

# Evaluating the Role of Disease Duration in Systemic Therapy Response Among Patients with Moderate-to-Severe Psoriasis

Min Dai<sup>1,2</sup>, Yuxiong Jiang<sup>1,2</sup>, Yujing Xi<sup>3</sup>, Lezhen Xu<sup>4</sup>, Dawei Huang<sup>1,2</sup>, Yu Wang<sup>1,5</sup>, Yifan Hu<sup>1,5</sup>, Qian Yu<sup>1,2,5</sup>, Yuling Shi<sup>1,2,5</sup>

<sup>1</sup>Department of Dermatology, Shanghai Skin Disease Hospital, Tongji University School of Medicine, Shanghai, People's Republic of China; <sup>2</sup>Institute of Psoriasis, Tongji University School of Medicine, Shanghai, People's Republic of China; <sup>3</sup>Kashi Prefecture Second People's Hospital, Kashi, Xinjiang, People's Republic of China; <sup>4</sup>Department of Dermatology, The Third Affiliated Hospital of Naval Medical University, Shanghai, People's Republic of China; <sup>5</sup>Psoriasis Clinical Research Center, Tongji University, Shanghai, People's Republic of China

Correspondence: Yuling Shi; Qian Yu, Shanghai Skin Disease Hospital, Tongji University School of Medicine, Shanghai, 200443, People's Republic of China, Email shiyuling1973@tongji.edu.cn; yuervictory@163.com

**Background:** Psoriasis is a chronic immune-mediated inflammatory disease. Systemic therapy is usually applicable to patients who have failed topical treatment or phototherapy, but the value of early systemic therapy remains unclear.

**Purpose:** This study aimed to evaluate the impact of disease duration on the clinical efficacy and patients reported outcomes in moderate to severe psoriasis patients treated with systemic agents.

**Methods:** Our research was based on the SPEECH, an observational, prospective, multicenter registry. Adult patients with moderate to severe psoriasis receiving systemic therapy (including biologics, methotrexate or acitretin) were divided into groups based on disease duration: <2 years, 2–10 years, and ≥10 years. The clinical efficacy was assessed using PASI (Psoriasis Area and Severity Index), BSA (Body Surface Area), PGA (Physician Global Assessment). The Dermatology Life Quality Index (DLQI), PtGA (Patient Global Assessment) and the Hospital Anxiety and Depression Scale (HADS) were used to assess the patients reported outcomes. The treatment outcomes were analyzed at 3 months and 6 months. Using multiple logistic regression to analyze the differences between patients with different disease duration, and conducting subgroup analysis and sensitivity analysis to test the robustness of the research results.

**Results:** A total of 1908 patients who met the criteria were included in the analysis. After 3 months of treatment, the PASI75 response rates for the three groups of patients (<2 years, 2–10 years, and ≥10 years) were 55%, 55% and 60%, respectively all  $p$  value >0.05. No significant differences were observed among the three groups in the rates of achieving BSA <1/3, PGA 0/1, DLQI 0/1, PtGA 0/1, HADS-A = 0, and HADS-D = 0. Notably, these outcomes still showed no significant differences at 6 months. Subgroup and sensitivity analyses also yielded consistent results.

**Conclusion:** Disease duration does not significantly affect clinical efficacy or patients reported outcomes in patients with moderate-to-severe psoriasis receiving systemic therapy. These results indicate that early systemic therapy does not improve treatment outcomes in real clinical settings, thereby supporting the continued efficacy of step-up treatment strategy and providing novel insights into clinical practice management.

**Keywords:** psoriasis, disease duration, systemic therapy, clinical efficacy, patients reported outcomes

## Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease, with a global prevalence of approximately 2% to 3%. It is often associated with significant physical, psychological, and social burdens.<sup>1</sup> It typically follows a course of remission and recurrence; many patients only experience mild rash flares, but some may have a longer disease duration before receiving more intensive treatment.<sup>2</sup> The present treatment approach uses a step-up regimen—starting with topical drugs, progressing to phototherapy, and reserving systemic drugs for patients with poor control under conventional

treatment.<sup>3,4</sup> This method minimizes overtreatment of mild disease but often delays effective systemic intervention until the disease has persisted for a longer duration. This raises the question whether early systemic treatment could yield better outcomes?

In recent years, systemic therapy, including traditional drugs such as methotrexate and acitretin, as well as biologics targeting specific inflammatory pathways, have significantly improved patients' symptoms.<sup>5–9</sup> However, the response to systemic therapy varies greatly among individuals, influenced by multiple factors including disease severity, comorbidities, age of onset, treatment history, and family history.<sup>10–12</sup> In other chronic immune-mediated inflammatory diseases, like Crohn's disease and rheumatoid arthritis, researchers have reported the role of disease duration on treatment response, with early use of systemic treatments leading to better clinical outcomes.<sup>13,14</sup> Similar to psoriasis, earlier systemic therapy may have greater advantages. However, there is still a lack of study data on the impact of disease duration on systemic therapy outcomes in psoriasis.

