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ORIGINAL RESEARCH

Impact of Treatment Interruption on the Effectiveness of Interleukin (IL)-17A Inhibitors in Plaque Psoriasis: A Retrospective Analysis

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Background: Plaque psoriasis is a chronic, recurrent, immune-mediated inflammatory skin disease. This study aimed to investigate effectiveness of interleukin (IL)-17A inhibitor treatment and effectiveness after treatment interruption in plaque psoriasis patients and analyze the related factors.

Methods: This study retrospectively collected clinical characteristics and related treatment status of plaque psoriasis patients treated with IL-17A inhibitors, and evaluated the treatment effectiveness, reasons for treatment interruption, effectiveness after treatment interruption, and risk factors affecting treatment effectiveness.

Results: This study ultimately included 106 patients with plaque psoriasis, including 61 males (57.55%) and 45 females (42.45%), aged 41.0 (31.0–54.0) years and with a disease duration of 12.0 (8.0–20.0) months. Among them, 71 cases (67%) achieved PASI90 after receiving IL-17A inhibitor treatment, and 35 cases (33.02%) achieved PASI75. A total of 50 patients (50/106, 47.17%) interrupted treatment, 23 patients (23/50, 46%) maintained a therapeutic effect of PASI90 or above, and 27 patients (27/50, 54%) had a therapeutic effect lower than PASI75, with median time of treatment interruption of 1.0 (1.0–3.5) months. Univariate analysis findings showed that duration of IL-17A inhibitor treatment interruption and reasons for interruption had significant statistical significance on treatment effectiveness (all $P<0.05$). In multivariate analysis, treatment interruption (OR=7.154, 95% CI: 2.528–20.24) and reasons such as stress/anxiety (OR: 14.889, 95% CI: 1.160–23.480) were risk factors affecting treatment effectiveness.

Conclusion: Interleukin (IL)-17A inhibitor treatment interruption plays critical effects on the treatment of plaque psoriasis. Early and long-term adherence to IL-17A inhibitor treatment can control the course of the disease and improve the long-term health of psoriasis patients.

Keywords: plaque psoriasis, interleukin (IL)-17A inhibitors, interrupt, COVID-19 pandemic, treatment outcomes

Introduction

Plaque psoriasis is a chronic, recurrent, immune-mediated inflammatory skin disease.[1] The lesions show red scaly plaques, which are common in elbows, knees, trunk, scalp, etc. Plaque psoriasis affects about 29.5 million adults worldwide, and is often accompanied by a variety of comorbidities, resulting in a significant disease burden.[2] Usually, the treatment method follows the severity of the disease. In recent years, targeted therapy with biological agents has become an important means for the treatment of moderate and severe psoriasis. Interleukin 23 (IL-23)/helper T cell 17 (Th17) pathway, as a key pathway in the pathogenesis of plaque psoriasis, achieves therapeutic effect through targeted inhibition of inflammatory cytokines.[3] However, since the beginning of the 2019 coronavirus pandemic, psoriasis patients have been unable to maintain treatment due to COVID-19 infection, drug access problems, inconvenient treatment for patients, concerns about new coronavirus vaccination, safety issues of biological agent treatment and other reasons, which has a certain impact on the treatment effect.[4]

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There is a lack of data on the treatment of patients with IL-17A inhibitors during the COVID-19 pandemic. The purpose of this study is to study the course, persistence and related factors of plaque psoriasis patients receiving IL-17A inhibitor during the COVID-19 pandemic.

Materials and Methods

Patients

This study, as a single center, retrospective cross-sectional study, selected patients diagnosed with plaque psoriasis in the Dermatology Department of our Hospital from September 1, 2021 to March 1, 2023.

Ethical Statement

This study has been reviewed by the Ethics Committee of Liyang People's Hospital (Approval No. AF/SC-08/1.02023006). This study complies with the Declaration of Helsinki. Due to this is a retrospective study, we stated that we will keep the patients' medical records we have covered confidential.

Inclusive Criteria and Exclusive Criteria

Inclusion criteria: (1) Adults aged 18 and above. (2) After a diagnosis of moderate to severe plaque psoriasis, the patient received biological treatment for at least 3 months. The biological treatment consisted of interleukin-17A (IL-17A) inhibitors (such as Secukinumab and Ixekizumab). (3) Patients with complete treatment data, baseline clinical information, and contact information. (4) All patients achieved PASI75 or PASI90 after receiving treatment for 3 months. (5) All patients had unlimited treatment time and follow-up until December 31, 2023.

