent TB Receiving Secukinumab

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ABSTRACT

Introduction: The utilization of biologics in patients with psoriasis with latent tuberculosis infection (LTBI) has garnered significant attention. Although the tuberculosis (TB) safety profile of second-generation biologics, including secukinumab, has been partially confirmed in both clinical trials and real-world studies, the necessity for prophylactic therapy in patients with LTBI prior to administering this class of biologics remains a topic of controversy.

Methods: This study enrolled 62 patients with psoriasis with LTBI who underwent secukinumab with routine TB reexamination. Patients were divided into two groups based on whether they received antituberculosis therapy (ATB; $n = 48$) or not (NTB; $n = 16$). We performed a propensity score-matched (PSM) analysis between ATB and NTB subgroups and retrospectively reviewed their interferon-gamma release assays (IGRA) and radiographic results.

Results: No active TB case was reported on the basis of medical records and chest radiographs in either two group. Before PSM, the mean reexamining IGRA value was significantly elevated in patients who received prophylactic therapy ($P = 0.00$), but no significant increase was observed in patients who were not. After PSM, there was no significant IGRA value enhancement whether or not patients received prophylactic treatment.

Conclusion: Our data provide additional information on the safety profile of secukinumab in patients with psoriasis with LTBI. Furthermore, our presentation of the reexamined IGRA results revealed no significant elevation in the ATB or NTB group. As such, we believe further exploration is necessary to determine whether anti-TB medication is required prior to administering secukinumab.

Yue Xiao, Wenyao Mi, and Jinqiu Wang share first authorship.

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PLAIN LANGUAGE SUMMARY

In the past decade, biologics have revolutionized psoriasis treatment. Among patients receiving biologics, tuberculosis infection is a big concern. Secukinumab, an interleukin-17 inhibitor, belongs to the second-generation biologics. Clinical trials and real-life experience have partially reported its tuberculosis safety. In 2020, a systematic review of randomized clinical trials of secukinumab found no reactivate tuberculosis case. However, when participants tested positive for latent tuberculosis infection at screening in the clinical trials, they received antituberculosis treatment. Should patients with latent tuberculosis infection receive antituberculosis medication before receiving secukinumab? The answer is controversial and lacks evidence. This study enrolled patients with psoriasis with latent tuberculosis infection who underwent secukinumab with routine tuberculosis reexamination. Then, the patients were divided into two groups based on whether they received antituberculosis therapy and not. We observed that neither of these two groups presented tuberculosis activation cases. We also matched patients who received antituberculosis therapy and those who did not. The interferon-gamma release assay showed no significant increase after balancing the baseline. Our data indicated that secukinumab is safe among patients with latent tuberculosis infection even when they did not receive antituberculosis treatment.

Keywords: Latent tuberculosis infection; Psoriasis; Safety; Secukinumab; Tuberculosis

Key Summary Points

Why carry out this study?

The necessity of antituberculosis (TB) medication before the administration of secukinumab is a growing concern. According to psoriasis biologics treatment guidelines and results of clinical trials, pretreatment anti-TB is required and recommended.

However, in real life, patients' conditions are more complex, and it might not be appropriate for them to receive anti-TB medication mainly because of safety concerns. Moreover, the real-world experience in this topic is quite limited.

In this study, we aim to profile the TB safety of secukinumab among patients with psoriasis and latent tuberculosis infection (LTBI).

Furthermore, to provide evidence on the necessity of TB prophylaxis treatment before receiving secukinumab, we elucidate tuberculosis infection status changes and interferon-gamma release assay (IGRA) level among patients who received anti-TB medication and those who did not.

What was learned from the study?

Our data has provided additional information on the safety profile of secukinumab in patients with psoriasis and latent tuberculosis infection and de-emphasized applying pretreatment anti-TB medication prior to administering secukinumab.

Our presentation of the reexamined IGRA results revealed no significant elevation in the patients who received or did not receive anti-TB medication.

INTRODUCTION

In the past decades, the biologics that target core cytokines like tumor necrosis factor (TNF)-α and interleukin (IL)-17 have revolutionized the treatment of psoriasis [1]. They have improved the overall therapeutic efficacy of psoriasis treatment and allowed patients with psoriasis to pursue a lesion-free life with the goal of clinical remission achieved [2]. Nonetheless, aside from the impressive treatment effects, physicians still have concerns about the safety of biologics, in particular, the potential activation of latent infectious issues, including tuberculosis (TB), hepatitis B virus (HBV), human immunodeficiency virus (HIV), etc. [3, 4]. Moreover, TB remains one of the most notorious infectious diseases because of its worldwide prevalence and insidious systemic damage [5].

Therefore, TB screening workup is critical for the safe use of biologics, especially in regions with moderate to high TB burden. Many effective measures could be taken to know the TB infection status of patients, including taking the history of typical clinical symptoms, performing chest X-ray or chest CT, and conducting TB laboratory tests (interferon-gamma release assays, IGRAs, or tuberculin skin test, TST). On the basis of the above, patients who met the diagnostic criteria of active TB were not suited for biologics because the active TB infection status has been emphasized as an absolute contraindication for biologics by guidelines for psoriasis in different countries and regions [6–8].

