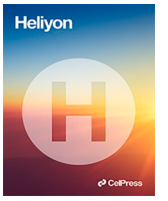
Heliyon 10 (2024) e24096

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Decreased risk of COVID-19 and long COVID in patients with psoriasis receiving IL-23 inhibitor: A cross-sectional cohort study from China

Yifan Hu [a,c,1], Dawei Huang [a,c,1], Yuxiong Jiang [a,c,1], Qian Yu [b,c], Jiajing Lu [a,c,**], Yangfeng Ding [a,c,***], Yuling Shi [a,c,*]

[a] Department of Dermatology, Shanghai Skin Disease Hospital, Tongji University School of Medicine, Shanghai, 200443, China
[b] Department of Dermatology, Shanghai Tenth People's Hospital, Institute of Psoriasis, Tongji University School of Medicine, Shanghai, 200072, China
[c] Institute of Psoriasis, Tongji University School of Medicine, Shanghai, 200443, China

ARTICLE INFO

Keywords:
COVID-19
Psoriasis
IL-23 inhibitor

ABSTRACT

Background: Although clinical trials and real-world data suggest that the risk of COVID-19 and its complications is not exacerbated in patients with psoriasis treated by biological agents, the evidence for this is still limited.
Objectives: We aimed to assess the outcomes of COVID-19 among Chinese patients with psoriasis treated by IL-23 inhibitor, and to compare these variables in patients receiving other therapies.
Methods: A cross-sectional cohort study was conducted to compare psoriasis treatment with IL-23 inhibitor to other treatment methods. All the patients received a questionnaire that contained questions about their psoriasis treatment, COVID-19 symptoms, and related risk factors. The prevalence of COVID-19 was calculated, and logistic regression analyses were performed to determine the association between treatment method and COVID-19 risk. The symptoms of COVID-19 and long COVID were described for each treatment group.
Results: Between December 2022 and February 2023, 732 patients with psoriasis were included in the final analysis. 549 patients had a SARS-CoV-2 infection during the study period. Our results showed that individuals who worked outdoors had a decreased risk of COVID-19, as did those who had other allergic disease. With regard to the effect of the treatment regimens, IL-23 inhibitor treatment was associated with a decreased risk of COVID-19 compared to almost all the other treatments except acitretin. Fever was the most common symptom, but the maximum temperature and duration of fever were comparable among the treatment groups. Patients treated with IL-23 inhibitor were more likely to be asymptomatic after recovery compared to patients treated with methotrexate, narrow-bound ultra violet B, or TNF-α inhibitor.

* Corresponding author. Shanghai Skin Disease Hospital, Tongji University School of Medicine, Shanghai, 200443, China.
** Corresponding author. Department of Dermatology, Shanghai Skin Disease Hospital, Tongji University School of Medicine, Shanghai, 200443, China.
*** Corresponding author. Department of Dermatology, Shanghai Skin Disease Hospital, Tongji University School of Medicine, Shanghai, 200443, China.
E-mail addresses: bonnie166166@126.com (J. Lu), mmmm_111111@126.com (Y. Ding), shiyuling1973@tongji.edu.cn (Y. Shi).
[1] These authors have contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e24096
Received 21 July 2023; Received in revised form 28 December 2023; Accepted 3 January 2024
Available online 9 January 2024

Conclusions: IL-23 inhibitor treatment may lower the risk of COVID-19 and long COVID. Thus, IL-23 inhibitor treatment might be beneficial and positively considered for patients with psoriasis who require systemic treatment during periods when there is a surge in COVID-19 cases.

1. Introduction

Psoriasis is a chronic, inflammatory, immune-mediated skin disease that affects both the physical and mental health of patients. It affects over 60 million people worldwide, and in China, the incidence rate is 0.47 % [1]. In general, treatment strategies for plaque psoriasis are designed based on psoriasis severity, location, the presence of psoriatic arthritis, the presence of associated medical conditions, and patient satisfaction and preference [2]. Treatment for mild-to-moderate psoriasis mainly involves application of topical ointment. For moderate-to-severe psoriasis, the treatments include conventional systemic therapy with various agents, e.g., acitretin, methotrexate, narrow-bound ultra violet B (NB-UVB), and traditional Chinese medicine, as well as administration of biological agents, e.g., TNF-α inhibitors, IL-17 inhibitors, and IL-23 inhibitors [3].

According to WHO's weekly epidemiological update on COVID-19, as of March 2023, there were more than 759 million confirmed cases of COVID-19 and more than 6.8 million COVID-19-related deaths. Understandably, the disease has been a great burden on mankind. COVID-19 not only causes severe acute respiratory syndrome, but also affects other organs: for example, COVID-19 is commonly associated with skin diseases [4–6]. China has optimized its epidemic prevention and control measures since December 2022, and centralized isolation and treatment for COVID-19 is no longer mandatory.

The COVID-19 pandemic has had a monumental impact on medical practice and patient behavior. Several clinical trials and real-world data show that systemic therapies do not increase susceptibility to COVID-19, and preventive cessation is unnecessary for patients with psoriasis [7–11]. For example, Khalaf's study showed that TNF inhibitor treatment was associated with a decreased risk of COVID-19-associated hospitalization relative to methotrexate treatment and may be positively considered in patients with moderate-to-severe psoriasis warranting systemic treatment during the pandemic [11]. However, data on patients with psoriasis who were receiving IL-23 inhibitor treatment during the COVID-19 pandemic are still limited. In this study, we have tried to fill in this information gap by collecting and analyzing data related to COVID-19 from patients with psoriasis in China. This study was conducted between December 2022 and February 2023, and data were collected through medical records and questionnaires answered by the patients. The aim was to investigate the association between various psoriasis treatments and the risk of COVID-19 and sequelae after recovery from COVID-19.