Exclusion criteria: (1) Unable to contact or unwilling to accept follow-up. (2) Stop treatment if adverse reactions occur during the process of receiving IL-17A inhibitors. (3) After receiving IL-17A inhibitors for 3 months, the target of PASI75 cannot be maintained, and other drugs are used for treatment.

Data Collection

This study analyzed the demographic characteristics, lifestyle habits, and clinical characteristics of patients. Demographic characteristics: age, sex, weight, comorbidity, vaccination of COVID-19 vaccine. Lifestyle habits: smoking history and drinking history. Clinical characteristics: Age of patients diagnosed as disease, total time of use of biologics, whether treatment has been interrupted, duration of treatment interruption, reasons for inability to maintain treatment, and clinical course after treatment interruption.

Observation Indicators

The present study evaluated the therapeutic effects of IL-17A inhibitors on patients with plaque psoriasis. This study also evaluated the reasons for patients' treatment interruption, changes in treatment effectiveness after interruption, and analyzed the risk factors that affect treatment effectiveness. In this study, "treatment interruption" was defined as the patient completely stopping the use of IL-17A inhibitors for ≥4 weeks for any reason, and not receiving other systemic biological agents during this period.

Statistical Analysis

Statistical analysis was conducted using SPSS 24.0 software. The descriptive analysis used ratio or rate (%) to represent categorical variables, and M (Q1, Q3) was used to describe continuous variables. Wilcoxon signed rank sum test was used for continuous variables, and Chi-square test or Fisher's exact test was used for categorical variables to compare the factors affecting treatment effectiveness. A p-value less than 0.05 was considered statistically significant. The univariate logistic regression analysis was performed by defining the baseline patient characteristics as independent variables and the inability of IL-17A inhibitor treatment to achieve PASI75 as the dependent variable. The significant correlation ($P<0.05$) in the univariate analysis was defined as the independent variable and the treatment effect as the dependent variable, and a multivariate logistic regression analysis was conducted to identify the risk factors affecting the treatment

effect. The results of categorical variables were expressed using odds ratios (OR) and their 95% confidence intervals (CI), with P<0.05 indicating the statistical significance. When the 95% CI was relatively large, the Bootstrap resampling technique was used to estimate the CI of parameters.

Results

Clinical Characteristics

A total of 123 patients received IL-17A inhibitor treatment, and 3 of them switched to other treatment methods due to ineffective treatment during the treatment process. The other patients had better tolerance. During follow-up, 8 patients did not respond to questionnaire and telephone surveys, and 6 patients were lost to follow-up. Finally, this study included 106 eligible patients, including 61 males (57.55%) and 45 females (42.45%), with a median age of 41.0 (31.0–54.0) years and a median duration of illness of 12.0 months (8.0–20.0). Meanwhile, the sample size of the involved patients has been calculated, suggesting that the sample of 106 patients is adequate to detect the meaningful differences or associations. A total of 63 cases (59.43%) had moderate disease severity, while 43 cases (40.57%) had severe disease severity. A total of 71 patients (67.0%) achieved PASI90 after receiving IL-17A inhibitor treatment, and 35 patients (33.0%) achieved PASI75. A total of 27 cases (25.47%) received treatment with Ixekizumab, with 18 cases (18/27, 67%) achieving a PASI90 therapeutic effect and 9 cases (9/27, 33%) achieving a PASI75 therapeutic effect. A total of 79 cases (74.53%) received treatment with secukinumab, with 53 cases achieving PASI90 (53/79, 67%) and 26 cases (26/79, 33%) achieving PASI75. Among the patients using IL-17A inhibitors, 57 (53.77%) maintained treatment for at least 1 year, of which 36 (63.16%) maintained PASI90 effectiveness and 21 (36.84%) maintained PASI75 effectiveness. All above results were shown in the Table 1.