In comparison, patients with asymptomatic latent TB infection (LTBI) who presented as TB laboratory test positive are not contradicted in biological treatment, and the risk of TB activation varies among biologics. The World Health Organization (WHO) recommended that patients with LTBI receiving TNFα inhibitors (TNFi), the first-generation biologics, take TB preventive treatment on the basis of accumulating evidence indicating an elevated risk for TB activation secondary to TNFα monoclonal antibodies [9, 10]. Consistently, current guidelines around the world still recommend that patients with LTBI should be treated with anti-TB medication before using either first- or second-generation biologics [6–8]. While for the second-generation biologics, which target the T helper (Th)17/IL-23 pathway, recent clinical trials and real-world data of IL-17 inhibitors (IL-17i) have not witnessed the TB activation effect [10–12]. Therefore, the evidence is lacking on the necessity of prophylactic anti-TB in patients with LTBI receiving IL-17i, and many real-world issues remain to be studied.

In this retrospective, observational study, we focused on TB safety among patients with psoriasis and LTBI who received secukinumab (SEC), the first nationally approved, insurance-covered IL-17i in China, since 2019 and 2021. In order to provide evidence on the necessity of TB prophylaxis treatment before receiving secukinumab, we also profiled the tendency in TB status and TB-IGRA value changes in patients who received TB prophylaxis treatment and those who were not in regions with such a high TB burden.

METHODS

Study Design and Participants

We retrospectively detected the patients with psoriasis who underwent TB-IGRA test(s) between January 2018 and August 2022 from the West China Hospital, a tertiary medical center. Patients were included if they: 1. were over 18 years old with no sex restriction; 2. were diagnosed with plaque psoriasis or psoriasis vulgaris (ICD-10 code 40.0), with or without psoriatic arthritis (according to the Classification Criteria for Psoriatic Arthritis, CASPAR) [13]; 3. received SEC with the recommended regime (300 mg, subcutaneous injection, at 0, 1, 2, 3, 4 weeks, then every 4 weeks) for over 24 weeks; 4. tested TB-IGRA positive before the treatment of SEC and diagnosed with LTBI; 5. TB-IGRA was reexamined and chest imaging from 24 to 72 weeks after SEC initiation. Patients were excluded if they: 1. had a chest radiograph (X-ray or CT) with signs of active TB; 2. had clinical symptoms at the active clinical stage of TB (such as fever, reduced appetite,

weight loss, night sweats, anemia, cough for 14 days, etc.) [14]; 3. initiated SEC over 12 weeks after pretreatment TB-IGRA examination.

Ethics and Data Collection

This study was conducted in line with the declaration of Helsinki (2013 revision). This retrospective research was approved by the biomedical research ethics committee of West China Hospital of Sichuan University (Approval no. 2022-1880). Informed consent was waived because of the retrospective study design and fully anonymous data. The baseline demographic, clinical, and follow-up information, including age, gender, height, weight, smoking status, psoriasis conditions, laboratory results, etc., were retrospectively collected through the hospital information system. We also successfully matched these enrolled patients with the cohort named PSOWCH (Psoriasis cohort of West China Hospital) and acquired detailed information such as baseline Psoriasis Area and Severity Index (PASI) and body surface area (BSA).

Subgroups

As a result of the absence of a gold standard diagnosis for LTBI, we observed that patients with suspicious imaging findings were referred to infectious disease specialists for further diagnosis and consultation in the real-world medical process. The patients were divided into two subgroups: the anti-TB group (ATB) and the no anti-TB group (NTB). The ATB group contains patients who received monotherapy of isoniazid (300 mg, once daily); or isoniazid (300 mg, once daily) plus rifampin (450 mg, once daily); or those patients with old pulmonary tuberculosis or suspicious chest CT findings who received isoniazid (300 mg, once daily) plus rifampin (450 mg, once daily) plus ethambutol under the guidance of an infectious disease doctor (Supplementary Table 1). Patients in the NTB group did not receive anti-TB medication because of the activated HBV co-infection, abnormal liver function, or decline in patient status.

TB-IGRA

TB-IGRA was examined several times: at screening (a time window from 3 months before the SEC recommended by the manufacturer (Wantai, Beijing, China). The interferon-γ (IFNγ) levels in the test tube (T), nil tube (N), and positive control tube (P) were separately detected, recorded as TB-IGRA (T), TB-IGRA (N), TB-IGRA (P), TB-IGRA (P-N), TB-IGRA (T-N). TB-IGRA results were positive, negative, or intermediate (Table 1). TB-IGRA reversion was defined as a result changing from positive to

Table 1 Interpretation of TB-IGRA results

IGRA levels (pg/ml)			Results
TB-IGRA (N)	TB-IGRA (P-N)	TB-IGRA (T-N)	
≤ 400	Any value	≥ 14 and ≥ TB-IGRA (N)/4	Positive
	≥ 20	< 14	Negative
	≥ 20	≥ 14 but < TB-IGRA (N)/4	Negative
	< 20	< 14	Intermediate
	< 20	≥ 14 but < TB-IGRA (N)/4	Intermediate
> 400	Any value	Any value	Intermediate

Cutoff value of TB-IGRA is 14 pg/ml as recommended by the manufacturer
N nil tube, *P* positive control tube, *T* test tube, *TB-IGRA* tuberculosis interferon-gamma release assays