2. Methods

2.1. Study design and study population

This population-based multicenter study investigated the incidence of COVID-19, medical interventions for COVID-19, and COVID-19-associated mortality between December 2022 and February 2023 in a cohort of patients with psoriasis. Patients undergoing psoriasis treatment at six hospitals in China (Shanghai Skin Disease Hospital, Shanghai Tenth People's Hospital, Ruijin Hospital, Changhai Hospital, Huashan Hospital, and Yueyang Hospital) were considered for this study. Patients who had immunosuppression or were receiving immunomodulatory treatment for indications other than psoriasis were excluded. The written informed consent of each patient was obtained before they were given the study questionnaire. This study was approved by Shanghai Skin Disease Hospital Ethics Committees and was conducted in accordance with the tenets of the Declaration of Helsinki (IRB approval number: 2020-36).

2.2. COVID-19-related outcomes

The medical records of eligible patients were checked to determine whether they had a confirmed diagnosis of COVID-19 based on the SARS-CoV-2 PCR test or serology IgM, IgG or the rapid test antigen. Next, data were obtained on the medical interventions for COVID-19 administered to patients with a confirmed COVID-19 diagnosis admitted to the respiratory clinic or emergency ward for medical care. COVID-19-associated mortality was defined as death ascribed to COVID-19 or its complications in patients with a confirmed COVID-19 diagnosis. Long COVID was defined as the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation according to the WHO definition.

2.3. Variables collected and analyzed

Data on the following variables related to patient characteristics were collected through the questionnaire: age, sex, residential address, occupation (Indoor work refers to working in a relatively enclosed environment, while outdoor work refers to working in areas without sound insulation, shading, or insulation facilities), body mass index (BMI), duration of psoriasis, relevant comorbidities (pulmonary diseases such as chronic obstructive pulmonary disease, chronic bronchitis, asthma, and others; allergic diseases such as urticaria, atopic dermatitis, eczema, allergic rhinitis, and others), psoriasis treatment [topical ointment (emollients, corticosteroids, vitamin D, calcineurin inhibitors, combination topical agents et al.), acitretin, methotrexate, NB-UVB, TNF-α inhibitor (Adalimumab),

IL-17 inhibitors (Secukinumab and Ixekizumab), IL-23 inhibitor (Ustekinumab), and traditional Chinese medicine (XiaoYinFang, LongKuiYinXiao et al.)]. All the treatments followed the drug instructions or doctor's advice.

The variables associated with COVID-19 were as follows: previously confirmed COVID-19, risk factors (including occupational risk), vaccination status, date of first vaccination, number of vaccinations, type of vaccination, symptoms of COVID-19 (fever, dizziness, headache, fatigue, muscle soreness, cough, expectoration, pharyngalgia, catarrhal symptoms, decrease in blood oxygen saturation [≤93 %], increase in heart rate [>100 times/minute], shortness of breath [>30 times/minute], dyspnea, chest tightness, chest pain, abnormal taste or smell, nausea, diarrhea, and secondary bacterial infection), drugs used for the treatment of COVID-19 (antipyretics, cough expectorant, antiviral drugs, antibiotics, glucocorticoids, gamma globulin, thymofaxin, and traditional Chinese medicine), course of COVID-19 infection, and long COVID (persistent low fever, dizziness, headache, slowness of thinking/difficulty, fatigue, muscle aches, persistent cough, sputum production, shortness of breath, difficulty breathing, chest tightness, chest pain, rapid heart rate, nausea, diarrhea, abnormal taste or smell, and secondary bacterial infection).

2.4. Statistical analysis

The SPSS 26.0 software was used for data entry and statistical analysis. Potential confounding factors were first selected by univariate analysis, with P value < 0.05 considered as the inclusion criterion. Quantitative variables were expressed as mean ± standard deviation for normally distributed variables and median and interquartile range for variables with a skewed distribution. Qualitative variables were presented as frequency counts and proportions (%). Student's *t*-test was used to compare normally distributed quantitative variables between two groups. Logistic regression models were constructed with IL-23 inhibitor treatment as the independent variable, COVID-19 as the dependent variable, and the following covariates: age, occupation, previous infection, vaccination, allergic diseases, topical ointment, acitretin, methotrexate, NB-UVB, TNF-α inhibitor, IL-17 inhibitors, and traditional Chinese medicine. $p < 0.05$ was considered to indicate statistical significance.

3. Results

3.1. Patients and treatments

We identified 1135 patients with psoriasis who were eligible based on their electronic records and sent them the study

