



BRIEF REPORT

The Tuberculosis Positive Conversion Rate Among Psoriasis Patients Treated with Adalimumab and Secukinumab: A Single-Center Retrospective Study in China

Yue Xiao · Hui Chen · Qin Zou · Yiyi Wang · Yuanxia Gu ·
Jinqiu Wang · Wei Yan · Wei Li

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ABSTRACT

Introduction: The tuberculosis (TB) positive conversion rate among psoriasis patients who received biologics has been reported worldwide, particularly in regions with low TB risk. Nonetheless, the TB-related safety of biologics such as adalimumab and secukinumab remains elusive in areas with high TB risk. According to the World Tuberculosis Report 2021, China is the country with the second highest TB burden, but data on TB conversion are also limited. Thus, we performed a retrospective, single-center study to profile the TB infection status conversion ratio among psoriasis patients treated with adalimumab and secukinumab in China.

Methods: Patients were enrolled between April 2019 and February 2021 from West China

Hospital, Sichuan University. Baseline and relevant clinical information were summarized, and proper statistical analysis was used under different conditions.

Results: Five (5.43%) patients suffered TB conversion in the adalimumab group, two of whom developed active TB within the first 6 months. In the secukinumab group, four (5.26%) patients had TB positive conversion with no reports of active TB.

Conclusion: Our data show a relatively high rate of TB conversion among these psoriasis patients after mean treatment duration of 17.13 months. We recommend that, in patients who receive adalimumab, TB be reevaluated after the first 3 months and then monitored semiannually for the next 2 years. For patients treated with secukinumab, annual examination is sufficient.

Yue Xiao, Hui Chen, and Qin Zou contributed equally to this work.

Keywords: Adalimumab; Biologics; Psoriasis; Secukinumab; Tuberculosis

Y. Xiao · Q. Zou · Y. Wang · Y. Gu · J. Wang ·
W. Yan · W. Li (✉)
Department of Dermatology and Venereology, Rare
Diseases Center, West China Hospital, Sichuan
University, Chengdu 610041, Sichuan, China
e-mail: liweihx_hxyy@scu.edu.cn

H. Chen
West China School of Medicine, Sichuan University,
Chengdu 610041, Sichuan, China

Q. Zou
West China School of Nursing, Sichuan University,
Chengdu 610041, Sichuan, China

Key Summary Points

Why carry out this study?

The tuberculosis conversion rate among psoriasis patients treated with biologics is a growing concern. In areas with low tuberculosis risk such as the USA, the safety of biologics in tuberculosis infection has been identified. The tuberculosis positive conversion rate is low, and there are no reports of active tuberculosis. Thus, annual tuberculosis screening is sufficient. However, data on tuberculosis positive conversion or active tuberculosis in high-risk areas remains to be elucidated. We aimed to add evidence regarding tuberculosis infection status conversion in high-risk regions through this study and recommend a tuberculosis screening timeline for psoriasis patients receiving biologics.

What was learned from the study?

Our study profiled a comparatively high tuberculosis-positive conversion rate in China, emphasizing the importance of tuberculosis screening in these high-burden countries.

We recommended a new tuberculosis screening timeline for patients treated with adalimumab. They should undergo tuberculosis screening after the first 3 months of treatment and then semiannually after its completion.

psoriasis treatment in the recent decades, and their use has grown widely because of efficacy and safety. However, there are still risks regarding their application in clinical practice [3, 4]. In addition to common adverse effects such as upper tract infection and local injection reaction, tuberculosis (TB) infection remains a significant concern.

Recently, accumulating evidence based on real-world experience has illustrated the TB conversion rate among psoriasis patients treated with biologics in regions with low TB risk such as the USA and Italy. There are no reports of active TB, while the incidence of latent tuberculosis infection (LTBI) varies in these two regions [3, 4]. Hence, the specific risk of LTBI or active TB among patients treated with biologics in different regions remains to be further explored. China is the country with the second highest TB burden, accounting for 8.50% of all estimated incident TB cases worldwide, according to the 2021 World Tuberculosis Report, and with a high rate of multidrug-resistant TB (MDR-TB), which makes the condition more complex [5]. In 2020, the prevalence of tuberculosis in Sichuan Province was 55.19/100,000, which is the national average in China [6]. Herein, aiming to provide evidence for areas with high TB risk, we retrospectively examined the TB conversion rate among psoriasis patients treated with adalimumab (ADA) or secukinumab (SEC) in China. We chose these two commonly adopted drugs as a tumor necrosis factor inhibitor (TNFi) and interleukin (IL)-17 inhibitor (IL-17i), included in the healthcare insurance in China in 2020 and 2021, respectively.