Table 1 The Basic Characteristics of IL-17A Inhibitor Used by Patients During the COVID-19 Pandemic

	Total (n=106)	PASI90 or More (n=71)	PASI75 (n=35)	χ^2/Z	P
Age	41(31.00–54.00)	40(31.00–58.00)	43 (33.50–53.00)	0.430[a]	0.667
Gender				0.129[b]	0.835
Male	61 (57.55%)	40 (56.34%)	21 (60.00%)		
Female	45 (42.45%)	31 (43.66%)	14 (40.00%)		
Time of illness (month)	12 (8.00–20.00)	12(8.00–17.00)	15 (9.00–21.00)	1.545[a]	0.122
Smoking				1.133[b]	0.587
Never	65 (61.32%)	44 (61.97%)	21 (60.00%)		
Occasionally	25 (23.58%)	18 (25.35%)	7 (20.00%)		
Often	16 (15.09%)	9 (12.68%)	7 (20.00%)		
Drinking				0.620[b]	0.779
Never	64 (60.38%)	42 (59.15%)	22 (62.86%)		
Occasionally	10 (9.43%)	6 (8.45%)	4 (11.43%)		
Often	32 (30.19%)	23 (32.39%)	9 (25.71%)		
Weight				2.048[b]	0.374
Normal	76 (71.70%)	54 (76.06%)	22 (62.86%)		
Overweight	11 (10.38%)	6 (8.45%)	5 (14.29%)		
Obesity	19 (17.92%)	11 (15.49%)	8 (22.86%)		
Complication				2.695[b]	0.777
No	69 (65.09%)	45 (63.38%)	24 (68.57%)		
Hypertension	17 (16.04%)	12 (16.90%)	5 (14.29%)		
Diabetes	6 (5.66%)	4 (5.63%)	2 (5.71%)		
Hyperlipidemia	5 (4.72%)	4 (5.63%)	1 (2.86%)		
Renal insufficiency	3 (2.83%)	1 (1.41%)	2 (5.71%)		
Cardiovascular disease	6 (5.66%)	5 (7.04%)	1 (2.86%)		

(*Continued*)

Table 1 (Continued).

	Total (n=106)	PASI90 or More (n=71)	PASI75 (n=35)	χ^2/Z	P
IL-17A inhibitors					
Ixekizumab	27 (25.47%)	18 (25.35%)	9 (25.71%)	0.002[b]	0.968
Sikuximab	79 (74.53%)	53 (74.65%)	26 (74.29%)		
Total time of using L-17A inhibitor				1.490[b]	0.705
>3 months, ≤6 months	20 (18.87%)	15 (21.13%)	5 (14.29%)		
>6 months, ≤12 months	29 (27.36%)	20 (28.17%)	9 (25.71%)		
>12 months	57 (53.77%)	36 (50.70%)	21 (60.00%)		
Severity of illness before treatment				1.389[b]	0.294
Moderate (BSA: 3–10%)	63 (59.43%)	45 (63.4%)	18 (51.4%)		
Severe (BSA: ≥10%)	43 (40.57%)	26 (36.6%)	17 (48.6%)		

Note: BSA: body surface area; [a]Z value, [b]χ^2 value.

Patients' Treatment Interruption

Among patients receiving IL-17A inhibitor treatment, 50 cases (50/106, 47.17%) interrupted treatment (31 males and 19 females), of which 23 cases (23/50, 46%) maintained effectiveness above PASI90, and 27 cases (27/50, 54%) had effectiveness lower than PASI75 (Table 2). The median month for treatment interruption was 1.0 (1.0–3.5). Among the 50 patients who interrupted treatment, 31 patients because of COVID-19 infection, 7 patients were unable to obtain drugs, 3 patients had economic reasons, and 10 patients had their own reasons (anxiety/worry/stress, etc) (Table 2).

Analysis of Reasons for Effect of IL-17A Inhibitor on Treatment Effectiveness

The univariate logistic regression results showed that the duration of interrupted IL-17A inhibitors (OR=0.205, 95% CI: 0.092–0.459), treatment stop (OR=0.142, 95% CI: 0.056–0.361), and stress/anxiety (OR=0.048, 95% CI: 0.006–0.404) had a significant effect on treatment effectiveness (Table 3). However, there was no statistical significance whether there was COVID-19 infection (OR=0.856, 95%: 0.354–2.065) (Table 3). The multivariate logistic regression results showed that after incorporating multiple variables, treatment interruption (OR=7.154, 95% CI: 2.528–20.248) and stress/anxiety (OR: 14.889, 95% CI: 1.160–23.480) were identified as risk factors affecting treatment effectiveness (Table 4). Among the enrolled cases in this study, there were 7 patients who interrupted treatment during the follow-up period due to inability to obtain medication, and 3 patients due to economic reasons (Table 4). Due to the small number of cases, they were not included in the regression analysis.