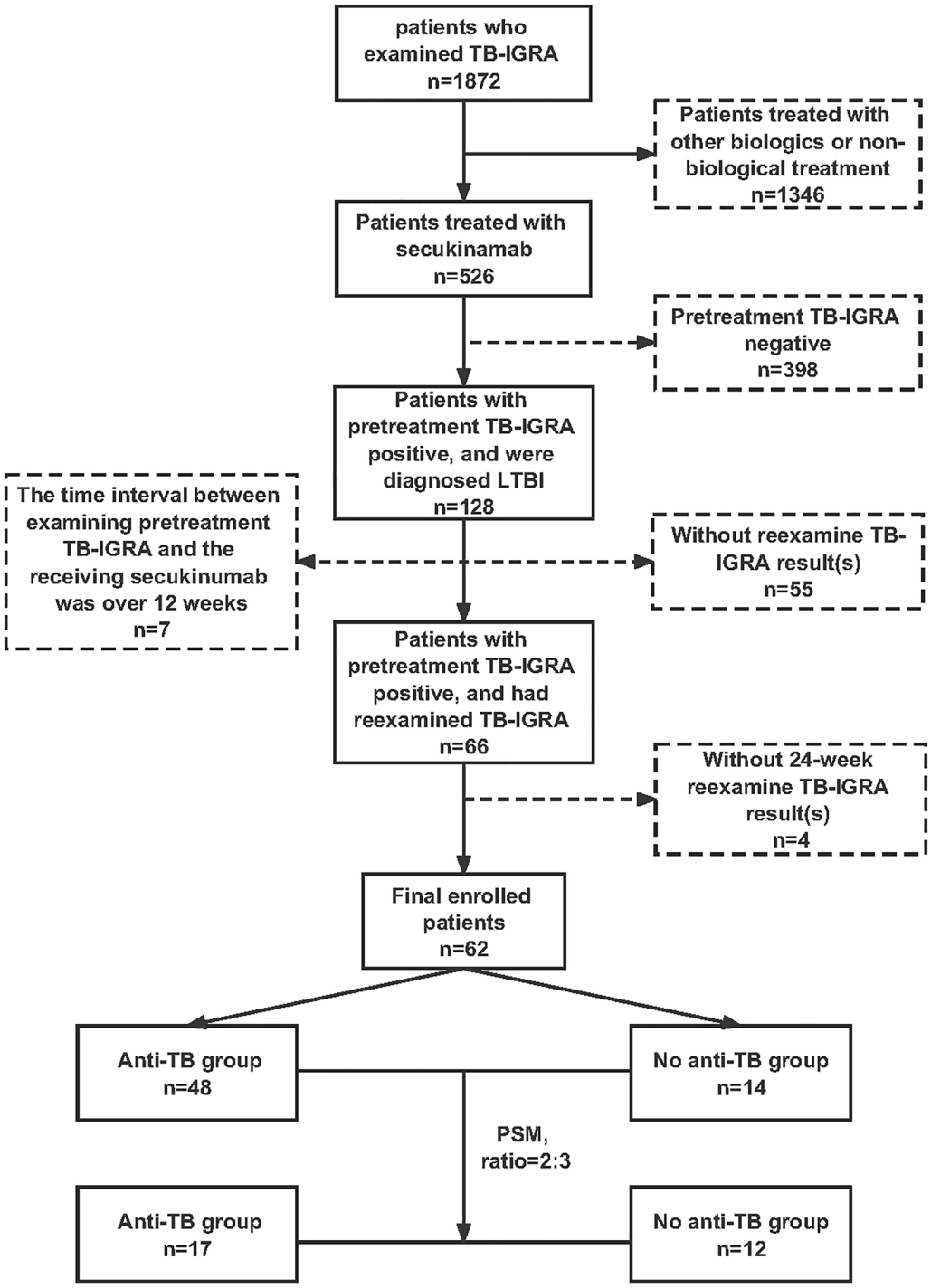

Fig. 1 Flowchart of patients' enrollment

Table 2 Baseline and clinical characteristics of patients with psoriasis and LTBI who received secukinumab (n = 62)

Variables	Total (n = 62)	Before PSM			After PSM		
		ATB (n = 48)	NTB (n = 14)	P value	ATB (n = 17)	NTB (n = 12)	P value
Age, years, mean (SD)	45.60 (12.82)	46.77 (13.91)	41.40 (7.50)	0.06	40.35 (11.61)	40.67 (6.44)	0.93
Gender, male, counts (%)	48 (77.42)	35 (72.92)	13 (92.86)	0.16	14 (82.35)	11 (91.67)	0.62
BMI[a], kg/m^2, mean (SD)	23.92 (3.16)	23.79 (3.20)	24.36 (3.08)	0.56	24.12 (4.03)	24.42 (3.32)	0.83
Smoking status							
Never smoke, counts (%)	31 (50.00)	25 (52.08)	8 (57.14)	0.76	8 (47.06)	6 (50.00)	> 0.99
Smokers[b], counts (%)	31 (50.00)	23 (47.92)	6 (42.86)		9 (52.94)	6 (50.00)	
Comorbidities							
PsA, counts (%)	14 (22.58)	10 (20.83)	4 (28.57)	0.72	5 (29.41)	2 (16.67)	0.66
Type 2 diabetes, counts (%)	3 (4.84)	3 (6.25)	0 (0.00)	> 0.99	0 (0.00)	0 (0.00)	> 0.99
HBV, counts (%)	5 (8.06)	4 (8.33)	1 (7.14)	> 0.99	2 (11.76)	1 (8.33)	> 0.99
HCV, counts (%)	0 (0.00)	0 (0.00)	0 (0.00)	> 0.99	0 (0.00)	0 (0.00)	> 0.99
HIV, counts (%)	0 (0.00)	0 (0.00)	0 (0.00)	> 0.99	0 (0.00)	0 (0.00)	> 0.99
Psoriasis status							
Duration of psoriasis, years, mean (SD)	17.85 (9.53)	18.40 (9.46)	16.00 (9.88)	0.36	14.82 (6.30)	15.75 (10.55)	0.82
PASI, mean (SD)	10.34 (6.69)	10.66 (6.65)	9.24 (6.97)	0.32	10.28 (6.07)	10.12 (7.18)	0.78
BSA, mean (SD)	16.55 (15.67)	16.19 (14.59)	17.79 (19.50)	0.40	18.24 (16.75)	20.33 (19.99)	0.72
Previous immunosuppressant[c]							
MTX, counts (%)	24 (38.71)	19 (39.58)	5 (35.71)	> 0.99	6 (35.29)	4 (33.33)	> 0.99
CsA, counts (%)	3 (3.23)	2 (4.17)	0 (0.00)	> 0.99	0 (0.00)	0 (0.00)	> 0.99
Biologics[d], counts (%)	3 (4.84)	3 (6.25)	0 (0.00)	> 0.99	2 (5.88)	0 (0.00)	> 0.99
TB prophylactic treatment							
INH, counts (%)	–	18 (37.50)	–	–	6 (35.29)	–	–
HR, counts (%)	–	25 (52.08)	–	–	9 (52.94)	–	–
HRE, counts (%)	–	5 (10.42)	–	–	2 (11.77)	–	–
TB-IGRA							
Baseline TB-IGRA, pg/ml, mean (SD)	138.80 (145.80)	157.90 (152.50)	73.35 (98.19)	0.00*	86.43 (84.63)	81.41 (104.40)	0.50