METHODS

This single-center retrospective analysis included psoriasis patients between April 2019 and February 2021 in the West China Hospital of Sichuan University and was approved by the biomedical research ethics committee of this medical center (approval no. 2021-581). This study was performed in accordance with the Helsinki Declaration of 1964. No informed consent was required because the retrospective

INTRODUCTION

Psoriasis is a common immune-mediated disease that affects approximately 2% of the population worldwide [1]. Its chronic, refractory, and multiorgan-affected characteristics are strongly associated with decreased quality of life [1, 2]. Biologic agents are pathogenesis-based therapeutic strategies that have revolutionized

study design and the data were anonymized. The inclusion and exclusion criteria are outlined below:

The inclusion criteria were: (1) ≥ 18 years old; (2) moderate to severe chronic plaque psoriasis (Psoriasis Area Severity Index (PASI) ≥ 3 , or Body Surface Area (BSA) $\geq 3\%$, and Dermatology Life Quality Index (DLQI) ≥ 6); (3) conventional treatment failure or intolerance (including methotrexate, acitretin, phototherapy, traditional Chinese medicine); (4) treated with biologics adalimumab or secukinumab; (5) completed QuantiFERON-TB Gold (QFT) twice (at baseline and during follow-up). The exclusion criteria were: (1) QFT positive at baseline; (2) treated less than 12 weeks.

Demographic data and relevant clinical information are summarized, including gender, age at initiation of biologic, previous treatment, bionäive or not, duration of psoriasis, duration of treatment (ADA/ SEC), and QFT results at screening and follow-ups.

Statistical analysis was performed using SPSS software (version 26.0; IBM SPSS Statistics). Categorical variables are expressed as count (%), while continuous variables are described as mean \pm standard deviation (SD).

RESULTS

In this retrospective, single-center study, 168 psoriasis patients were enrolled according to the criteria. There were 111 male (66.07%) and 57 female (33.93%) patients, with mean age of 39.04 ± 11.16 years. The Psoriasis Area Severity Index (PASI) was measured as 10.60 ± 6.78 , and Body Surface Area (BSA) was 15.67 ± 15.27 . This cohort included 76 patients who received SEC and 92 patients treated with ADA, both serving as monotherapy without a combination of other systematic medications. We recorded previous treatment received by patients before using biologics; the most frequently chosen systematic medication was methotrexate (88, 52.38%). Other demographic and clinical features are presented in Table 1.

In this cohort, nine patients suffered TB conversion with the result of QFT changing from negative to positive, among whom five

Table 1 Baseline information and clinical characteristics

Baseline information	Total patients (<i>n</i> = 168)
Age, years	39.04 ± 11.16
Gender (male)	111 (66.07)
BMI, kg/m ²	23.76 ± 3.71 , <i>n</i> = 126
PASI	10.60 ± 6.78
BSA	15.67 ± 15.27
Smoking	46 (36.51), <i>n</i> = 126
Alcohol	30 (22.73), <i>n</i> = 132
Duration of psoriasis, years	14.35 ± 8.68
Duration of Ada/Sec, months	17.13 ± 7.42
Family history	28 (22.05), <i>n</i> = 127
Bionäive, yes	142 (84.52)
Previous therapy ^a	
Methotrexate	88 (52.38)
Acitretin	72 (42.86)
Cyclosporine	9 (5.36)
Traditional Chinese medicine	55 (32.74)
Phototherapy	79 (47.02)
TB	<i>n</i> = 168
QFT conversion	9 (5.36)
LTBI	7 (4.17)
Active TB	2 (1.19)
Ada	<i>n</i> = 92
QFT conversion	5 (5.43)
LTBI	3 (3.26)
Active TB	2 (2.17)
Sec	<i>n</i> = 76
QFT conversion	4 (5.26)
LTBI	4 (5.26)

Table 1 continued

Baseline information	Total patients (<i>n</i> = 168)
Active TB	0 (0.00)

Categorical variables expressed as *n* (%), and continuous variables as mean ± standard deviation

^aThese systematic treatments were stopped before using biologics. The total may be > 100% as some patients previously received more than one systematic treatment

Ada adalimumab, *BMI* body mass index, *BSA* body surface area, *F* female, *LTBI* latent tuberculosis infection, *M* male, *PASI* Psoriasis Area Severity Index, *QBT* QuantiFERON TB Gold, *Sec* secukinumab, *TB* tuberculosis, *TCM* traditional Chinese medicine

(5.43%) patients received ADA and four (5.26%) were treated with SEC. Of the five patients who suffered QFT conversion in the ADA group, two (2.17%) developed active TB. In contrast, there were no active TB cases in the SEC group (Table 1).