To our knowledge, large-scale, real-world studies specifically designed to investigate the influence of psoriasis disease duration on treatment outcomes are lacking. Previous studies have not addressed whether the duration of psoriasis affects treatment efficacy in clinical practice. Additionally, it is unclear whether the chronicity of the disease alters the efficacy of specific systemic therapies. This lack of evidence limits the development of personalized treatment strategies, particularly for patients with long-term disease.

To address this issue, this multicenter prospective observational study utilized data from the SPEECH registry to explore whether early systemic therapy truly improves clinical or patients reported outcomes. Patients with moderate-to-severe psoriasis were stratified into three groups based on disease duration at enrollment: short duration (<2 years), medium duration (2–10 years), and long duration (>10 years). Participants received various systemic therapies, including biologics, methotrexate, and acitretin. Although treatment switching may occur in clinical practice, our analyses focused on patients who maintained a single systemic therapy for at least six months, thereby ensuring reliable evaluation of treatment response. Furthermore, we examined potential contributors to disease progression, including treatment type, patient demographics, and clinical characteristics, to explore whether specific therapies were associated with greater disease stability or risk of deterioration. This study provides novel insights into the relationship between psoriasis disease course and systemic therapy efficacy in real clinical settings.

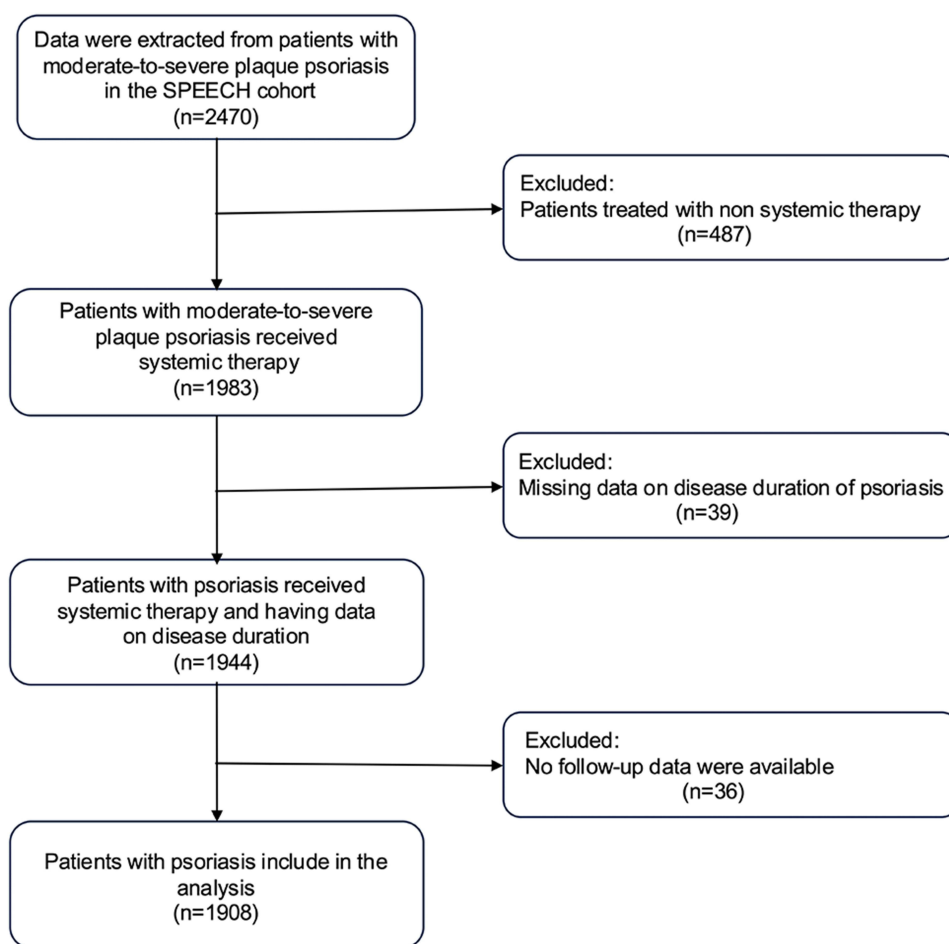
## Material and Methods

### Study Design

The SPEECH registry is a multicenter prospective observational study that records the clinical features of psoriasis in the Chinese population and the safety and efficacy of different treatment methods such as biologics, conventional systemic therapy, and phototherapy.<sup>15</sup> The SPEECH registry is registered at seven dermatology centers in Shanghai, China. All data were prospectively collected at each visit using standardized case report forms and entered into a central electronic database by trained dermatology staff to ensure data completeness and accuracy. This study received ethical approval from the Institutional Review Board of Shanghai Dermatology Hospital (#2020-36), along with approvals from the ethics committees of all other participating centers.

