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RESEARCH LETTER

Safety of Biologics for Psoriatic Patients with Latent Tuberculosis

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Although biologics are effective for psoriasis, immunosuppressive therapy can increase the risk of tuberculosis (TB) reactivation. To determine whether biological therapy for psoriasis increases the risk for TB reactivation, we performed a patients' chart review to determine the incidence and the relative risk of TB reactivation in psoriatic patients with latent TB infection (LTBI), who received biological therapy, with vs without prior anti-TB therapy.

In addition to routine test for HIV, a total of 1208 patients, including 881 males and 327 females aged 39.0 ± 11.4 years, with moderate-to-severe psoriasis were screened for TB infection prior to biological therapy at our department from January 2020 to June 2021. All patients were negative for HIV and syphilis. LTBI was defined as a positive for Interferon-gamma release assay (IGRA) without any indications of active TB infection according to chest X-rays or CTs, and clinical symptoms. TB reactivation means development of active TB or re-infection of TB in patients who have recovered from previous TB infection. All patients included in this analysis were positive for Interferon-gamma release assay, without any indications of active TB infection at baseline, indicating that they had recovered from previous TB infection. TB reactivation was diagnosed by specialists at the Chest Hospital, based on the findings of chest CTs or X-rays, and clinical symptoms. Of 180 patients who were LTBI (IGRA positive), 69 patients were given prophylaxis therapy (either isoniazid in combination with rifampicin or isoniazid alone) prior to biological therapy. Among the 111 patients without prophylaxis therapy, 37 patients received biological therapy. Thirteen out of the 37 patients without prophylaxis therapy and 43 out of 69 patients with prophylaxis therapy completed 12-week follow-up. Thirty cases receiving prophylaxis therapy and 11 cases receiving no prophylaxis therapy completed 24-week follow-up (Detailed in Figure S1). At the end of 24-week follow-up, the rates of TB reactivation in LTBI patients with and without prophylaxis therapy were 13% (4/30) and 27% (3/11) (relative risk=2.045, 95% CI: 0.5604–6.899. P>0.05), respectively (Table 1). The rates of other adverse events also did not differ significantly between the groups with vs without prophylaxis therapy at either 12-week (46% vs 70%, p=0.19) or 24-week follow-up (91% vs 77%, p=0.41) (Table 2). However, the incidence of overall adverse events was

Table 1 TB Reactivation at 24-Week Follow-up

	Prophylaxis Therapy (N=69)	No Prophylaxis Therapy (N=37)	TB Reactivation at 24-Week Follow-Up	
			Anti-TB therapy (N=30)	No Anti-TB Therapy (N=11)
Males	54	25	22	7
Females	15	12	8	4
Age (yr)*	45.43 ± 1.69 (21)	47.27 ± 2.69 (19)	44.40 ± 2.33 (19)	51.18 ± 6.36 (47)
Adalimumab	9	6	0 (0/4)	1 (1/2)
Secukinumab	27	18	4 (4/13)	1 (1/6)
Ixekizumab	17	10	0 (0/4)	0 (0/2)
Ustekinumab	2	1	0 (0/1)	0 (0/0)
Guselkumab	14	2	0 (0/8)	1 (1/1)

Notes: *Data are expressed as mean ± standard error of mean (interquartile range).

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Table 2 Adverse Events

Follow-up time	No Prophylaxis Therapy		Prophylaxis Therapy		Adalimumab		Secukinumab		Ixekizumab		Ustekinumab		Guselkumab	
	12 Weeks	24 Weeks	12 Weeks	24 Weeks	12 Weeks	24 Weeks	12 Weeks	24 Weeks	12 Weeks	24 Weeks	12 Weeks	24 Weeks	12 Weeks	24 Weeks
Number of cases	13	11	43	30	8	6	23	19	12	6	1	1	12	9
Serious Adverse Events														
ALT or AST>40	2	3	15	8	3	3	4	3	4	2	1	1	5	2
CREA≥133	3	1	6	2	3	–	2	2	3	1	–	–	1	–
TC>5.2 or TG>2.3	0	1	5	5	1	–	1	3	3	1	–	–	–	2
ANA(+)	0	0	0	1	–	–	–	1	–	–	–	–	–	–
Non-Serious Adverse Events														
Folliculitis	1	2	1	2	1	1	1	3	–	–	–	–	–	–
Eczema	0	0	2	2	–	–	1	–	–	–	–	–	1	2
Anemia	0	0	0	0	–	–	–	–	–	–	–	–	–	–
Urticaria	0	2	0	1	–	1	–	2	–	–	–	–	–	–
Chicken pox	0	1	0	1	–	–	–	2	–	–	–	–	–	–
Herpes zoster	0	0	1	1	–	–	–	–	–	–	–	–	1	1
Total	6	10	30	23	8	5	9	16	10	4	1	1	8	7

Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; CREA, Creatinine; TC, Total cholesterol; TG, Triglyceride; ANA, antinuclear antibodies.

significantly higher at 24-week follow-up compared to 12-week follow-up in the group without prophylaxis therapy (91% vs 46%, p<0.05). In contrast, the incidence of overall adverse events did not differ significantly between 12-week and 24-week in the group with prophylaxis therapy (70% vs 77%, p=0.60) (Table 2).

Active TB occurs in approximately 0.1–0.2% of psoriatic patients receiving biological therapy.[1] Anti-TB therapy has been recommended for individuals receiving immunosuppressive agents.[2] Studies suggest that prophylaxis therapy can prevent TB reactivation in individuals who receive biologics and anti-TB therapy has been recommended.[3,4] We demonstrate here that pretreatments with prophylaxis therapy reduced the rate of TB reactivation in psoriatic patients receiving biologics (13% vs 27%). However, a solid conclusion cannot be drawn due to the small sample size. Although evidence suggests that it may not be necessarily crucial to screen LTBI prior to some biological therapies when weighing benefits and costs,[5] prophylaxis therapy becomes necessary when using biologics in patients with LTBI because some biological agents such as Ustekinumab and etanercept can increase the risk for TB reactivation.[6,7] In addition, the incidence of overall adverse events was higher at 24-week than at 12-week follow-up in patients without prophylaxis therapy. Whether the increased adverse events at 24 weeks were associated with TB reactivation is unclear. Nonetheless, the present study shows that pretreatment with prophylaxis therapy tends to lower the incidence of TB reactivation and overall adverse events in psoriatic patients, suggesting the possible benefits of prophylaxis therapy for psoriatic patients with LTBI, who are undergoing biological treatment. However, study in large cohort is needed to confirm the results of the present study and to differentiate the contribution of individual biological agent to TB reactivation and adverse events. Additionally, it cannot exclude the possibility that the incidence of active TB following biological treatment may include some new infected cases because the positive rate of TB is extremely high in Guangdong, China.

Data Sharing Statement

All data pertinent to this report are presented in the manuscript.

Ethics Statement

This work was reviewed and approved by the ethics committee of Dermatology Hospital, Southern Medical University (#GDDHLS-20190304). Patients' consent was not required because this was a retrospective study in which all patients' information was deidentified. This study was carried out in compliance with the Declaration of Helsinki.

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Disclosure

The authors have no conflicts of interest.

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