We summarize the detailed characteristics of the patients who presented with TB positive conversion. In the SEC group, patients continued the treatment after QFT conversion and did not develop TB activation. Two cases of active TB occurred after the first 3 months of treatment with ADA. In the ADA group, for patients who developed LTBI or active TB, their therapeutic regime was adjusted from ADA to SEC after regular anti-TB treatment. We then closely monitored their TB infection status and did not find any sign of active TB during follow-up (Table 2).

DISCUSSION

This single-center retrospective study reports the QFT conversion rate among patients treated with ADA (5.43%) or SEC (5.26%) in China, an area with high burden of TB and MDR-TB, with a mean treatment duration of 17.13 months.

TB is an infectious disease that starts with inhalation of *Mycobacterium tuberculosis*, one of

the leading causes of death [5, 7]. LTBI is an asymptomatic TB infectious condition that can exist persistently with a risk of developing active TB, which can be detected through QFT [7]. In this study, the total QFT conversion rate of psoriasis patients treated with ADA and SEC was 5.36% (9/168). In 2016, Gao et al. observed that the QFT conversion rate was 3.10% among 12 749 baseline IGRA-negative participants in rural regions in China within 1-year follow-up [8]. We found that the QFT conversion rate of psoriasis patients who received biologics in our study (5.36%) was higher than that of the general population in China (3.10%). Thus, changes in TB infection status among psoriasis patients treated with biologics are of concern.

In fact, previous data have indicated the incidence of LTBI and active TB among psoriasis patients treated with different biologics based on clinical trials. TNFi, predominantly the subclass of anti-TNF- α monoclonal antibodies, has been shown to be a risk factor of TB infection [9]. Leonard et al. summarized 18 clinical trials of ADA-treated psoriasis and reported 16 events of TB infection, including nine active TB cases and seven LTBI cases [10]. By contrast, biologics targeting IL-17 or IL-12/23 are not associated with progression of TB activation [11, 12]. A pooled analysis that included 19 clinical trials of SEC-treated psoriasis reported four new LTBI cases among 8436 baseline-negative psoriasis patients [11]. Additionally, Lebwohl et al. also pooled safety data from clinical trials of ustekinumab-treated psoriasis and reported no TB cases, while they did not mention the incidence of LTBI [12]. Although random clinical trials can provide high-quality evidence, one of their limitations is that the studied population cannot wholly represent the population treated in everyday life. Such real-world experience is essential and urgently required.

A long-term single-center retrospective study in the USA, an area with low TB risk, reported 1 LTBI case per 428 patient-years and no active TB cases among patients using biologic agents, including TNFi, IL-17i, and IL-12/23i [3]. In Italy, another area with low TB risk, a 9-year retrospective study indicated a 6.50% QFT conversion rate with no reports of active TB among psoriasis patients after a median of

Table 2 Clinical characteristics of psoriasis patients with TB positive conversion

No.	Gender (F/M)	Age at biologic initiation	Complications	Previous treatment	Biologics	Duration of biologic at time of TB positive (months)	Symptoms of TB	Evidence	Type of TB infection	Anti-TB	Biologic switching	Follow-up after TB positive conversion (months)
1	M	31	PsA; vitiligo; depression	TCM	SEC	12	None	QuantiFERON Gold	LTBI	None	None	13
2	M	38	Hyperuricemia; hypodipemia; thyroid nodule	TCM	SEC	16	None	QuantiFERON Gold	LTBI	INH (5 months)	None	None
3	F	40	None	TCM	SEC	13	None	QuantiFERON Gold	LTBI	None	None	11
4	M	34	None	MTX; acitretin	SEC	8	None	QuantiFERON Gold	LTBI	None	None	2
5	M	62	PsA; type 2 diabetes	Phorootherapy	ADA	3.5	None	QuantiFERON Gold	LTBI	HR (4 months)	ADA withdrawal	15
6	M	49	PsA	MTX (6 months); Era (3 months)	ADA	3	Fever & chills	QuantiFERON Gold; chest ray; bronchoscopy	Active TB	HR (6 months)	SEC	14
7	M	28	PsA; anemia; protein malnutrition	Acitretin	ADA	6	Fever	QuantiFERON Gold; chest ray	Active TB	HRZE (4 months)	(1) ETA; (2) SEC	25
8	M	56	Nonalcoholic fatty liver	MTX; acitretin	ADA	6	None	QuantiFERON Gold; chest ray	LTBI	HR (3 months)	SEC	10
9	M	52	PsA	MTX	ADA	3.5	None	QuantiFERON Gold; chest ray	LTBI	HR (3 months)	SEC	4