Table 2 Basic Information on Interruption of IL-17A Inhibitor Treatment in Patients

	Total (n=106)	PASI90 or more (n=71)	Less than PASI75 (n=35)	χ^2/Z	P
Gender				0.129[b]	0.835
Male	61 (57.55%)	40 (56.34%)	21 (60.00%)		
Female	45 (42.45%)	31 (43.66%)	14 (40.00%)		
Interruption time (month)	0.00 (0.00–1.00)	0.00 (0.00–1.00)	1.00 (1.00–3.50)	5.590[a]	<0.001
Treatment interruption				18.838[b]	<0.001
No	56 (52.83%)	48 (67.61%)	8 (22.86%)		
Yes	50 (47.17%)	23 (32.39%)	27 (77.14%)		
Treatment interruption reason				34.576[b]	<0.001
No.	56 (52.83%)	49 (69.01%)	7 (20.00%)		
COVID-19 infection	31 (29.25%)	20 (28.17%)	11 (31.43%)		
Unable to obtain medication	7 (6.60%)	2 (2.82%)	5 (14.29%)		
Economic reasons	3 (2.83%)	0 (0.00%)	3 (8.57%)		
Anxiety/worry/stress	10(9.43%)	1 (1.41%)	9 (25.71%)		

Note: [a]Z value, [b]χ^2 value.

Table 3 Univariate Logistic Analysis of the Efficacy of IL-17A Inhibitor Therapy in Patients

Independent Variable	OR (95% CI)	*P*
Interruption time (month)	0.205 (0.092–0.459)	<0.001
Treatment interruption	0.142 (0.056–0.361)	<0.001
COVID-19 infection	0.856 (0.354–2.065)	0.729
Stress/anxiety	0.048 (0.006–0.404)	<0.005

Table 4 Multivariate Logistic Analysis of the Efficacy of IL-17A Inhibitor Therapy in Psoriasis Patients

Independent Variable	OR (95% CI)	*P*
Interruption time (month)	0.129 (0.011–1.456)	0.099
Treatment interruption		
No	1	
Yes	7.154 (2.528–20.248)	<0.001
Stress/anxiety		
No	1	
Yes	14.889 (1.160–23.480)[a]	0.004[a]

Note: [a]Bootstrap Heavy self-service sampling.

Discussion

The outbreak of the COVID-19 pandemic has increased the risk of treatment interruption for patients with psoriasis. Existing studies mostly focus on efficacy and safety during continuous treatment or the incidence of drug interruption. However, this study explores the heterogeneous effects of IL-17A inhibitor treatment interruption on patients, their impact on loss of response, and the impact on the efficacy after drug interruption in COVID-19 infected patients who have been vaccinated. This study showed that the use of IL-17A inhibitors has achieved significant therapeutic effects in the treatment of plaque-like moderate to severe psoriasis. Among the 123 patients who received biologics, except for 3 who were ineffective, all patients achieved PASI75 effectiveness. A total of 57 psoriasis patients who have been continuously using IL-17A inhibitors for one year have achieved ideal therapeutic effects without experiencing adverse reactions. Since patients who discontinued the use of IL-17A inhibitors due to adverse reactions have already been excluded according to the exclusion criteria, this study did not conduct a detailed analysis of treatment interruptions caused by adverse drug reactions. This study mainly focuses on treatment interruptions not related to safety (such as COVID-19 infection, psychological factors, etc), rather than the safety of drugs. Actually, common adverse drug reactions of IL-17A inhibitors (such as Candida infection, injection site reactions) are usually mild to moderate and controllable. In clinical studies evaluating the effectiveness and safety of biologics, Huang et al[5] extended the duration of treatment to range from 3 months to a maximum of 5 years. This indicates the safety and effectiveness of IL-17A inhibitors. Therefore, adverse drug reactions were not the main driving factors for drug interruption in the study cohort. IL-17A inhibitors have become an important treatment for psoriasis. During the COVID-19, many patients and medical staff raised whether the use of IL-17A inhibitors had the risk of infection with COVID-19. A large number of studies have shown that the use of IL-17A inhibitors will not increase the susceptibility of COVID-19 and the severity of COVID-19.[6,7]