Table 2 continued

Variables	Total (n = 62)	Before PSM			After PSM		
		ATB (n = 48)	NTB (n = 14)	P value	ATB (n = 17)	NTB (n = 12)	P value
Time interval between TB-IGRA1 and TB-IGRA2, months, mean (SD)	12.00 (3.94)	12.23 (4.12)	11.21 (3.26)	0.39	10.94 (3.27)	11.00 (3.49)	0.99

Categorical variables expressed as counts (%), and continuous variables as mean (SD)

ATB anti-TB group, *BMI* body mass index, *BSA* body surface area, *CsA* cyclosporin, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *HIV* human immunodeficiency virus, *HR* isoniazid + rifampicin, *HRE* isoniazid + rifampicin + ethambutol hydrochloride, *INH* isoniazid, *LTBI* latent tuberculosis infection, *MTX* methotrexate, *NTB* no anti-TB group, *PASI* Psoriasis Area Severity Index, *PsA* psoriatic arthritis, *PSM* propensity score-matched study, *SD* standard deviation

[a]BMI classification is according to the WHO suggestions for the Chinese population

[b]Smokers included current smokers and ex-smokers

[c]Total percentage of previous treatment is over 100% as some of the patients received more than one treatment

[d]Biologics group included adalimumab (1 patients), etanercept (1 patient), infliximab (1 patient)

*$P < 0.05$ and considered significant

negative. We also documented each patient's TB-IGRA (T-N) results, which represent the result of the specific value of IFNγ.

Propensity Score Matching (PSM)

PSM was used to adjust the relevant confounders. The data were imported in R (version 1.1.456), and PSM was done through the MatchIt package. The variables, including age, gender, pretreatment TB-IGRA results, and the time interval between pretreatment and follow-up TB-IGRA, were included in the logistic PSM model. The matching method was the "nearest", and the match ratio was 2:3, i.e., 2 in the NTB group vs. 3 in the ATB group . The match ratio was not set as 1:1 because that would cause a loss of patients. The caliper value was set as 0.2 (range 0–1). We adopted the ggplot2 package to show each variety's distributional balance and the covariate balance of the model. In the Love plot, which displayed the matching effect of those covariates, the m. threshold was adjusted as 0.1 (the standardized mean difference of the covariate < 0.1 was considered significant).

Statistical Analysis

The statistical analysis was performed using GraphPad Prism version 9.0.0, and proper statistical methods were obtained for different data types. The categorical variables were expressed as count (%) and were compared using Fisher's exact test. The continuous variables were shown as mean (standard deviation). The unpaired *t* test was applied for unmatched continuous data. The Mann–Whitney test was chosen when the data did not assume a Gaussian distribution. The Wilcoxon test was used for paired samples without normal distribution. All the *P* values were two-tailed, and $P < 0.05$ was considered statistically significant.

RESULTS

In this study, we screened 1872 patients with psoriasis who were ever examined by TB-IGRA, and 526 out of them received secukinumab. On the basis of their TB-IGRA records, we excluded 398 patients (75.67%, 398/526) with pretreatment TB-IGRA negative results; then excluded patients without proper TB-IGRA reexamination results. Eventually, we enrolled 62 patients