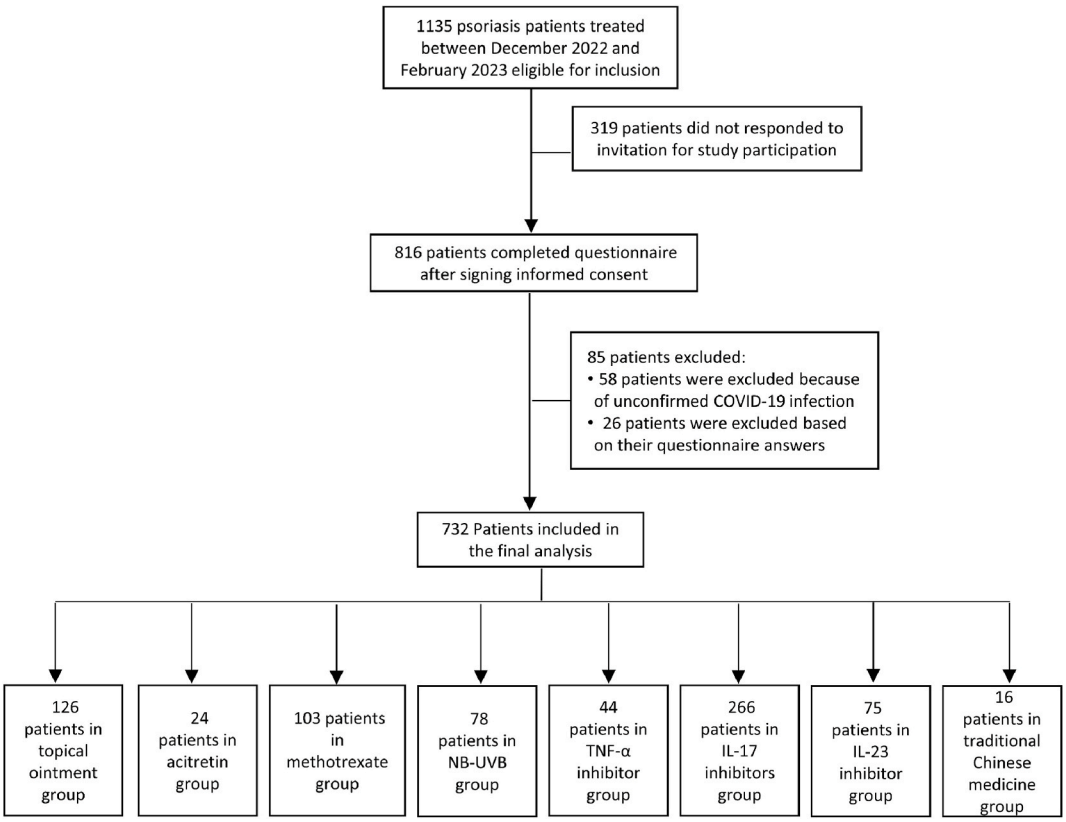


Fig. 1. Flowchart of patient inclusion.

questionnaire. Among them, 816 patients completed the questionnaire (response rate = 71.9 %). Based on the study criteria, 58 patients were excluded because their diagnosis was not confirmed, and 26 patients were excluded because they were using immunosuppressive drugs. The final analysis included 732 patients with psoriasis (Fig. 1).

The patients included in our analysis were from 24 provinces across China, but the majority were from Shanghai. The region-wise distribution of patients is shown in Fig. S1. Among the 732 patients, 518 (70.8 %) were male and 214 (29.2 %) were female. The patients' age ranged from 7 to 90 years. Of the 732 patients, 649 (88.7 %) were engaged in indoor work and 83 (11.3 %) were engaged in outdoor work. Our results showed that patients who worked outdoors had a decreased risk of COVID-19 (adjusted odds ratio [OR], 0.528; 95 % CI, 0.314–0.890) (Fig. 2).

With regard to the psoriasis treatment methods administered, 126 patients were treated with topical ointment; 24, with acitretin; 103, with methotrexate; 78, with NB-UVB; 44, with TNF-α inhibitor; 266, with IL-17 inhibitors; 75, with IL-23 inhibitor; and 16, with traditional Chinese medicine. Detailed data on the patients are presented in Table 1.

3.2. COVID-19-related characteristics of the cohort

Of the 732 patients, 549 patients had a SARS-CoV-2 infection during the study period (December 2022 to February 2023), and 303 patients had a prior SARS-CoV-2 infection before the study period. Among these 303 patients, 271 still had COVID-19 during the study period (Table 2). The results of logistic regression analysis indicated that patients with a prior SARS-CoV-2 infection may have had a higher risk of infection in the study period (adjusted OR, 4.334; 95 % CI, 2.798–6.714) (Fig. 2). At the time of participation in this study, 517 patients (70.6 %) had received at least one vaccination. The vaccines they received were all SARS-CoV-2 inactivated vaccine. Among the patients with COVID-19, 399 (72.7 %) had received at least one vaccination. However, we found that there was no significant correlation between vaccination status and COVID-19 infection (adjusted OR, 1.379; 95 % CI, 0.932–2.039) (Fig. 2).

As shown in Table 2, 372 (67.8 %) of the patients with COVID-19 did not have pulmonary disease previously, while 8 (1.5 %) had chronic obstructive pulmonary disease, 65 (11.8 %) had chronic bronchitis, 20 (3.6 %) had asthma, and 84 (15.3 %) had other pulmonary diseases such as emphysema pulmonum, pulmonary bulla, and pulmonary nodules. Among the patients with COVID-19, 340 (61.9 %) did not have any allergic disease previously. However, 43 (7.8 %) had urticaria, 8 (1.5 %) had atopic dermatitis, 62 (11.3 %) had eczema, 71 (12.9 %) had allergic rhinitis, and 25 (4.6 %) had other allergic disease (such as food allergy, drug allergy, eosinophilia, and high immunoglobulin E levels). Our results showed that people who had other allergic diseases had a decreased risk of COVID-19 (adjusted OR, 0.401; 95 % CI, 0.200–0.803) (Fig. 2).

3.3. COVID-19 outcomes according to treatment regimen

As shown in Table 1, among the patients in the cohort who had a confirmed COVID-19 diagnosis, 102 (18.6 %) were from the topical ointment group; 17 (3.1 %), from the acitretin group; 75 (13.7 %), from the methotrexate group; 61 (11.1 %), from the NB-UVB group; 38 (6.9 %), from the TNF-α inhibitor group; 200 (36.4 %), from the IL-17 inhibitor group; 42 (7.7 %), from the IL-23 inhibitor group; 14 (2.6 %), from the traditional Chinese medicine group. Multivariate analysis showed that IL-23 inhibitor treatment was a