During the COVID-19 epidemic, doctors advised patients not to stop using IL-17A inhibitors because of COVID-19 infection. However, according to the follow-up results, there were still 31 patients who stopped treatment due to COVID-19 infection (Table 1). There are mainly three categories of reasons for the interruption of COVID-19-related treatment: COVID-19 infection (for patients with mild symptoms, the treatment is suspended, and the infection is given priority; for patients with severe symptoms, they need to be hospitalized for treatment, and the drug withdrawal time is extended), the crunch of medical resources (during the pandemic, due to isolation policies and the limited admission capacity of

hospitals, patients are unable to attend follow-up appointments on time or obtain medications), and concerns about vaccination (due to short-term discomfort after vaccination, such as redness and swelling at the injection site, patients stop taking the medications on their own, but there are no serious adverse reactions). There are also factors for interruptions that are not related to COVID-19, including difficulties in obtaining medications, economic burdens, psychological stress, and so on. However, this study did not conduct data analysis on the susceptibility of patients with psoriasis who used IL-17A inhibitors to COVID-19. According to the relevant foreign guidelines,[8] in order to maintain the therapeutic effect, patients who used biological agents should first treat the infection and isolate them at home after infecting COVID-19. In this study, in order to ensure the effectiveness, we monitored the patients infected with COVID-19 and learned about the relevant clinical conditions. After that, we let the patients first receive treatment for COVID-19 infection. It is recommended to interruption treatment when the clinical symptoms are serious and maintain treatment for mild symptoms. The results showed that there was no statistical significance between whether COVID-19 was infected or not and the effectiveness of IL-17A biological agents in the Univariate logistic analysis (P=0.729). Meanwhile, the results of this study showed that after patients interrupted treatment, the median interruption time for achieving PASI90 or above was 0.00 (0.00–1.00) months, and the median interruption time for achieving PASI75 was 1.00 (1.00–3.50) months. There was a difference in the duration of interruption and treatment effectiveness.

The COVID-19 pandemic in 2019 has also had a negative impact on the compliance of psoriasis patients with biologic therapy. In this study, 50 patients (47.17%) interrupted treatment, and 31 patients were interrupted due to COVID-19 infection. At the beginning of the COVID-19 pandemic, 28% of psoriasis patients receiving biological agents were interrupted by Yalici-Armagan.[9] These results indicate that the COVID-19 is a serious challenge for psoriasis patients who use biological agents. Compared with Yalici-Armagan's report,[9] our study indicated that 10 psoriasis patients interrupted treatment due to self-reasons such as stress/anxiety/depression, which was an important independent risk factor affecting the effectiveness of IL-17A inhibitor therapy. This study did not separately investigate factors such as stress, anxiety, and depression, and the sample size was small, which has certain limitations. However, its results are consistent with Topaloğlu Demir et al's report,[10] which shows that the risk factors for clinical recurrence caused by interrupting biologic therapy are the presence of additional triggering factors (including stress, infection, and other related factors) and the use of alcohol. However, in this study, there was no significant correlation between alcohol and treatment effectiveness in both univariate and multivariate logistic regression analyses, which may be due to the heterogeneity of risk factors caused by differences in culture or lifestyle. In addition, during the clinical follow-up of this study, we found that patients would request to stop treatment from their doctors, as the skin lesion clearance rate almost reached PASI100 and they believed they had recovered. At this point, clinical doctors need to communicate with patients to improve their treatment compliance.[11] Therefore, with the COVID-19 pandemic, understanding and addressing the non-sustained risk factors for psoriasis treatment is crucial for improving medication behavior.

Psoriasis, as a chronic and recurrent skin disease, has a long-term treatment time. Although research is underway on patients stopping or reducing treatment doses after achieving treatment goals with biologics, the optimal time has not yet been determined. The research results of Topaloğlu Demir et al[10] indicate a significant correlation between the total time of discontinuing biologics and clinical skin lesion recurrence. In this study, 50 patients (47.17%) interrupted the use of biologics, 27 patients experienced a decrease in treatment effectiveness from PASI90 to PASI75, and 23 patients maintained PASI90. The underlying mechanism may lie in that patients who maintained PASI 90 might have more thoroughly cleared the inflammatory cells during IL-17 treatment period, while those with a decline in efficacy might have a residual inflammatory microenvironment that has not been completely suppressed. Furthermore, patients who interrupted the treatment due to psychological factors were more prone to recurrence (OR=14.889) in this study, which may be related to the activation of the IL-17 pathway by stress hormones. In the multivariate logistic regression analysis, there was no statistically significant correlation between the duration of interruption of IL-17A inhibitors and clinical effectiveness. According to the consensus of the International Psoriasis Council (IPC), relapse should be defined as "an increase in the PASI score by ≥50% compared to the lowest value or an absolute PASI score ≥5".[2] Therefore, we consider that although it did not increase the baseline indicators by 50%, the efficacy decreased to PASI75 indicating the loss of response of PASI (LOR), as Smith et al's report.[12] Although a decrease from a PASI 90 response may not be directly equivalent to recurrence as defined in the traditional sense, the increase in disease activity it reflects still holds clinical

significance (for example, a decline in the patient's quality of life and an increase in the inflammatory burden).[12] There was no obvious clinical relapse and no correlation with clinical effectiveness, but there was decreased PASI90, the key factor of which may be the shorter duration of drug interruption.