### Participants

All participants in this study are selected from the SPEECH cohort and met the following inclusion criteria: 1. Adults diagnosed with moderate-to-severe plaque psoriasis who were treated with biologic agents (such as guselkumab, ustekinumab, ixekizumab, secukinumab, or adalimumab), methotrexate, or acitretin; 2. Treatment was administered according to established protocols without modifications in dosage or treatment intervals. To ensure reliable evaluation of treatment response, only patients who remained on a single systemic therapy for at least six months were included in the analysis. Key exclusion criteria are the absence of baseline information on disease duration (Figure 1).



**Figure 1** Study flowchart.

## Data Collection and Outcome Measures

Demographic and clinical data were drawn from all participants at baseline, including age, gender, education level, disease duration, family history of psoriasis, BMI, lifestyle (smoking, drinking), early-onset psoriasis (age of onset <40 years), comorbidities (obesity, psoriatic arthritis, hyperlipidemia, and hypertension). To ensure consistency, treatment adherence and clinical assessments were regularly recorded and reviewed at each visit by on-site investigators.

Additionally, disease characteristics were assessed using measures such as Psoriasis Area and Severity Index (PASI), Body Surface Area (BSA), Dermatology Life Quality Index (DLQI), Physician Global Assessment (PGA), Patient Global Assessment (PtGA), Hospital Anxiety and Depression Scale - Anxiety (HADS-A) and Depression (HADS-D). Treatment efficacy was assessed at 3 months (12 weeks) and 6 months (28 weeks) after treatment, using criteria such as the PASI 75 ( $\geq 75\%$  improvement in PASI), BSA <1/3 (clear to almost clear), PGA 0/1 (clear to almost clear), DLQI 0/1 (little to no impact on life), PtGA 0/1 (clear to almost clear), and HADS-A or HADS-D = 0 (complete resolution of anxiety or depression symptoms) at 3 months and 6 months post-treatment.

## Statistical Analyses

The primary analysis used a modified intention-to-treat (mITT) dataset and employed multiple imputation to fill in the missing treatment efficacy data. By grouping patients according to disease duration (<2 years, 2–10 years, and  $\geq 10$  years). Continuous variable hypothesis Follow a normal distribution, represented by the mean (SD), and statistical comparisons are conducted using the Student's *t*-test. Non-normally distributed continuous variables are represented as median (interquartile range) and compared using the Mann–Whitney *U*-test. Categorical variables are expressed as n (%),

and analyzed using the  $\chi^2$  test or Fisher's exact probability method. Using the group with a disease duration of <2 years as a reference, logistic regression analysis was employed to evaluate the treatment response of patients with different disease durations. The adjusted odds ratio (aOR) and its 95% confidence interval (CI) were computed. To visualize response trends, line charts were generated, and intergroup differences were assessed using the Kruskal–Wallis and Dwass–Steel–Critchlow–Fligner (DSCF) tests. Additionally, subgroup analyses were performed to investigate potential interactions and factors. Sensitivity analysis was conducted based on the per-protocol (PP) dataset to further validate the robustness of the study findings. All statistical models were adjusted for potential confounders, such as gender, age, education level, early-onset psoriasis, family history of psoriasis, psoriatic arthritis (PsA), obese (BMI>28), baseline PASI, BSA score, different categories of treatment drugs, the hospital to which the patient belonged, and prior systemic therapy history. Statistical analyses were performed with R software version 4.2.2, and results with  $p$ -value <0.05 were deemed statistically significant.

## Results

### Clinical Characteristics According to Disease Duration

Among the initially registered 2470 patients, 1947 fulfilled the inclusion criteria for this analysis. Due to incomplete baseline information, 39 patients were excluded, leaving 1908 patients eligible for the final analysis (Figure 1). Participants were divided into three groups based on the duration of the disease: <2 years, 2–10 years, and  $\geq 10$  years. In the comparison of baseline characteristics across the three patient groups, it was noted that patients in the short disease duration group (<2 years) had more females (29.1% vs 18.3% vs 25.0%), higher education levels, more obesity (24.1% vs 19.0% vs 16.8%). In addition, patients in the short disease duration group had lower baseline PASI and BSA scores. Moreover, patients in the long disease duration group ( $\geq 10$  years) were more likely to receive biologic therapy and had early-onset psoriasis ( $p < 0.05$ ). There were no significant differences in the remaining covariates (Table 1).