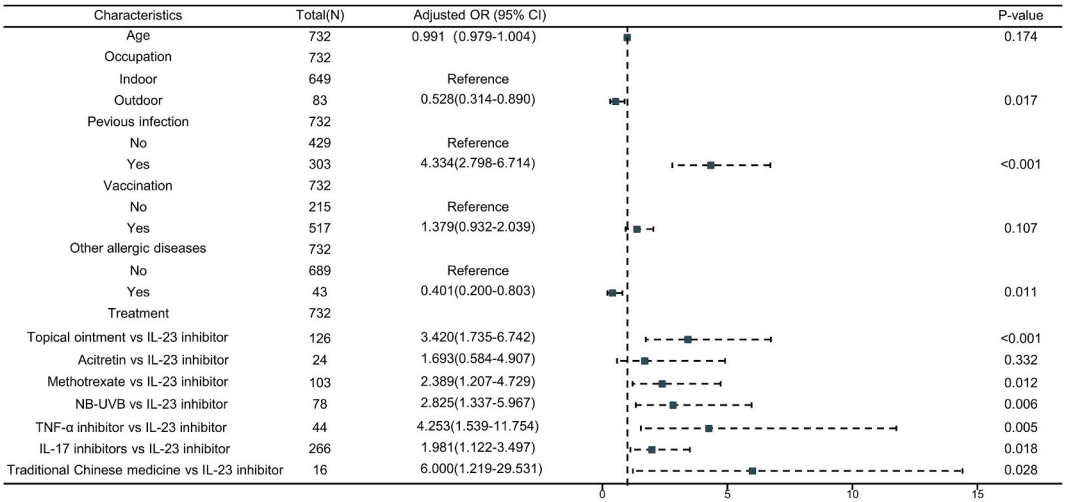


Fig. 2. Multivariable logistic regression assessing factors associated with COVID-19 infection comparing other treatments versus IL-23 inhibitor.
Multivariable logistic regression models were constructed with IL-23 inhibitor treatment as the independent variable, covid-19 infection as the dependent variable, and the following covariates: age, occupation, previous infection, vaccination, allergic diseases, topical ointment, acitretin, methotrexate, NB-UVB, TNF-α inhibitor, IL-17 inhibitors and traditional Chinese medicine. Adjusted odds ratios were computed for all treatment comparisons with the IL-23 inhibitor cohort. $P < 0.05$ was considered significant.
OR, odds ratio; CI, Confidence interval; NB-UVB, Narrow Bound Ultra Violet B; IL, interleukin; TNF, tumor necrosis factor.

Table 1
Descriptive characteristics of the study population.

Projects	All patients (n = 732)	Covid-19 (+) (n = 549)	Covid-19 (−) (n = 183)
Age (y),median(IQR)	48.0 (37.0–62.0)	46.0 (36.0–60.0)	53.0 (41.0–65.0)
BMI(kg/m^2),median(IQR)	23.8 (20.9–27.8)	23.7 (20.8–26.8)	24.1 (21.1–26.7)
Sex, no.(%)			
Male	518 (70.8 %)	384 (69.9 %)	134 (73.2 %)
Female	214 (29.2 %)	165 (30.1 %)	49 (26.8 %)
Occupation, no.(%)			
Indoor	649 (88.7 %)	496 (90.3 %)	153 (83.6 %)
Outdoor	83 (11.3 %)	53 (9.7 %)	30 (16.4 %)
Treatment, no.(%)			
Topical ointment	126 (17.2 %)	102 (18.6 %)	24 (13.1 %)
Acitretin	24 (3.3 %)	17 (3.1 %)	7 (3.8 %)
MTX	103 (14.1 %)	75 (13.7 %)	28 (15.3 %)
NB-UVB	78 (10.7 %)	61 (11.1 %)	17 (9.3 %)
TNF-α inhibitor	44 (6.0 %)	38 (6.9 %)	6 (3.3 %)
IL-17 inhibitors	266 (36.3 %)	200 (36.4 %)	66 (36.1 %)
IL-23 inhibitor	75 (10.2 %)	42 (7.7 %)	33 (18.0 %)
Traditional Chinese medicine	16 (2.2 %)	14 (2.6 %)	2 (1.1 %)

Table 2
Characteristics compared between COVID-19(+) and COVID-19(−) groups.

Projects	All patients (n = 732)	Covid-19 (+)			Covid-19 (−) (n = 183)
		PCR (n = 549)	Serology IgM(n = 549)	Serology IgG(n = 271)	Rapid test antigen (n = 536)	
Previous infection, no.(%)						
Yes	303 (41.4 %)	271 (49.4 %)	271 (49.4 %)	271 (100 %)	271(50.6 %)	32 (17.5 %)
No	429 (56.6 %)	278 (50.6 %)	278 (50.6 %)	–	265 (49.4 %)	151 (82.5 %)
Covid-19 vaccination, no.(%)						
Yes	517 (70.6 %)	399 (72.7 %)	–	–	–	118 (64.5 %)
No	215 (29.4 %)	150 (27.3 %)	–	–	–	65 (35.5 %)
Pulmonary disease, no.(%)						
None	498 (68.0 %)	372 (67.8 %)	–	–	–	126 (68.9 %)
COPD	13 (1.8 %)	8 (1.5 %)	–	–	–	5 (2.7 %)
Chronic bronchitis, no. (%)	80 (10.9 %)	65 (11.8 %)	–	–	–	15 (8.2 %)
Asthma	26 (3.6 %)	20 (3.6 %)	–	–	–	6 (3.3 %)
Others	115 (15.7 %)	84 (15.3 %)	–	–	–	31 (16.9 %)
Allergic disease, no.(%)						
None	446 (60.9 %)	340 (61.9 %)	–	–	–	106 (57.9 %)
Urticaria	59 (8.1 %)	43 (7.8 %)	–	–	–	16 (8.7 %)
AD	15 (2.0 %)	8 (1.5 %)	–	–	–	7 (3.8 %)
Eczema	76 (10.4 %)	62 (11.3 %)	–	–	–	14 (7.7 %)
Allergic rhinitis	94 (13.3 %)	71 (12.9 %)	–	–	–	23 (12.6 %)
Others	42 (5.7 %)	25 (4.6 %)	–	–	–	17 (9.3 %)