There are differences in median interruption time required to achieve PASI90 vs PASI75 after treatment resumption. This may be due to the drug's half-life and residual effects. IL-17A inhibitors have a relatively long half-life. Stopping the drug for a short period of time cannot completely eliminate the drug's effects, and it can still maintain some of the therapeutic efficacy. Patients who achieved PASI 90 after resuming treatment have inhibited the formation of the "immune memory" of skin inflammation through early treatment. The residual immunomodulatory effect after drug interruption is stronger, which delays the rebound of the disease. In a summary analysis of a Phase III study, the median time for PASI 50 response to disappear after interruption of IL-17A biologics was approximately 3.75 months.[13] In a prospective international cohort, the drug retention rate (probability of continuing treatment) of psoriasis patients using biologics within the first 3 years of treatment was studied, which was associated with the composite endpoint of interruption. In this study, Secukinumab was associated with a lower risk of the composite endpoint. The most common outcome was interruption, and the results showed that the interruption time of Secukinumab was 9.25 months, with an interruption risk comparable to that of Ustekinumab.[14] Early intervention with IL-17 inhibitors may promote the sustained maintenance of lesion clearance in patients by inhibiting the establishment of inflammatory memory in psoriatic skin tissue. In this study, the onset time (months) of psoriasis patients was 12 (8.0–20.0), and the therapeutic effect reached PASI75.

The PASI 90 response rate in the Secukinumab group (n=79, 53/79) and the Ixekizumab group (n=27, 18/27) was both 67%, suggesting that there was no significant difference in the short-term therapeutic effects between the two types of drugs (P>0.05). The half-life of Ixekizumab (~13 days) is shorter than that of Secukinumab (~27 days), which may lead to differences in the duration of the therapeutic effect after drug withdrawal. However, in this study, perhaps due to the small sample size of Ixekizumab (n=27), no statistical significance was observed. In subsequent studies, the sample size should be expanded to clarify the dynamic changes in the therapeutic effect of the two types of drugs after drug withdrawal. The STEPIn studies[15,16] showed that after 52 weeks of treatment with Secukinumab, all 20 gene sets selected from the MAD-5 transcriptome at the lesion site in newly diagnosed (disease course≤ 1 year) adult patients with moderate to severe plaque psoriasis returned to a non-lesion state,[17] suggesting that Secukinumab has the potential to reverse the course of psoriasis at the DNA level and achieve immune modification. Early initiation of biologic therapy and increased opportunities for disease modification have become major trends in the treatment of psoriasis. Early use of biologics can not only control the condition, achieve treatment goals, but also improve long-term health outcomes.[18]

PASI score is currently the most widely used assessment indicator of disease severity in clinical studies of psoriasis. PASI score takes into account degree of erythema, infiltration, and desquamation of the skin lesions, as well as the affected area, and can objectively and standardly reflect the treatment effect of psoriasis. Therefore, it is used as the main efficacy assessment indicator in this study. Certainly, we recognize the value of body surface area (BSA) and dermatology life quality index (DLQI) in evaluating treatment effect of psoriasis. The reasons for not using these scores are as follows: First, since this study is a retrospective study, the data mainly come from electronic medical records and follow-up records, and BSA and DLQI score data were not completely collected in patients' medical records. To maintain consistency and integrity of data, we chose to use PASI score, which is an indicator with complete and reliable data. Second, this study mainly focuses on the changes in the efficacy of IL-17A inhibitors in relieving psoriasis skin lesions and after the interruption of treatment, and the PASI score has good sensitivity in reflecting the range of skin lesions, erythema, scaling, and degree of infiltration. Based on these two points, we believe that the PASI score can effectively evaluate the main research objectives in this study. In this study, we indeed did not conduct a separate analysis of the efficacy in specific difficult-to-treat areas (such as the scalp, nails, hands, and feet, etc). The main reason is that in this retrospective study, the detailed information on the distribution of skin lesions of the patients is limited. Therefore, it is impossible to directly analyze the impact of difficult-to-treat areas on the maintenance of the therapeutic effect after treatment interruption, which is one of the limitations of this study. Nevertheless, the PASI score has been widely used to evaluate the systemic treatment effect of psoriasis and has been used as the main efficacy indicator in clinical studies of IL-17A inhibitors.[3] In this study, although the overall

