[7, 8]. This is very important because these patients can unknowingly infect other persons and contribute to the spread of the infection: their isolation is therefore necessary [8]. Further studies are required to establish whether urticaria involves mainly the limbs (as in our patients and those reported by other authors [7, 10]), itching is mild [5, 10] (also in one of our patients) and whether it is possible that urticaria, as a first clinical manifestation, occurs in patients with COVID-19 of mild to moderate severity [5, 8]. ■

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## Safety of biologics for psoriasis patients during the COVID-19 pandemic: the experience from Wuhan, China

Patients with psoriasis have an increased risk of systemic comorbidities, which may be associated with the development of severe manifestations of coronavirus disease 2019 (COVID-19) [1, 2]. However, the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection for the subset of psoriasis patients on biologic therapies remains unclear [3]. Continuing biologic therapy during the COVID-19 pandemic is an area of concern and inquiry for patients and providers [4, 5].

Wuhan, the epicentre of the outbreak in China, reported more than 50,000 confirmed cases of COVID-19. The local government enforced strict lockdown measures from January 23rd to April 8th, 2020. We set out to conduct a survey of psoriatic patients receiving biologic treatments in Wuhan City. Self-administered, online questionnaires were sent out to 118 registered psoriatic patients through smartphones (WeChat). In total, 107 patients completed the questionnaires (response rate: 90.7%) during March 2020, revealing 102 cases of psoriasis vulgaris (95.3%), three cases of erythrodermic psoriasis (2.8%), and two cases of pustular psoriasis (1.9%). The average age was 39.99 ± 1.29 years (range: 15-86 years) and there were 73 males (68.2%). Forty-three (40.2%) patients had underlying comorbidities, including 15 (14.0%) with psoriatic arthritis, 10 (9.3%) with hypertension, 16 (15.0%) with obesity (BMI >27.5 kg/m$^2$) [6], and five (4.7%) patients with diabetes. Additionally, 14 (13.1%) patients had at least two comorbidities. IL-17 inhibitors were used in 90 patients (84.1%) and TNF-α inhibitors were used in 17 patients (15.9%).

The survey showed that none of the 107 patients with psoriasis were diagnosed with COVID-19, including 55 (51.4%) patients who were either local residents or had travelled to Wuhan after November 2019. Since the government of Wuhan City administered a comprehensive SARS-CoV-2 nucleic acid test on 11 million citizens in May 2020, we conducted telephone interviews for our patients in July 2020. One hundred and two patients completed this follow-up; 90 (88.2%) patients underwent the nucleic acid amplification test and 61 patients (59.8%) underwent the antibody test, all reported as negative.

Two patients with psoriatic arthritis (*table 1*) developed fever during the COVID-19 pandemic. A 35-year-old woman with a history of tuberculosis , receiving adalimumab (80 mg monthly) injections, was hospitalized in an isolation ward and became afebrile after treatment with antibiotics. The second was a 37-year-old man on secukinumab therapy (300 mg monthly), who received antibiotic treatment as an outpatient, and recovered. Four patients (3.7%) had a history of close contact with a COVID-19 patient, but none of these patients developed any COVID-19 symptoms. Notably, a 16-year-old girl on secukinumab therapy (150 mg monthly), whose mother and grandparents had confirmed COVID-19 infection, had negative serologic and radiologic screening tests. We subsequently learned that she was in the habit of wearing a facemask even around family members, and washed her hands frequently.

We also analysed the possible reasons why the patients in our study did not contract COVID-19. Firstly, the majority of patients (99 cases, 92.5%) were younger than 60 years of age. Secondly, most patients (64 cases, 59.8%) did not have underlying comorbidities. Also, many patients rigorously followed infection control guidelines. Moreover, in our cohort, IL-17 inhibitors, which have been reported to be comparatively less immunosuppressive [7], were prescribed more often than TNF-α

**Table 1.** Clinical characteristics of patients with psoriasis using biological agents during the COVID-19 pandemic in Wuhan.

| Characteristics | Number of patients (%) |
|---|---|
| **Gender** | |
| Male | 73 (68.2) |
| Female | 34 (31.8) |
| **Age (years)** | |
| 15–44 | 69 (64.5) |
| 45–59 | 30 (28.0) |
| >60 | 8 (7.5) |
| **Clinical classification** | |
| Psoriasis vulgaris | 102 (95.3) |
| Erythrodermic psoriasis | 3 (2.8) |
| Pustular psoriasis | 2 (1.9) |
| **Biological agent** | |
| IL-17 inhibitors | |
| Secukinumab | 87 (81.3) |
| Ixekizumab | 3 (2.8) |
| TNF-alpha inhibitors | |
| Adalimumab | 11 (10.3) |
| rhTNFR:Fc | 5 (4.7) |
| Infliximab | 1 (0.9) |
| **History of infectious diseases** | |
| Tuberculosis | 3 (2.8) |
| **Comorbidities** | 15 (14.0) |
| Psoriatic arthritis | 16 (15.0) |
| Obesity | 10 (9.3) |
| Hypertension | 5 (4.7) |
| Diabetes | 2 (1.9) |
| Cardiovascular disease | 2 (1.9) |
| Gout | 9 (8.4) |
| Dyslipidaemia | 3 (2.8) |
| Others* | |
| **Local residents or travelled to Wuhan after November 2019** | 55 (51.4) |
| **Close contact with a COVID-19 patient** | 4 (3.7) |
| **Suspected symptoms of COVID-19** | |
| Fever | 2 (1.9) |
| **SARS-CoV-2 nucleic acid amplification test**** | 90 (88.2) |
| Positive | 0 (0.0) |
| **SARS-CoV-2 antibody test**** | 61 (59.8) |
| Positive | 0 (0.0) |
| **Confirmed COVID-19 infection** | 0 (0.0) |