significant factor associated with a decreased risk of COVID-19 (Fig. 2): IL-23 inhibitor vs. topical ointment (adjusted OR, 3.420; 95 % CI, 1.735–6.742), IL-23 inhibitor vs. acitretin (adjusted OR, 1.693; 95 % CI, 0.584–4.907), IL-23 inhibitor vs. methotrexate (adjusted OR, 2.389; 95 % CI, 1.207–4.729), IL-23 inhibitor vs. NB-UVB: (adjusted OR, 2.825; 95 % CI, 1.337–5.967), IL-23 inhibitor vs. TNF-α inhibitor: (adjusted OR, 4.253; 95 % CI, 1.539–11.754), IL-23 inhibitor vs. IL-17 inhibitors (adjusted OR, 1.981; 95 % CI, 1.122–3.497), IL-23 inhibitor vs. traditional Chinese medicine (adjusted OR, 6.000; 95 % CI, 1.219–29.531). Thus, our results showed that treatment with IL-23 inhibitor was associated with a lower risk of COVID-19 than almost all the other treatments except acitretin.

No COVID-19-associated mortality occurred. Further, the need for medical interventions for COVID-19 was comparable between different groups, as shown in Table 3.

3.4. Symptoms of COVID-19 in different treatment groups

Table 3 presents the symptoms of COVID-19 in different treatment groups. Fever was the most common symptom, as it was found in 78.7 % of the patients, but the maximum temperature and duration of fever were comparable among the treatment groups (Table S3).

Compared to the IL-23 inhibitor group, the acitretin group had a higher incidence of fever, the IL-17 inhibitors group had a higher incidence of expectoration, and the traditional Chinese medicine group had a higher incidence of chest tightness. Among the 549 patients with COVID-19, only 22 (4 %) required medical intervention at a hospital. Antipyretics were the most common drugs used for COVID-19 treatment, and they were used in 42.5 % of the patients. The next most common drug was cough expectorant agents, and they were followed by traditional Chinese medicine, antibiotics, antiviral drugs, gamma globulin, glucocorticoids, and thymofaxin (Table S1). There was no significant difference in the proportions of patients using various COVID-19 medications among the psoriasis treatment groups.

Table 3
Symptoms of covid-19 infections in different groups.

Projects	All patients (n = 549)	Topical ointment (n = 102)	Acitretin (n = 17)	Methotrexate (n = 75)	NB-UVB (n = 61)	TNF-α inhibitor (n = 38)	IL-17 inhibitors (n = 200)	IL-23 inhibitor (n = 42)	Traditional Chinese medicine (n = 14)
Symptoms, no.(%)									
None	18 (3.3 %)	3 (2.9 %)	1 (5.9 %)	3 (4.0 %)	1 (1.6 %)	1 (2.6 %)	9 (4.5 %)	0 (0.0 %)	0 (0.0 %)
Fever	432 (78.7 %)	83 (81.4 %)	9 (52.9 %) *	51 (68.0 %)	53 (86.9 %)	33 (86.8 %)	159 (79.5 %)	35 (83.3 %)	9 (64.3 %)
Dizziness	152 (27.7 %)	30 (29.4 %)	4 (23.5 %)	17 (22.7 %)	17 (27.9 %)	9 (23.7 %)	60 (30.0 %)	12 (28.6 %)	3 (21.4 %)
Headache	184 (33.5 %)	35 (34.3 %)	5 (29.4 %)	24 (32.0 %)	21 (34.4)	11 (28.9 %)	68 (34.0 %)	17 (40.5 %)	3 (21.4 %)
Fatigue	329 (59.9 %)	64 (62.7 %)	10 (58.8 %)	41 (54.7 %)	36 (59.0 %)	21 (55.3 %)	129 (64.5 %)	21 (50 %)	7 (50.0 %)
Muscle soreness	294 (53.6 %)	54 (52.9 %)	11 (64.7 %)	33 (44.4 %)	35 (57.4 %)	22 (57.9 %)	109 (54.5 %)	23 (54.8 %)	7 (50.0 %)
Cough	375 (68.3 %)	69 (67.6 %)	9 (52.9 %)	57 (76.0 %)	41 (67.2 %)	25 (65.8 %)	135 (67.5 %)	29 (69.0 %)	10 (71.4 %)
Expectoration	233 (42.2 %)	46 (45.1 %)	6 (35.3 %)	31 (41.3 %)	22 (36.1 %)	18 (47.4 %)	83 (41.5 %) *	19 (45.2 %)	8 (57.1 %)
Pharyngalgia	169 (30.8 %)	31 (30.4 %)	5 (29.4 %)	22 (29.3 %)	17 (27.9 %)	9 (23.7 %)	68 (34.0 %)	12 (28.6 %)	5 (35.7 %)
Catarrhal symptoms	201 (36.6 %)	40 (39.2 %)	4 (23.5 %)	27 (36.0 %)	20 (32.8 %)	14 (36.8 %)	72 (36.0 %)	17 (40.5 %)	7 (50.0 %)
Decreased blood oxygen saturation	10 (1.8 %)	2 (2.0 %)	0 (0.0 %)	3 (4.0 %)	2 (3.3 %)	1 (2.6 %)	1 (0.5 %)	0 (0.0 %)	1 (7.1 %)
Increased heart rate	60 (10.9 %)	9 (8.8 %)	1 (5.9 %)	6 (8.0 %)	11 (18.0 %)	5 (13.2 %)	24 (12.0 %)	3 (7.1 %)	1 (7.1 %)
Shortness of breath	13 (2.4 %)	3 (2.9 %)	0 (0.0 %)	2 (2.7 %)	2 (3.3 %)	0 (0.0 %)	5 (2.5 %)	1 (2.4 %)	0 (0.0 %)
Dyspnea	16 (2.9 %)	4 (3.9 %)	1 (5.9 %)	1 (1.3 %)	2 (3.3 %)	0 (0.0 %)	7 (3.5 %)	1 (2.4 %)	0 (0.0 %)
Chest tightness	56 (10.2 %)	15 (14.7 %)	3 (17.6 %)	6 (8.0 %)	6 (9.8 %)	1 (2.6 %)	21 (10.5 %)	1 (2.4 %)	3 (21.4 %) *
Chest pain	21 (3.8 %)	4 (3.9 %)	1 (5.9 %)	2 (2.7 %)	0 (0.0 %)	0 (0.0 %)	13 (6.5 %)	1 (2.4 %)	0 (0.0 %)
Abnormal taste/ smell	136 (24.8 %)	26 (25.5 %)	1 (5.9 %)	21 (28.0 %)	18 (29.5 %)	9 (23.7 %)	49 (24.5 %)	9 (21.4 %)	3 (21.4 %)
Nausea	46 (8.4 %)	9 (8.8 %)	1 (5.9 %)	4 (5.3 %)	8 (13.1 %)	4 (10.5 %)	16 (8.0 %)	4 (9.5 %)	0 (0.0 %)
Diarrhea	76 (13.8 %)	14 (13.7 %)	2 (11.8 %)	3 (4.0 %)	11 (18.0 %)	7 (18.4 %)	28 (14.0 %)	6 (14.3 %)	5 (35.7 %)
Secondary bacterial infection	38 (6.9 %)	10 (9.8 %)	1 (5.9 %)	4 (5.3 %)	3 (4.9 %)	3 (7.9 %)	13 (6.5 %)	4 (9.5 %)	0 (0.0 %)
Others	9 (1.6 %)	2 (2.0 %)	0 (0.0 %)	1 (1.3 %)	1 (1.6 %)	1 (2.6 %)	4 (2.0 %)	0 (0.0 %)	0 (0.0 %)