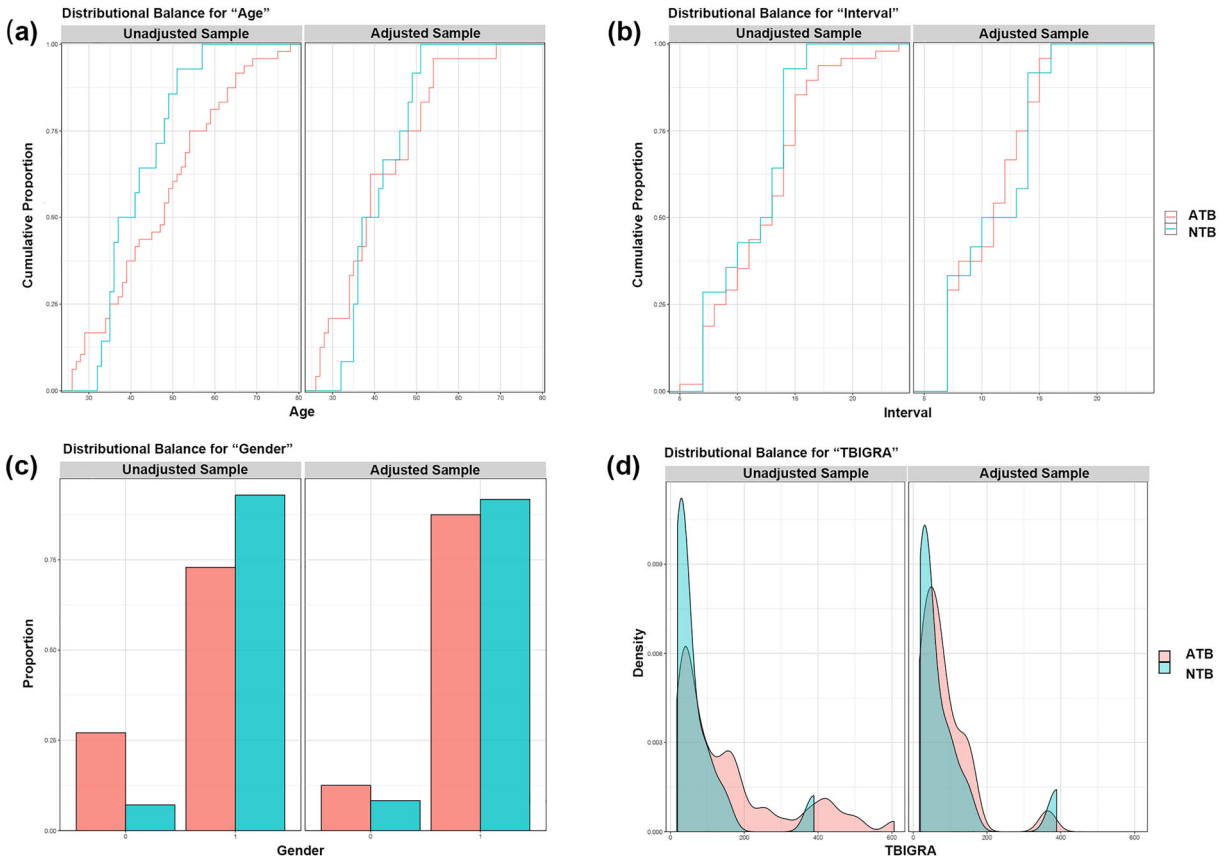

Fig. 2 **a–d** Matching effect of **a** age, **b** time interval between pretreatment TB-IGRA examination and reexamined one, **c** gender, and **d** pretreatment TB-IGRA value in the anti-TB group (ATB) and no anti-TB group (NTB)

who received SEC from June 2019 to May 2022, met the inclusion and exclusion criteria, and these patients were grouped by receiving anti-TB treatment (ATB, $n = 48$) or not (NTB, $n = 14$) (Fig. 1). Among patients in the ATB subgroup, 37.50%, 52.08%, and 10.42% of them, respectively, received monotherapy of isoniazid, isoniazid plus rifampin, and isoniazid plus rifampin plus ethambutol, i.e., the three different prophylactic regimes (Table 2).

Baseline disparities were noted between the unmatched ATB group ($n = 48$) and the NTB group ($n = 14$). The mean age of the ATB group was 46.77 (standard deviation, SD, 13.91); the mean age was younger in the other group, 41.40 (7.50) years old ($P = 0.06$). Our results also showed a remarkably significant difference in the pretreatment TB-IGRA results between these two groups ($P = 0.00$). Other demographic data (gender, $P = 0.16$; body mass index, BMI, $P = 0.56$) and clinical characteristics (duration of psoriasis, $P = 0.36$; PASI, $P = 0.32$; BSA, $P = 0.40$; the time interval between TB tests, $P = 0.39$) were comparable, along with even distribution in smoking status ($P = 0.76$) and comorbidities (PsA, $P = 0.72$; type 2 diabetes, $P = 0.99$; HBV, $P = 0.99$; HCV, $P = 0.99$; HIV, $P = 0.99$). The baseline and clinical characteristics are detailed in Table 2.

To reduce the impact of confounding variables, we adopted PSM with a matching ratio of 3:2 and a caliper value of 0.2. Between matched ATB group ($n = 17$) and the NTB group ($n = 12$), covariates including age, gender, pretreatment TB-IGRA, and the time interval between TB tests were well-balanced as shown in Fig. 2a–d. In addition, a Love plot graphically displayed the covariate balance before and after being adjusted with an m.threshold of 0.1 (Fig. 3).