**Table 1** Demographic and Patient Characteristics of the Study Cohort

Characteristic	Disease Duration, Years			P-Value
	<2, N = 234	2–10, N = 515	$\geq 10$ , N = 1159	
Age, years; Median (IQR)	52 (37, 65)	43 (33, 58)	52 (39, 64)	<0.001
Gender				0.002
Male	166 (70.9%)	419 (81.7%)	868 (75.0%)	
Female	68 (29.1%)	94 (18.3%)	289 (25.0%)	
BMI, kg/m <sup>2</sup>	25.1(22.1, 27.8)	24.5(22.4, 27.2)	24.5(22.5, 27.0)	0.468
Early onset of psoriasis				<0.001
Yes	52 (22.4%)	139 (27.0%)	317 (27.5%)	
No	180 (77.6%)	375 (73.0%)	837 (72.5%)	
Smoking, n (%)				0.067
Yes	92 (39.5%)	250 (48.6%)	532 (45.9%)	
No	141 (60.5%)	264 (51.4%)	626 (54.1%)	
Alcohol, n (%)				0.279
Yes	52 (22.4%)	139 (27.0%)	317 (27.5%)	
No	180 (77.6%)	375 (73.0%)	837 (72.5%)	

(Continued)

Table 1 (Continued).

Characteristic	Disease Duration, Years			P-Value
	<2, N = 234	2–10, N = 515	≥10, N = 1159	
Education level, n (%)				0.012
High school graduate or less	110 (49.1%)	198 (40.8%)	555 (50.4%)	
Some college	52 (23.2%)	124 (25.6%)	239 (21.7%)	
College graduate or higher	62 (27.7%)	163 (33.6%)	307 (27.9%)	
Obese, n (%)				0.027
Yes	56 (24.1%)	97 (19.0%)	192 (16.8%)	
No	176 (75.9%)	413 (81.0%)	951 (83.2%)	
Hypertension, n (%)				0.656
Yes	57 (24.4%)	140 (27.2%)	295 (25.5%)	
No	177 (75.6%)	375 (72.8%)	864 (74.5%)	
Psoriatic arthritis, n (%)				0.175
Yes	42 (17.9%)	71 (13.8%)	199 (17.2%)	
No	192 (82.1%)	444 (86.2%)	960 (82.8%)	
History of allergy, n (%)				0.515
Yes	30 (12.9%)	52 (10.1%)	131 (11.3%)	
No	202 (87.1%)	462 (89.9%)	1,024 (88.7%)	
Family history of psoriasis, n (%)				<0.001
Yes	38 (16.4%)	80 (15.7%)	304 (26.3%)	
No	194 (83.6%)	431 (84.3%)	850 (73.7%)	
Prior systemic therapy, n (%)				<0.001
Yes	58 (24.8%)	177 (34.4%)	556 (48.0%)	
No	176 (75.2%)	338 (65.6%)	603 (52.0%)	
Treatment, n (%)				0.002
Acitretin	45 (19.2%)	104 (20.2%)	170 (14.7%)	
Methotrexate	83 (35.5%)	157 (30.5%)	335 (28.9%)	
Biologics	106 (45.3%)	254 (49.3%)	654 (56.4%)	
Baseline PASI score	12 (8, 17)	13 (10, 18)	13 (10, 19)	0.003
Baseline BSA score	14 (9, 24)	15 (10, 25)	17 (11, 29)	<0.001
Baseline PGA score	3 (2, 3)	3 (2, 3)	3 (2, 3)	0.230
Baseline HADS-A score	4.0 (2.0, 8.0)	4.0 (1.0, 7.0)	4.0 (1.0, 7.0)	0.242

(Continued)

**Table 1** (Continued).

Characteristic	Disease Duration, Years			P-Value
	<2, N = 234	2–10, N = 515	≥10, N = 1159	
Anxiety symptom (>8), n (%)				0.288
Yes	51 (25.5%)	85 (20.3%)	196 (20.8%)	
No	149 (74.5%)	333 (79.7%)	747 (79.2%)	
Baseline HADS-D score	5.0 (2.0, 8.0)	4.0 (2.0, 8.0)	4.0 (2.0, 8.0)	0.662
Depression symptom (>8), n (%)				0.680
Yes	54 (27.0%)	116 (27.8%)	241 (25.6%)	
No	146 (73.0%)	302 (72.2%)	702 (74.4%)	

**Abbreviations:** n, number; BMI, Body Mass Index; PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index; BSA, Body Surface Area; PGA, Physician's Global Assessment; HADS-A, Hospital Anxiety and Depression-Anxiety; HADS-D, Hospital Anxiety and Depression-Depression.