3.5. Long COVID in different treatment groups

During the study period, we also collected 534 patients' data on their symptoms 4 weeks after their acute infection period (Table S2). As shown in Fig. 3, only 139 patients were asymptomatic after the infection, and the remaining patients had several symptoms of varying degrees that affected different systems. Among them, persistent cough was the most common symptom, as it was reported in 42.5 % of the patients. It was followed by fatigue, expectoration, and abnormal sense of smell and taste. These findings indicate that COVID-19 has a long-term impact on patients. Interestingly, 39.0 % of the patients treated with IL-23 inhibitor were asymptomatic after recovery, and this was significantly different from the percentage of asymptomatic patients in the methotrexate, NB-UVB, and TNF-α inhibitor groups. Patients treated with IL-23 inhibitor also had a lower incidence of fatigue, muscle aches, shortness of breath, diarrhea, and abnormal taste or smell after recovery than those who received other treatments, although the difference was not statistically significant. These findings indicate that there may be various persistent symptoms or sequelae after recovery from COVID-19, and that IL-23 inhibitor may, to a certain extent, reduce the occurrence of such symptoms.

4. Discussion

This is the first large-scale population-based cross-sectional cohort study to estimate COVID-19 outcomes among patients with psoriasis after the COVID-19 policy adjustment in China. Our results showed that, relative to other treatments, IL-23 inhibitor treatment in these patients conferred significant protection against COVID-19. Moreover, patients treated with IL-23 inhibitor were more likely to be asymptomatic after recovery than patients treated with methotrexate, NB-UVB or TNF-α inhibitor. With regard to risk mitigation behaviors, we found that patients who worked outdoors had a decreased risk of COVID-19 (adjusted OR, 0.528; 95 % CI, 0.314–0.890). Patients who work indoors may be exposed to an increased risk of infection due to poor air flow in indoor environments. We also found that there was no significant correlation between vaccination status and COVID-19 (adjusted OR, 1.379; 95 % CI, 0.932–2.039). As a large number of elderly patients in China are not vaccinated due to concerns for their chronic disease, this might have had an impact on our results. Moreover, our results showed that patients who had a prior SARS-CoV-2 infection did not seem to have a lower risk of infection during the study period. Several studies have assessed the characteristics of patients with COVID-19 reinfection, but the causes and risk factors of reinfection are still not fully understood [12–15]. We speculate that the reason for re-infection may be exposure to different strains.

Allergic diseases, characterized by type-2 polarization of the immune system, are considered as one of the major risk factors for severe COVID-19 [16]. Ren's study showed that while allergic rhinitis and asthma act as protective factors against COVID-19, asthma increases the risk of hospitalization for COVID-19 [17]. Further, Gani reviewed the risk of COVID-19 in patients with allergic rhinitis and found that allergic rhinitis seems to provide protection against COVID-19. In line with these studies, there is accumulating evidence to suggest that Th2-predominant inflammation may reduce the risk of COVID-19 and disease severity [18–20]. In our study, we did not find a relationship between COVID-19 and allergic rhinitis. However, our results showed that patients who had other allergic diseases had a lower risk of COVID-19 (adjusted OR, 0.401; 95 % CI, 0.200–0.803), and this is consistent with the findings of previous literature.