PASI score met the standard (such as PASI90), the remaining lesions in difficult-to-treat areas may affect the patients' subjective feelings or accelerate LOR. Some previous studies[19–22] pointed out that the remaining lesions in difficult-to-treat areas such as the scalp or nails may accelerate the loss of response, even if the overall PASI score is high. Future studies will incorporate site-specific assessment indicators (such as the scalp PASI and the Nail Psoriasis Severity Index [mNAPSI]) to more comprehensively evaluate the impact after treatment interruption. Although this study did not directly record lesion distribution in difficult-to-treat areas, it still provides the following implications for clinical practice. In one aspect, doctors need to assess whether patients have lesions in refractory areas before drug withdrawal and inform them of the potential risk of recurrence. In another aspect, targeted examinations for local lesions (such as dermoscopy of the scalp and nails) should be increased for patients who stop taking drugs to make up for the limitations of the PASI score.

This study has important research and clinical guiding significance. First, it fills the gap in correlation of mechanisms and clarifies that psychological stress is a risk factor for the decline in efficacy after treatment interruption, which is independent of infection and economic factors. Second, it quantifies the impact of short-term interruption (≤3 months) and long-term interruption (>3 months) on the maintenance rate of PASI90 (46% vs 27%), providing a basis for formulating individualized drug interruption strategies in clinical practice. Third, it confirms that against the backdrop of an extremely high vaccination rate, COVID-19 infection does not significantly reduce the efficacy, supports the safety of biological agents during the pandemic, and alleviates the doctor-patient conflict caused by patients' voluntary drug interruption due to concerns about infection.

Of course, this study has certain limitations. First, as a single-center retrospective study, small sample sizes and some confounding factors are inevitable In the future, the sample size can be expanded through multi-center cooperation, and patients from different regions, ethnic groups, and economic backgrounds can be included to verify the universality of the results. Second, the practicality of using PASI score alone to judge treatment effectiveness is limited. In addition to PASI score, we will integrate the BSA, the DLQI, and patient-reported outcomes (PROs) to comprehensively assess the physical and psychological impacts of treatment interruption. Furthermore, we will formulate individualized treatment decisions for patients, such as developing a biomarker-driven predictive model to identify patients with a high risk of recurrence after drug interruption. Third, this study only explored effect of IL-17 inhibitor treatment interruption on plaque psoriasis, but no other biologic treatments investigated. In future studies, TNF-α inhibitors, IL-23 inhibitors, and JAK inhibitors will be used to explore their effects on plaque psoriasis after drug interruption, and to evaluate the relevant mechanisms of the impact of interrupting different biological agents.

Conclusion

Interleukin (IL)-17A inhibitor treatment interruption plays critical effects on the treatment of plaque psoriasis. Early and long-term adherence to IL-17A inhibitor treatment can control the course of the disease and improve the long-term health of patients, to achieve disease modification of psoriasis as early as possible. Improving the continuity and compliance of treatment is a new challenge that requires healthcare professionals and patients to jointly take relevant measures, such as using remote medical consultation, increasing psychosocial support, and providing clear information on the safety of using biologics, to minimize the negative impact of patient compliance.

Data Sharing Statement

Datasets used and/or analyzed in this study are available from the corresponding author on reasonable request.

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Disclosure

All of the authors declare no conflict of interests.