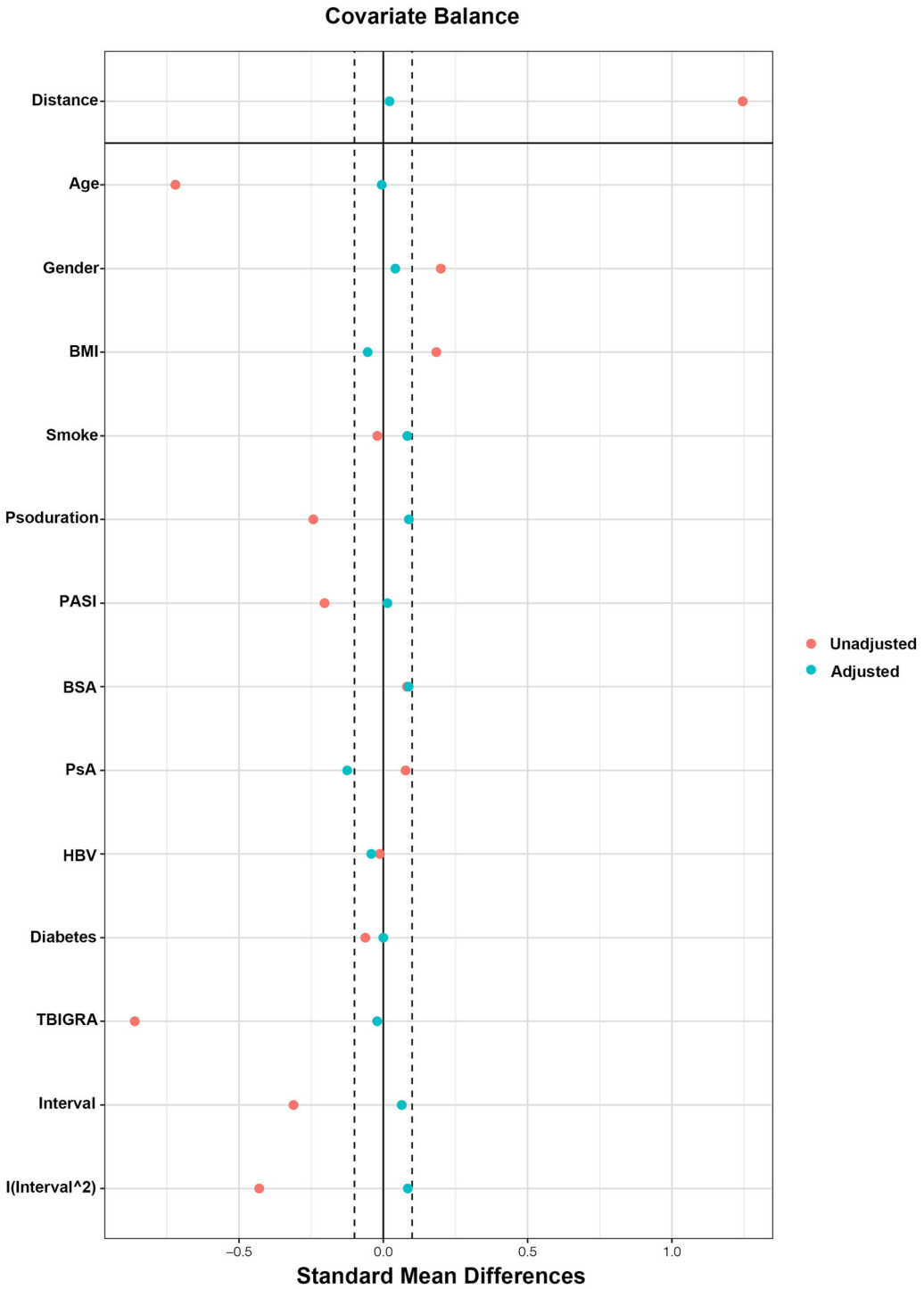

Fig. 3 Love plot showed the effect of propensity scoring matching (PSM). Red dots represent the standard mean differences of each variable before PSM, and the green dots indicate those after PSM

Table 3 LTBI status of patients with psoriasis treated with secukinumab

Variables	Total (n = 62)	Before PSM			After PSM		
		ATB (n = 48)	NTB (n = 14)	P value	ATB (n = 17)	NTB (n = 12)	P value
Treatment episode of SEC							
Follow-up, months, mean (SD)	23.37 (8.53)	24.68 (8.83)	18.91 (5.63)	0.025*	23.57 (9.87)	18.76 (6.10)	0.15
Time interval between TB-IGRA1 and TB-IGRA2, months, mean (SD)	12.00 (3.94)	12.23 (4.12)	11.21 (3.26)	0.39	10.94 (3.27)	11.00 (3.49)	0.99
Active TB, counts (%)	0 (0.00)	0 (0.00)	0 (0.00)	–	0 (0.00)	0 (0.00)	–
LTBI status							
Persistent positive, counts (%)	61 (98.38)	47 (97.92)	14 (100.00)	> 0.99	16 (94.12)	12 (100.00)	> 0.99
Reversion, counts (%)	1 (1.62)	1 (2.08)	0 (0.00)		1 (5.88)	0 (0.00)	

Categorical variables expressed as n (%). Reversion is defined as when the result of TB-IGRA changed from positive to negative

HR isoniazid + rifampicin, *HRE* isoniazid + rifampicin + ethambutol hydrochloride, *INH* isoniazid, *LTBI* latent tuberculosis infection, *SEC* secukinumab, *TB* tuberculosis

*$P < 0.05$ and considered significant

There was no active TB case reported with a mean therapeutic duration of 23.37 (SD 8.53) months in either ATB or NTB group. Regarding the LTBI status, 61 out of 62 patients were persistent TB-IGRA positive, and only one patient presented TB-IGRA reversion in the TB-IGRA reexamination. Furthermore, there was no significant difference in the distribution of LTBI status between the ATB and NTB groups either before or after PSM ($P > 0.99$) (Table 3). Then, we examined the tendency of TB-IGRA values between pretreatment result (TB-IGRA1) and almost 1-year reexamination (TB-IGRA2). Before PSM, the value of TB-IGRA2 was significantly elevated in the ATB group ($P = 0.00$), but no significant increase of TB-IGRA2 was observed in the NTB group (Fig. 4a, b). Intriguingly, after controlling the covariates imbalance through PSM, there was no significant difference between TB-IGRA1 and TB-IGRA2 either in the ATB or NTB group (Fig. 4c, d). Moreover, we also calculated the difference in mean and standard deviation between ATB and NTB groups and found no significance difference (Fig. 5).