Patient age documented at start of biologic use
 ADA adalimumab, ETA etanercept, F female, HR isoniazid + rifampicin, HRZE isoniazid + rifampicin + pyrazinamide + ethambutol, INH isoniazid, LTBI latent tuberculosis infection, M male, MTX methotrexate, SEC secukinumab, PsA psoriatic arthritis, TB tuberculosis, TCM traditional Chinese medicine

34-month biological treatment [4]. Notably, the incidence of active TB is quite different in regions with median to high TB risk. In Japan, a country with median TB burden, Sakae Kaneko et al. reported two LTBI cases (under treatment with TNFi and IL12/23i) and one active TB case (under treatment with TNFi for 5 months) among 1052 TB baseline-negative psoriasis patients [13]. In comparison, we reported a relatively high QFT conversion rate in the ADA group (5.43%) and SEC group (5.25%), and two active TB cases in the ADA group, indicating the importance of TB monitoring in high-burden areas.

Guidelines for biologics in treating psoriasis in different regions have emphasized the importance of routine TB screening, but the timeline for TB reassessment varies [14–16]. The EuroGuiDerm guideline recommends monitoring tuberculosis infection during the treatment according to local regulations [14]. The American Association of Dermatology recommended annual LTBI retesting for high-risk patients [16]. The Japanese guidance increased the TB reexamination frequency and advised TB monitoring at the 6th and 12th months for psoriasis patients using biologics [15]. The newly published Chinese biologic guideline suggests an extension of the TB monitoring timeline compared with the previous edition, where patients using TNFi should complete TB monitoring every 6 months, while those treated with other biologics such as IL-17i, IL-23i, and IL12/23i should be monitored annually.

Combining this with our data, we recommend a new timeline for TB screening. We observed that two patients who were baseline QFT negative were exposed to active TB after approximately 3 months of ADA therapy. We suggest that, in psoriasis patients who receive ADA in areas with high TB burden, it might be more reasonable to consider monitoring by TB tests after the first 3 months of treatment then semiannually for the next 2 years. However, we agree that annual LTBI monitoring is sufficient to ensure safety among patients treated with SEC.

This study has several limitations because of its retrospective design, limited sample size, and median follow-up of 17.13 months. In this

study, we only included two biologics (SEC and ADA) because other biologics, including ixekizumab (IL-17i), ustekinumab (IL-12/23i), and guselkumab (IL-23i), were not included in the healthcare insurance in China before 2022. Few patients chose them at our center between April 2019 and February 2021. Furthermore, this study was conducted during the coronavirus disease 2019 (COVID-19) period, which might have a bearing on the results obtained (restrictions in terms of wearing masks, social distancing rules, etc.).

CONCLUSIONS

Parallel with previous real-world experience, we confirm the safety of SEC regarding TB activation among psoriasis patients [4, 13]. In comparison, we recommend TB reevaluation in the first 3 months for patients treated with ADA in regions with high TB burden. More evidence regarding TB status conversion among psoriasis patients treated with biologics is needed in areas with high TB burden, especially long-term real-world studies.

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Author Contributions. All authors contributed to the study conception and design. Yue Xiao, Hui Chen, Yiyi Wang collected the data. Yuanxia Gu and Jinqiu Wang organized

the data and made tables. Yue Xiao, Hui Chen, and Qin Zou drafted the manuscript. Wei Yan and Wei Li did the manuscript editing.

Disclosures. Yue Xiao, Hui Chen, Qin Zou, Yiyi Wang, Yuanxia Gu, Jinqiu Wang, Wei Yan, Wei Li have nothing to disclose.

Compliance with Ethics Guidelines. This study was approved by the biomedical research ethics committee of West China Hospital, Sichuan University (Approval number: 2021–581), and performed in accordance with the Helsinki Declaration of 1964. No informed consent was required because the retrospective study design and the data was anonymized.

Data Availability. The data in this current study is available from the corresponding author.

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