References

1. Białecka A. Evaluation of pancreatic function in patients with plaque psoriasis. *Postepy Dermatol Alergol*. 2023;40:372–376. doi:10.5114/ada.2023.129400
2. Parisi R, Iskandar IYK, Kontopantelis E, et al. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. *BMJ*. 2020;369:m1590. doi:10.1136/bmj.m1590
3. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80:1029–1072.
4. Oguz Topal I, Kara Polat A, Zindancı İ, et al. Adherence to systemic therapy in patients with psoriasis during the COVID-19 pandemic: a multicenter study. *J Cosmet Dermatol*. 2022;21:39–47. doi:10.1111/jocd.14610
5. Huang YW, Tsai TF. Remission duration and long-term outcomes in patients with moderate-to-severe psoriasis treated by biologics or tofacitinib in controlled clinical trials: a 15-year single-center experience. *Dermatol Ther*. 2019;9:553–569. doi:10.1007/s13555-019-0310-5
6. MacKenna B, Kennedy NA, Mehrkar A, 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*. 2022;4:e490–506. doi:10.1016/S2665-9913(22)00098-4
7. Pahalyants V, Murphy WS, Klebanov N, et al. Immunosuppressive biologics did not increase the risk of COVID-19 or subsequent mortality: a retrospective matched cohort study from Massachusetts. *J Am Acad Dermatol*. 2022;86:252–255.
8. Gelfand JM, Armstrong AW, Bell S, et al. National Psoriasis Foundation COVID-19 task force guidance for management of psoriatic disease during the pandemic: version 1. *J Am Acad Dermatol*. 2020;83:1704–1716.
9. Yalici-Armagan B, Tabak GH, Dogan-Gunaydin S, et al. Treatment of psoriasis with biologics in the early COVID-19 pandemic: a study examining patient attitudes toward the treatment and disease course. *J Cosmet Dermatol*. 2021;20:3098–3102.
10. Topaloğlu Demir F, Polat Ekinci A, Aytekin S, et al. Clinical course of psoriasis patients that discontinued biologics during the COVID-19 pandemic. *J Cosmet Dermatol*. 2023;22:722–731. doi:10.1111/jocd.15638
11. Zolnierek KB, Dimatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care*. 2009;47:826–834. doi:10.1097/MLR.0b013e31819a5acc
12. Smith CH, Jabbar-Lopez ZK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol*. 2017;177:628–636. doi:10.1111/bjd.15665
13. Chiu HY, Hui RC, Tsai TF, et al. Predictors of time to relapse following ustekinumab withdrawal in patients with psoriasis who had responded to therapy: an 8-year multicenter study. *J Am Acad Dermatol*. 2023;88:71–78. doi:10.1016/j.jaad.2019.01.035
14. Thein D, Rosenø NAL, Maul JT, et al. Drug survival of Adalimumab, Secukinumab, and Ustekinumab in psoriasis as determined by either dose escalation or drug discontinuation during the first 3 years of treatment—a Nationwide Cohort Study. *J Invest Dermatol*. 2023;143:2211–8.e4. doi:10.1016/j.jid.2023.04.009
15. Iversen L, Conrad C, Eidsmo L, et al. Secukinumab demonstrates superiority over narrow-band ultraviolet B phototherapy in new-onset moderate to severe plaque psoriasis patients: week 52 results from the STEPIn study. *J Eur Acad Dermatol Venereol*. 2023;37:1004–1016. doi:10.1111/jdv.18846
16. Iversen L, Eidsmo L, Austad J, et al. Secukinumab treatment in new-onset psoriasis: aiming to understand the potential for disease modification - rationale and design of the randomized, multicenter STEPIn study. *J Eur Acad Dermatol Venereol*. 2018;32:1930–1939. doi:10.1111/jdv.14979
17. Tian S, Krueger JG, Li K, et al. Meta-analysis derived (MAD) transcriptome of psoriasis defines the "core" pathogenesis of disease. *PLoS One*. 2012;7:e44274.
18. Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: a Review. *JAMA*. 2020;323:1945–1960. doi:10.1001/jama.2020.4006
19. van de Kerkhof PCM, Loewe R, Mrowietz U, et al. Quality of life outcomes in adults with moderate-to-severe plaque psoriasis treated with dimethylfumarate (DMF): a post hoc analysis of the BRIDGE study. *J Eur Acad Dermatol Venereol*. 2020;34:119–126. doi:10.1111/jdv.15922
20. van de Kerkhof P, Guenther L, Gottlieb AB, et al. Ixekizumab treatment improves fingernail psoriasis in patients with moderate-to-severe psoriasis: results from the randomized, controlled and open-label phases of UNCOVER-3. *J Eur Acad Dermatol Venereol*. 2017;31:477–482. doi:10.1111/jdv.14033
21. Rich P, Gooderham M, Bachelez H, et al. Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with difficult-to-treat nail and scalp psoriasis: results of 2 phase III randomized, controlled trials (ESTEEM 1 and ESTEEM 2). *J Am Acad Dermatol*. 2016;74:134–142. doi:10.1016/j.jaad.2015.09.001
22. Bakirtzi K, Sotiriou E, Vakirlis E, et al. When the low may still be high: the heavy burden of residual psoriasis in difficult-to-treat areas despite a low DLQI score among patients under biologics or apremilast: a 5-year, prospective, case-control study. *J Eur Acad Dermatol Venereol*. 2022;36:e145–7. doi:10.1111/jdv.17703