DISCUSSION

In this retrospective study, our results supplemented the safety evidence of SEC in patients with LTBI as there was no TB activation case whether or not patients received anti-TB treatment. Furthermore, we interpreted the changes in TB-IGRA values and observed no significant enhancement with a mean time interval of 1 year after controlling confounders.

Notably, the WHO has estimated that a quarter of the world's population is infected with *Mycobacterium tuberculosis*, and people with LTBI represent a large pool of the population with the potential to develop active TB during their lifetime [15, 16]. In the present study, 24.33% (128/526) of patients with psoriasis who received secukinumab were detected as pretreatment TB-IGRA positive. This rate was in line with previous LTBI reports in the general population in China and even slightly higher.

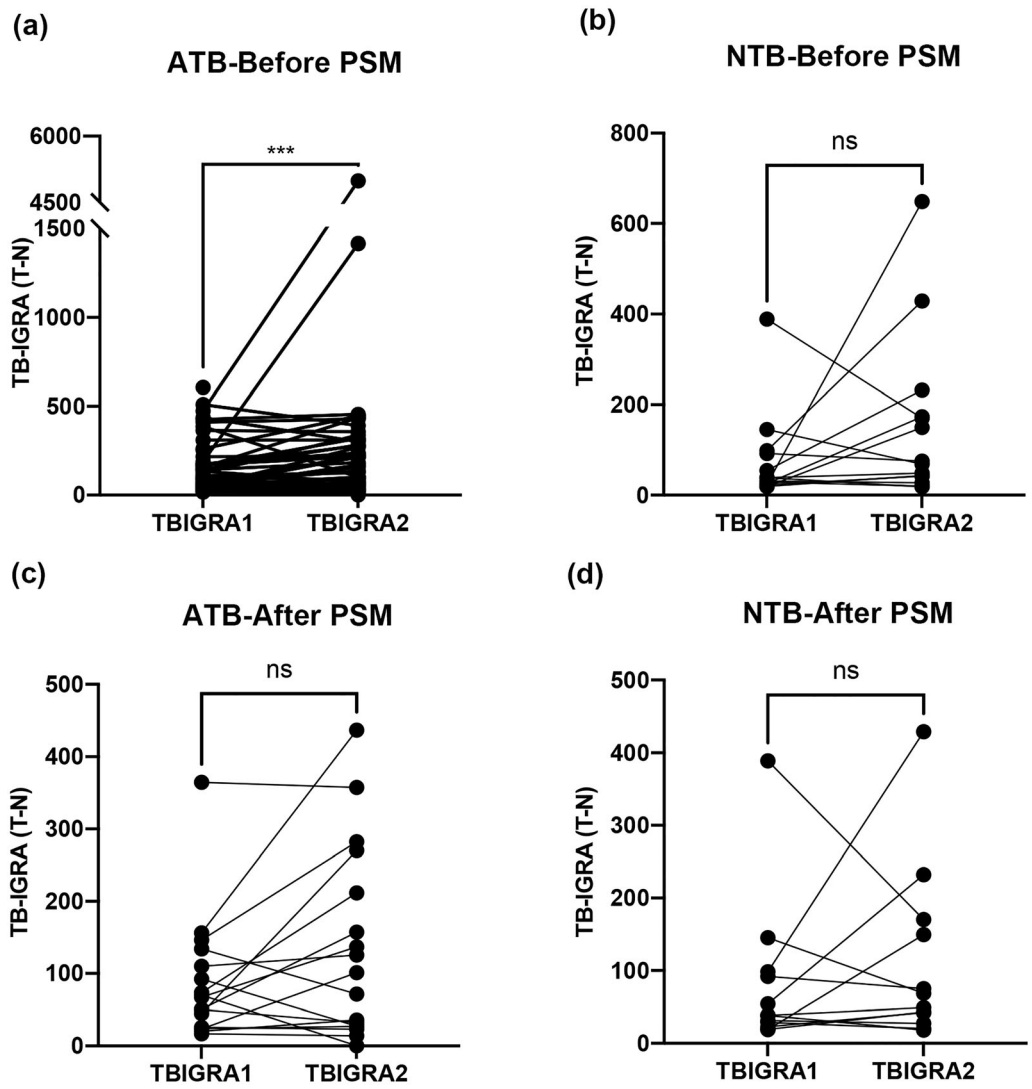

Fig. 4 **a** Mean TB-IGRA value among patients in the anti-TB group (ATB) significantly increased during follow-up before propensity scoring matching (PSM). **b** Changes in TB-IGRA values showed no significant enhancement among patients in the no anti-TB group (NTB) during follow-up before PSM. **c**, **d** After PSM, the changes of TB-IGRA values either in ATB and NTB showed no significant difference between the pretreatment results and the reexamined one

In a population-based, multicenter, prospective cohort study in the rural regions of China, the IGRA positive rate is 18.8% (3955/21022), and 3% of participants were assigned as indeterminate [17]. However, we need to know that the 24.33% does not represent the prevalence of LTBI in psoriasis because patients with LTBI were more likely to be prescribed second-generation biologics involving SEC in real-life experience. Thus, this selection bias is due to the substantial difference in TB risk between first- and second-generation biologics.