## Comparison of Treatment Efficacy

Using univariate logistic regression analysis to compare the efficacy outcomes among the three disease duration groups. In the unadjusted analysis, at 3 months, there were no significant differences in the proportions of the three different disease duration groups achieving BSA <1/3, PGA 0/1, PASI 75, DLQI 0/1, PtGA 0/1, HADS-A = 0, and HADS-D = 0. Even after adjusting for relevant covariates, these results remained non-significant (Table 2). Moreover, the results of the above at 6 months were similar, except that the PASI75 response rate was lower in the long disease duration group, but the adjusted OR showed no significant difference (Table 3).

The Kruskal–Wallis and DSCF tests were used to assess intergroup differences, and line graphs were used to illustrate the changes of various treatment outcomes over time in the three groups (Figure 2). The results showed that, except for the baseline, there were almost no significant differences in the outcomes at each time point among the three groups. Moreover, all three groups exhibited downtrend of the outcomes over time, reinforcing the consistency of treatment

**Table 2** Comparison of Clinical Efficacy and Psychological Outcome of Systemic Therapy in Different Disease Duration at 3 Months

Outcomes	Response Rate	Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-Value
<b>BSA&lt;1</b>					
<2 years	19%	Reference		Reference	
2~10 years	23%	1.27(0.86,1.87)	0.23	1.27(0.82,1.98)	0.29
≥10 years	23%	1.28(0.90,1.83)	0.17	1.06(0.69,1.65)	0.79
<b>BSA&lt;3</b>					
<2 years	43%	Reference		Reference	
2~10 years	47%	1.19(0.87,1.62)	0.28	1.34(0.92,1.95)	0.13
≥10 years	47%	1.16(0.87,1.54)	0.31	1.08(0.74,1.56)	0.69
<b>PGA 0/1</b>					
<2 years	32%	Reference		Reference	
2~10 years	29%	0.90(0.64,1.25)	0.52	1.09(0.72,1.64)	0.68
≥10 years	31%	0.99(0.73,1.34)	0.97	1.01(0.67,1.51)	0.96

(Continued)

**Table 2** (Continued).

Outcomes	Response Rate	Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-Value
<b>PASI 75</b>					
<2 years	55%	Reference		Reference	
2~10 years	55%	1.02(0.75, 1.40)	0.89	0.94(0.65, 1.41)	0.84
≥10 years	60%	1.24(0.94, 1.65)	0.13	0.86(0.59, 1.26)	0.45
<b>DLQI 0/1</b>					
<2 years	30%	Reference		Reference	
2~10 years	27%	0.87(0.62, 1.22)	0.40	1.12(0.75, 1.65)	0.58
≥10 years	34%	1.19(0.88, 1.61)	0.27	1.19(0.81, 1.75)	0.37
<b>PtGA 0/1</b>					
<2 years	18%	Reference		Reference	
2~10 years	16%	0.88(0.58, 1.33)	0.54	0.98(0.59, 1.61)	0.93
≥10 years	23%	1.37(0.96, 1.98)	0.086	1.31(0.81, 2.13)	0.27
<b>HADS-A=0</b>					
<2 years	35%	Reference		Reference	
2~10 years	37%	1.11(0.69, 1.78)	0.66	1.43(0.83, 2.48)	0.20
≥10 years	45%	1.52(0.99, 2.33)	0.058	1.79(1.05, 3.08)	0.034
<b>HADS-D=0</b>					
<2 years	22%	Reference		Reference	
2~10 years	27%	1.29(0.76, 2.19)	0.35	1.27(0.70, 2.29)	0.43
≥10 years	30%	1.46(0.90, 2.38)	0.13	1.37(0.77, 2.45)	0.29

**Abbreviations:** OR, Odds Ratio; CI, Confidence Interval; BSA, Body Surface Area; PGA, Physician's Global Assessment; PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index; PtGA, Patient Global Assessment; HADS-A, Hospital Anxiety and Depression-Anxiety; HADS-D, Hospital Anxiety and Depression-Depression.

**Table 3** Compare of Clinical Efficacy and Psychological Outcome of Systemic Therapy in Different Disease Duration at 6 Months

Outcomes	Response Rate	Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-Value
<b>BSA&lt;1</b>					
<2 years	35%	Reference		Reference	
2~10 years	32%	0.91(0.65, 1.26)	0.56	1.07(0.73, 1.57)	0.72
≥10 years	32%	0.91(0.67, 1.22)	0.52	0.98(0.67, 1.43)	0.92
<b>BSA&lt;3</b>					
<2 years	68%	Reference		Reference	
2~10 years	67%	0.98(0.71, 1.37)	0.93	1.11(0.74, 1.66)	0.63
≥10 years	65%	0.89(0.66, 1.20)	0.45	0.95(0.64, 1.41)	0.78
<b>PGA 0/1</b>					
<2 years	38%	Reference		Reference	
2~10 years	34%	0.84(0.61, 1.16)	0.28	1.20(0.80, 1.81)	0.38
≥10 years	42%	1.17(0.88, 1.56)	0.26	1.57(1.06, 2.33)	0.026
<b>PASI 75</b>					
<2 years	37%	Reference		Reference	
2~10 years	32%	1.24(0.90, 1.72)	0.19	1.20(0.81, 1.77)	0.36
≥10 years	28%	1.46(1.09, 1.96)	0.012	1.20(0.82, 1.76)	0.35