Various studies have demonstrated that the use of biological agents for the treatment of immune-mediated inflammatory disease is associated with a lower risk of COVID-19 [21–23]. However, most of our previous research only focused on the general risk of COVID-19 and its outcomes, and the risk associated with specific biological agents was not investigated. Nonetheless, Khalaf's study showed that treatment with TNF inhibitors were associated with a decreased risk of COVID-19-associated hospitalization relative to methotrexate treatment [11]. Further, a meta-analysis reported that the use of IL-17 inhibitors for psoriasis treatment does not increase the risk of COVID-19 or worsen the course of COVID-19 [8]. A nationwide cohort study in England assessed the risk of severe COVID-19 in adults with immune-mediated inflammatory diseases and in those on immune-modifying therapies. They found no increased risk of

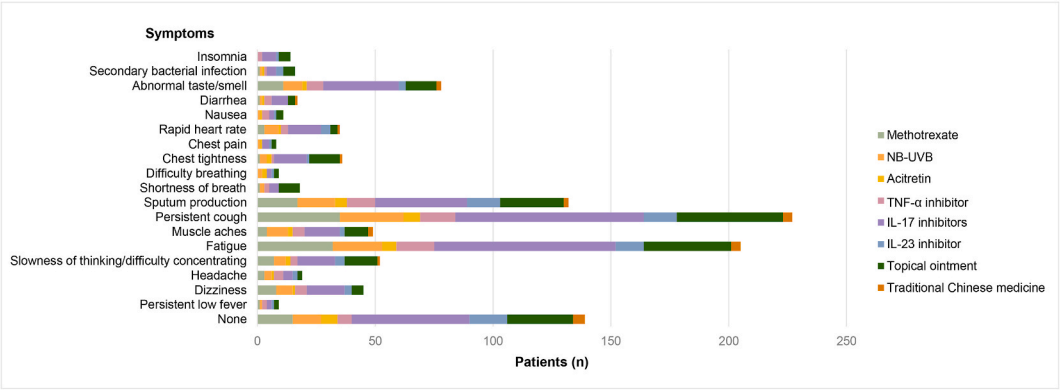


Fig. 3. Long COVID in different treatment groups. The ordinate represents different symptoms of long COVID, the abscissa represents the total number of patients with the symptoms. Different colors are used to distinguish the different treatment groups. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

adverse COVID-19 outcomes in those on most targeted immune-modifying drugs for immune-mediated inflammatory diseases compared with those on standard systemic therapy [24]. In the current study, multiple analyses were performed to compare the symptoms of COVID-19, COVID-19-associated medical interventions administered, mortality, and long COVID among patients treated with IL-23 inhibitor and other treatments. The results showed that IL-23 inhibitor treatment was associated with a decreased risk of COVID-19 compared to almost all other treatments except acitretin. Moreover, patients treated with IL-23 inhibitor were more likely to be asymptomatic after recovery than patients treated with methotrexate, NB-UVB, or TNF-α inhibitor. In agreement with our findings, it was reported that risankizumab (an IL-23 inhibitor) treatment in a patient with psoriasis did not worsen the clinical outcomes of COVID-19 [25]. Thus, based on these findings, IL-23 inhibitor could be positively considered in patients with psoriasis who need systemic treatment during periods when there is a surge in COVID-19 cases.

The main limitation of our study was its sampling bias. Although the general patient characteristics reflect the expected characteristics of a general psoriasis cohort with regard to age, sex, and BMI, our study did not investigate non-responders. Therefore, certain characteristics that could potentially influence our results may have been missed out. Also, our study was based on patient responses during surveys, which was also one of the limitations. Further, since a large number of elderly patients in China have not been vaccinated, correction for vaccination status is challenging and will have an impact on our results. Moreover, we were unable to evaluate the outcomes of COVID-19 in patients receiving treatments that are not commonly used in China, such as cyclosporine, fumaric acid ester, and other biological agents. As our study is mainly based on a questionnaire that was answered by the patients, we attribute the reason for the re-infection to be infection with different strains. We will conduct COVID-19 strain identification in the future to confirm our conjecture. Moreover, patients with re-infection could have genetic susceptibility to COVID-19 viruses, so we will conduct laboratory tests to validate this assumption too. The study was also limited by the small sample size of some treatment group. As only one IL-23 inhibitor-Ustekinumab was included in medical insurance during our study period and the price was relatively expensive, the number of patients who received IL-23 inhibitor treatment was relatively small, resulting in a smaller sample size for the IL-23 group. Further studies with larger sample sizes and longer follow-up periods are necessary to overcome this drawback and confirm the present findings. Besides, given the ongoing changes in the dynamics of the COVID-19 virus, the study's relevance may be diminished, and the data might not reflect the current situation.

In conclusion, the current large-scale, cross-sectional study revealed that compared to other treatment methods, IL-23 inhibitor treatment decreased the risk of COVID-19 and long COVID. These findings support the suggestion to avoid preventive cessation of IL-23 inhibitor treatment. In fact, in cases of moderate-to-severe plaque psoriasis that require systemic treatment, IL-23 inhibitor treatment should be positively considered. However, further studies with longer follow-up are warranted to provide broader insight into the influence of this class of drugs on COVID-19 risk.

Ethical approval

The research was approved by the Institutional Review Boards at all sites: Shanghai Skin Disease Hospital (#2020-36); Shanghai Tenth People's Hospital (#20KT110); Ruijin Hospital (#2020821); Huashan Hospital (#KY2021-733); Changhai Hospital (#2020-27); Yueyang Hospital of Integrated Traditional Chinese and Western Medicine (#2021-129).

Study ethics

The study was conducted according to the Declaration of Helsinki, and written informed consent was obtained from each participant.

Registration of clinical trial

ChiCTR2000036186.

Data availability statement

All data are already provided in the manuscript. For further if any may put a request to the corresponding author.