**The comorbidities of the three patients were bronchopneumonia, ankylosing spondylitis and thyroiditis. **Five patients could not be contacted by telephone, therefore 102 patients completed the follow-up from July 1st to 7th , 2020. Among the 102 patients, 90 (88.2%) received the nucleic acid amplification test and 61 underwent (59.8%) the antibody test.*

inhibitors. The latter are implicated in the development of serious infections by interfering with microbial defence mechanisms [8].

This retrospective study may not completely reflect the incident rate of COVID-19 infection in psoriasis patients on biologic therapies. However, our preliminary findings suggest that patients receiving biologic treatments do not have an increased risk of serious respiratory and/or other complications secondary to SARS-CoV-2 infection. Based on our survey, we propose that it is relatively safe for patients with psoriasis who do not show serologic or clinical evidence of COVID-19 infection to continue biologic therapies during the pandemic.

Nevertheless, our study has limitations. The sample size is relatively small, the methodology relies on self-administered questionnaires, and there were few older patients (only eight patients > 60 years). Future, multi-centre and multi-country collaborative studies, with larger patient populations, are needed to provide additional compelling evidence for the safety of biologic therapies during the COVID-19 pandemic. ■

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## Safety of secukinumab in psoriasis patients with latent tuberculosis infection

Tuberculosis (TB) has always represented a concern in the setting of systemic treatment for psoriasis, mainly with biologic therapy. Currently, latent tuberculosis infection (LTBI) treatment is mandatory in all patients starting biologic therapy [1]. Data suggest a variable risk of TB reactivation in patients with LTBI depending on the mechanism of action of treatment, even for agents within the same class [1]. Moreover, toxicity associated with LTBI treatment is considerable [2]. Isoniazid remains the first line for LTBI treatment and is associated with hepatotoxicity, with hepatitis rates of 0.5-1.0% and mortality in 0.05-0.1% of cases [2]. Alternatively, rifampin may be prescribed, but the several possible drug interactions and risk of resistance often limit its use [2]. Recent data suggests that novel biologics acting in the IL-23/IL-17 axis are not associated with TB reactivation and may be considered for patients in whom isoniazid or rifampin treatment is contraindicated or not tolerated [1, 3].

We report two cases with moderate to severe psoriasis and LTBI (*table 1*), in whom isoniazid or rifampin treatment was contraindicated or not tolerated [4]. Both patients were treated with secukinumab with an excellent, maintained clinical response, and showed no evidence of TB reactivation after two years of follow-up.

With the advent of biologics, the risk of TB has been highlighted, namely with TNF-α inhibitors [1, 5]. TB is caused by *Mycobacterium tuberculosis*, which is an intracellular pathogen that elicits a Th1 response. TNF-α is a key molecule that directly promotes an effective Th1 response. In contrast, IL-17A plays a protective role in the host defence at epithelial and mucosal barriers, serving as an important mediator for the clearance of extracellular pathogens [1]. An *in vitro* study examined the effect of TNF-α antibody, adalimumab and secukinumab, on dormant *Mycobacterium tuberculosis* H37Rv using a novel human three-dimensional microgranuloma model [5]. The results with adalimumab were indicative of mycobacterial reactivation, while, secukinumab treatment was

**Table 1.** Clinical information of the two patients with moderate to severe psoriasis and latent tuberculosis infection (LTBI).

| Patient No. | Sex | Age | Comorbidities | Duration of psoriasis | Previous failed treatment | Diagnosis of LTBI | Reason not to perform LTBI treatment | PASI score before biological treatment | PASI response after initiation of secukinumab |
|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 56 | Overweight | 17 years | Methotrexate, Cyclosporine | Positive IGRA<br>Positive Mantoux test | Generalized skin rash and small joint pain and oedema of both hands and feet due to isoniazid (symptoms resolved completely after withdrawal and reappeared after reintroduction of isoniazid, leading to the conclusion that isoniazid was the cause of these symptoms)<br>Previous treatment with rifampin for another indication | 16 | 1 year (PASI 100)<br>2 years (PASI 100) |
| 2 | F | 78 | Arterial hypertension<br>Type 2 diabetes *mellitus* | 5 years | Phototherapy, Methotrexate, Cyclosporine, Acitretin | Positive Mantoux test<br>Chest radiograph revealed fibrotic micronodules with apical topography in the left lung, presumably due to residual previous tuberculosis | High risk of isoniazid hepatitis: increased age and female gender | 18 | 1 year (PASI 90)<br>2 years (PASI 90) |