(Continued)

**Table 3** (Continued).

Outcomes	Response Rate	Unadjusted OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-Value
<b>DLQI 0/1</b>					
<2 years	35%	Reference		Reference	
2~10 years	34%	0.93(0.67,1.28)	0.65	1.34(0.92,1.96)	0.13
≥10 years	38%	1.09(0.82,1.47)	0.55	1.37(0.95,2.00)	0.092
<b>PtGA 0/1</b>					
<2 years	20%	Reference		Reference	
2~10 years	17%	0.87(0.58,1.28)	0.47	1.06(0.65,1.70)	0.83
≥10 years	22%	1.18(0.83,1.67)	0.36	1.24(0.78,1.98)	0.36
<b>HADS-A=0</b>					
<2 years	54%	Reference		Reference	
2~10 years	60%	0.81(0.45,1.46)	0.48	1.67(0.77,3.62)	0.19
≥10 years	52%	1.11(0.66,1.86)	0.69	1.89(0.89,4.03)	0.10
<b>HADS-D=0</b>					
<2 years	60%	Reference		Reference	
2~10 years	69%	0.69(0.37,1.27)	0.23	1.05(0.50,2.22)	0.89
≥10 years	65%	0.81(0.48,1.38)	0.45	0.95(0.46,1.96)	0.89

**Abbreviations:** OR, Odds Ratio; CI, Confidence Interval; BSA, Body Surface Area; PGA, Physician's Global Assessment; PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index; PtGA, Patient Global Assessment; HADS-A, Hospital Anxiety and Depression-Anxiety; HADS-D, Hospital Anxiety and Depression-Depression.

efficacy irrespective of disease duration. This underscored the stability of systemic therapy outcomes across different disease durations.

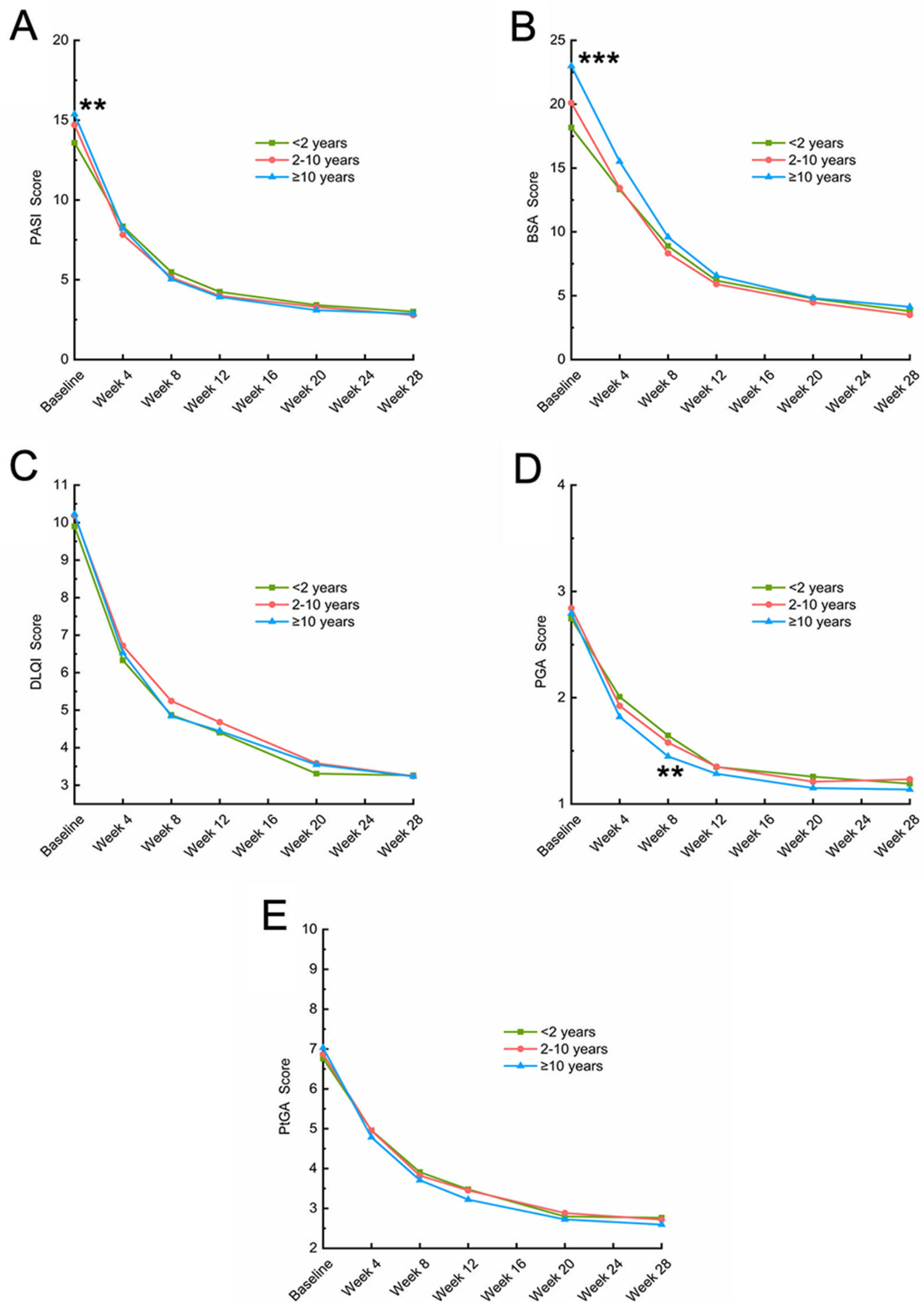
When using PASI75 as the primary efficacy endpoint, subgroup analyses showed no significant interaction between baseline variables and disease duration categories ( $p$  for interaction  $>0.05$ ; [Figures S1](#) and [S2](#)). Similarly, no significant interaction was observed between treatment type or prior systemic therapy history and disease duration in terms of treatment outcomes, indicating that the efficacy of systemic therapy is not affected by disease duration. These results support the robustness and consistency of our primary analysis.