CRediT authorship contribution statement

Yifan Hu: Writing – review & editing, Writing – original draft. **Dawei Huang:** Investigation, Data curation. **Yuxiong Jiang:** Investigation, Data curation. **Qian Yu:** Validation, Resources. **Jiajing Lu:** Writing – review & editing, Supervision. **Yangfeng Ding:** Validation, Data curation. **Yuling Shi:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was sponsored by grants from the National Key Research and Development Program of China (2023YFC2508106), National Natural Science Foundation of China (No. 82073429, 82273510, 82203908, 82003334, 82003335), Innovation Program of Shanghai Municipal Education Commission (No.2019-01-07-00-07-E00046) , Clinical Research Plan of SHDC (No. SHDC2020CR1014B) and Program of Shanghai Academic Research Leader (No. 20XD1403300).

Appendix ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e24096.

References

[1] X. Ding, T. Wang, Y. Shen, et al., Prevalence of psoriasis in China: a population-based study in six cities, Eur. J. Dermatol. 22 (5) (2012) 663–667.
[2] C. Griffiths, et al., Psoriasis, Lancet (London, England) 397 (10281) (2021) 1301–1315.
[3] A.W. Armstrong, C. Read, Pathophysiology, clinical Presentation, and treatment of psoriasis: a review, JAMA 323 (19) (2020) 1945–1960.
[4] Ö. Kutlu, A. Metin, Dermatological diseases presented before COVID-19: are patients with psoriasis and superficial fungal infections more vulnerable to the COVID-19? Dermatol. Ther. 33 (4) (2020) e13509.
[5] M. Goldust, et al., Skin cancer and COVID-19, Dermatol. Ther. 33 (6) (2020) e14050.
[6] X. Gu, X. Chen, M. Shen, Association of psoriasis with risk of COVID-19: a 2-sample Mendelian randomization study, J. Am. Acad. Dermatol. 87 (3) (2022) 715–717.
[7] K.V. Kwee, et al., Prevalence, risk and severity of SARS-CoV-2 infections in psoriasis patients receiving conventional systemic, biologic or topical treatment during the COVID-19 pandemic: a cross-sectional cohort study (PsoCOVID), J. Dermatol. Treat. 34 (1) (2023) 2161297.
[8] M. Liu, et al., Risk of COVID-19 infection, hospitalization and mortality in psoriasis patients treated with interleukin-17 inhibitors: a systematic review and meta-analysis, Front. Immunol. 13 (2022) 1046352.
[9] J.J. Wu, et al., The risk of COVID-19 in patients with psoriasis: a retrospective cohort study, J. Am. Acad. Dermatol. 87 (6) (2022) 1395–1398.
[10] A. Thatiparthi, et al., Biologic treatment Algorithms for moderate-to-severe psoriasis with comorbid conditions and special populations: a review, Am. J. Clin. Dermatol. 22 (4) (2021) 425–442.
[11] K. Kridin, et al., Tumor necrosis factor inhibitors are associated with a decreased risk of COVID-19-associated hospitalization in patients with psoriasis-A population-based cohort study, Dermatol. Ther. 34 (4) (2021) e15003.
[12] P. Brouqui, et al., COVID-19 re-infection, Eur. J. Clin. Invest. 51 (5) (2021) e13537.
[13] X. Ren, et al., Reinfection in patients with COVID-19: a systematic review, Glob Health Res Policy 7 (1) (2022) 12.
[14] S. Sotoodeh Ghorbani, et al., Epidemiologic characteristics of cases with reinfection, recurrence, and hospital readmission due to COVID-19: a systematic review and meta-analysis, J. Med. Virol. 94 (1) (2022) 44–53.
[15] T.L. Dao, V.T. Hoang, P. Gautret, Recurrence of SARS-CoV-2 viral RNA in recovered COVID-19 patients: a narrative review, Eur. J. Clin. Microbiol. Infect. Dis. 40 (1) (2021) 13–25.
[16] M. De Filippo, et al., Allergy and COVID-19, Acta Biomed. 92 (S7) (2021) e2021522.
[17] J. Ren, et al., Impact of allergic rhinitis and asthma on COVID-19 infection, hospitalization, and mortality, J. Allergy Clin. Immunol. Pract. 10 (1) (2022) 124–133.
[18] Y. Adir, et al., Asthma and COVID-19: an update, Eur. Respir. Rev. 30 (162) (2021).
[19] S. Liu, et al., Prevalence of comorbid asthma and related outcomes in COVID-19: a systematic review and meta-analysis, J. Allergy Clin. Immunol. Pract. 9 (2) (2021) 693–701.
[20] J.M. Yang, et al., Allergic disorders and susceptibility to and severity of COVID-19: a nationwide cohort study, J. Allergy Clin. Immunol. 146 (4) (2020) 790–798.
[21] F. Fagni, et al., COVID-19 and immune-mediated inflammatory diseases: effect of disease and treatment on COVID-19 outcomes and vaccine responses, Lancet Rheumatol 3 (10) (2021) e724–e736.
[22] Z. Izadi, et al., Association between tumor necrosis factor inhibitors and the risk of hospitalization or death among patients with immune-mediated inflammatory disease and COVID-19, JAMA Netw. Open 4 (10) (2021) e2129639.
[23] S.K. Mahil, et al., Factors associated with adverse COVID-19 outcomes in patients with psoriasis-insights from a global registry-based study, J. Allergy Clin. Immunol. 147 (1) (2021) 60–71.
[24] B. MacKenna, et al., Risk of severe COVID-19 outcomes associated with immune-mediated inflammatory diseases and immune-modifying therapies: a nationwide cohort study in the OpenSAFELY platform, Lancet Rheumatol 4 (7) (2022) e490–e506.
[25] C.J. Wang, A.K. Truong, COVID-19 infection on IL-23 inhibition, Dermatol. Ther. 33 (6) (2020) e13893.