Indeed, it has been confirmed that receiving TNFi, particularly anti-TNFα monoclonal antibodies, was one of the high-risk groups for developing active TB [18]. In 2022, our team also showed that two patients with psoriasis (2.17%, 2/92) with baseline IGRA negative results suffered active TB during follow-up in the high-burden region [19]. Previous research

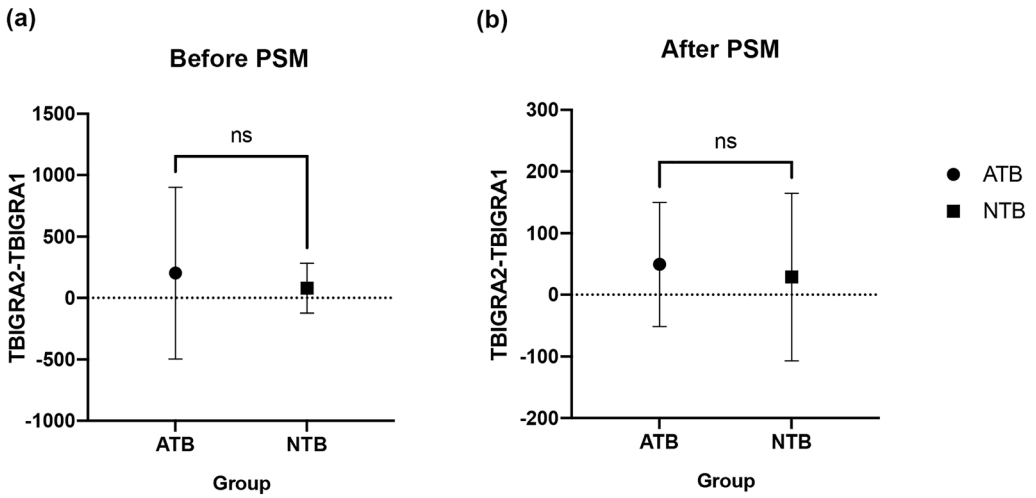

Fig. 5 There was no significant difference in the changes of TB-IGRA values between the anti-TB group (ATB) and the no anti-TB group (NTB) either **a** before or **b** after propensity scoring matching (PSM)

has indicated that prophylactic therapy can reduce the risk of developing active TB in such a high-risk group, and isoniazid monotherapy is 60–90% effective for 6–12 months [15]. In comparison, the TB risk in patients who received SEC differs from that of TNFi. No active TB case was reported in a systematic review containing several large-scale SEC clinical trials [11].

Despite the difference in TB risk, current national and regional guidelines for biologics in psoriasis still recommend anti-TB treatment for patients with LTBI before receiving biologics [6–8]. In 2020, Fowler and colleagues summarized the clinical trials of SEC, and they found 107 out of 2044 patients had a history of treated pulmonary TB and tested IGRA positive at screening. These patients received prophylactic therapy before enrollment and showed no evidence of TB reactivation during the 1-year follow-up [11]. However, the circumstances are more complex in the real world as patients might have multiple comorbidities, abnormal laboratory indexes, or safety concerns, and the side effects of anti-TB medication, such as liver damage, should be considered.

In this study, there was no TB activation case among 62 patients with psoriasis and LTBI during a mean therapeutic duration of 23.37 (SD 8.53) months, whether they received anti-TB treatment or not on the basis of medical records involving chest imaging results. In parallel, Shu et al. conducted an observational cohort study in a single center in China and observed no signs of active TB among 17 patients with LTBI but who did not receive chemoprophylaxis [20]. Also, a multicenter retrospective study in Italy, a region with a low TB risk, reported no active TB (n = 59), including ten patients (17%, 10/59) not receiving anti-TB medication [21]. The high tolerance of using SEC in patients with psoriasis and LTBI has been well profiled. Thus, consistent with the previous view, we also supposed that the necessity for prophylactic therapy prior to the administration of SEC might have been overestimated [20].

Compared with previous studies, we profiled the changes in TB-IGRA results in detail and observed an elevation in both the ATB and NTB groups with a 1-year mean time interval. Moreover, we even detected a significant difference in the former group with a higher mean baseline TB-IGRA level. After controlling the probable confounders involving baseline TB-IGRA, the pretreatment prophylactic therapy did not influence the elevating TB-IGRA value, and there was no significant increase in the ATB or NTB group. We considered that the increasing tendency of TB-IGRA values in the current study might be correlated with the high epidemic background rather than receiving prophylactic treatment based on previous evidence

[22]. Furthermore, combining the results of the TB status mentioned, we found that none of the patients developed active TB despite varying TB-IGRA values. This point is supported by a widely shared opinion that current TB tests, including IGRAs, cannot meet the requirements to predict either TB control or progression to active TB [23].

This study has limitations due to its retrospective study design, limited sample size, limited follow-up period, and enrollment of patients from a limited geographical region. Moreover, this study was conducted during the coronavirus 2019 (COVID-19) pandemic; before we collected the data, China was under the "COVID-19 zero policy" without this infection impact. However, the restrictions on wearing masks and traveling might affect the data. Additionally, we only enrolled patients who received SEC, the first IL-17A inhibitor included in health insurance care in mainland China with relatively abundant follow-up data in our center.

CONCLUSIONS

TB prophylaxis does not influence TB reactivation or significantly reduce the TB-IGRA level, which further underlines the safety of SEC in patients with psoriasis and baseline TB-IGRA positive results, even in a region with high TB burden. Documenting medical records of active TB symptoms and imaging features during follow-up is also re-emphasized. We considered that patients with LTBI should be referred to infectious disease specialists, and the anti-TB medication should be administered with discretion before initiating SEC. Future studies with population-based, long-term follow-up designs are warranted to validate TB safety for second-generation biologics among patients with psoriasis and LTBI in regions with different TB risks.

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Conflict of Interest. Yue Xiao, Wenyao Mi, Jinqiu Wang, Dingke Wen, Yiyi Wang, Yuanxia Gu, Dan Hao, Wei Yan, Xuerong Chen, and Wei Li declare that they have no conflict of interest.

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