## Sensitivity Analysis

Sensitivity analysis was also performed to verify the reliability of our results using the PP dataset. Disease duration was categorized into two groups based on the median:  $<15$  years and  $\geq 15$  years. Both univariate and multivariate logistic regression analyses showed no significant difference in efficacy between the two groups ([Tables S1](#) and [S2](#)). Furthermore, we conducted a hierarchical analysis according to treatment type (traditional agents vs biologics) and prior systemic therapy exposure. As presented in [Tables S3](#) and [S4](#), the results showed no significant differences in PASI75 response among different disease duration groups within each stratum. The Mantel-Haenszel pooled estimates further demonstrated no significant heterogeneity across strata. The results showed that disease duration did not affect the efficacy of systemic therapies, regardless of treatment type or prior systemic therapy, supporting the robustness and consistency of our primary analysis.

## Discussion

This large-scale, prospective, multicenter study provides valuable evidence on psoriasis management and treatment patterns, with patients receiving systemic therapy in routine clinical settings at seven hospitals in Shanghai, China. This study provides valuable insights into how disease duration affects clinical features and treatment outcomes of systemic therapy in Chinese psoriasis patients. Patients were divided into three groups based on disease duration:  $<2$  years, 2–10



**Figure 2** Line graphs comparing treatment outcomes over time among three groups. **(A)** Line graphs of PASI score and time; **(B)** Line graphs of BSA score and time; **(C)** Line graphs of DLQI score and time; **(D)** Line graphs of PGA score and time; **(E)** Line graphs of PtGA score and time. \*\*,  $p < 0.01$ ; \*\*\*,  $p < 0.001$ .

**Abbreviations:** PASI, Psoriasis Area and Severity Index; BSA, Body Surface Area; DLQI, Dermatology Life Quality Index; PGA, Physician's Global Assessment. PtGA, Patient Global Assessment.

years, and  $\geq 10$  years. A key finding of our study is that our study showed no significant correlation between disease duration and treatment response in terms of clinical efficacy (PASI75, PGA 0/1, BSA  $< 3$ ) and patients reported outcomes (DLQI 0/1, PtGA 0/1, HADS-A=0, HADS-D=0) at both 3 months and 6 months. This conclusion remained robust after adjusting for relevant covariates, and sensitivity analysis further verified the reliability of the results.

We observed that patients with a short disease duration ( $< 2$  years) had higher education levels, more female patients, more obese patients, and lower baseline PASI and BSA scores. However, these characteristics did not affect the treatment outcomes. Notably, patients with a longer disease duration were more likely to receive biological therapy and present with early-onset psoriasis, both of which usually associated with increased disease severity or longer treatment exposure. This is consistent with the findings from the British Association of Dermatologists Biologic Interventions Register (BADBIR), where longer disease duration was observed with biologics compared to traditional systemic therapy (23 vs 19 years,  $p < 0.001$ ).<sup>16</sup>

Our findings were consistent with prior clinical studies indicating that disease duration cannot independently predict the response to systemic or biological therapy. Most available studies have focused on biologics, consistently showing that treatment response is unaffected by disease duration. For instance, a prospective cohort study of 118 patients receiving etanercept found no significant difference in PASI improvement at week 24 between patients with disease durations  $< 20$  years versus  $\geq 20$  years ( $p = 0.170$ ).<sup>17</sup> Similarly, in another retrospective cohort study involving 135 patients receiving guselkumab, Hung et al reported no correlation between PASI 75 response and disease duration at week 36 (OR: 0.99, 95% CI 0.94–1.05), with comparable mean durations among responders and non-responders (18.42 vs 18.91 years).<sup>18</sup> Post-hoc analysis of large RCTs, including the NAVIGATE and VOYAGE trials ( $n = 1678$ ), indicated that the disease duration ( $< 15$  years vs  $\geq 15$  years) was not significantly associated with the PASI 90 response at week 40 (OR: 1.13, 95% CI: 0.88–1.47).<sup>19</sup> Furthermore, a recent meta-analysis including 4,649 patients found that disease duration was not significantly associated with biologic treatment response (OR 0.99, 95% CI 0.98–1.00,  $p = 0.17$ ), reinforcing that systemic therapy efficacy is generally independent of disease duration.<sup>20</sup>

Evidence regarding traditional systemic therapies is comparatively limited, but appears to suggest a similar trend. In our subgroup analyses, disease duration did not significantly influence treatment outcomes with methotrexate or acitretin. Although real-world evidence from prior studies has demonstrated the effectiveness of traditional systemic therapies in patients with moderate-to-severe psoriasis, they did not specifically evaluate whether disease duration influences treatment response. The BADBIR cohort identified predictors of reduced treatment effectiveness, including prior systemic exposure, male sex, comorbidities, and alcohol consumption, but disease duration was not among them.<sup>21</sup> Similarly, a systematic review of traditional systemic therapies found no evidence that disease duration significantly modified treatment response.<sup>22</sup> Additional analysis of treatment-switch patterns reported that disease duration did not affect the transition between traditional drugs and biologics.<sup>23</sup> Recent data further suggest that prior use of traditional drugs such as methotrexate or acitretin does not compromise the efficacy or drug survival of subsequent biologic therapy.<sup>24</sup> Collectively, these findings indicate that disease duration is not a major determinant of treatment outcomes for either traditional systemic agents or biologics. Importantly, prior exposure to traditional therapy does not diminish the effectiveness of subsequent biologics, thereby supporting the rationale for a step-up therapeutic strategy in clinical practice.

Although our research results indicated that early systemic therapy does not improve treatment outcomes in actual clinical settings, some studies report that early systemic treatment can actively control systemic inflammation to prevent or delay damage related to comorbidities, including psoriatic arthritis (PsA) and cardiovascular diseases.<sup>25–29</sup> Two different cohort studies indicated that compared to patients receiving phototherapy or topical medication, those undergoing systemic treatment have a significantly reduced risk of developing PsA.<sup>25,26</sup> Furthermore, new evidence suggested that biological therapy is beneficial in reversing the potential pathogenic processes of cardiovascular diseases, such as endothelial dysfunction and the progression of atherosclerotic plaques. In a large retrospective study, Song WJ et al found that compared to phototherapy, biologic therapy and non-biologic systemic therapy reduce the risk of new-onset MACE in psoriasis patients.<sup>27</sup> In order to determine whether early systemic intervention has a protective effect on psoriatic arthritis, or cardiovascular diseases, as well as whether these potential benefits make it worthwhile to upgrade treatment earlier, more long-term longitudinal studies are necessary in the future.

This study indicated that the early effectiveness of systemic therapy for psoriasis remains consistent, regardless of the disease duration, which may be related to the ability of biologics to modulate chronic inflammatory pathways and resident memory T cells in long-standing disease.<sup>30,31</sup> This suggests that even patients with long-standing psoriasis or delayed treatment initiation can achieve meaningful clinical responses, supporting the use of systemic therapy irrespective of disease duration.

Our research underscores that initiating systemic therapy early does not lead to better outcomes, and this observation supports the widely accepted step-up treatment strategy in current clinical practice.<sup>32</sup> Using systemic therapy for patients with poor response to topical treatment and phototherapy reduces unnecessary systemic drug exposure and its associated costs and risks.<sup>4</sup> In the absence of aggressive disease characteristics or rapid progression of joint involvement, systemic therapy may not need to be initiated immediately based solely on the disease duration. Conversely, the severity of the disease, the burden of symptoms, and the impairment of quality of life still be the main factors influencing clinical judgements. These findings provided clinical practice evidence, highlighting the importance of gradually and individually escalating systemic therapy regimens in the management of psoriasis.

It is important to recognize the limitations inherent in our study. First, like many observational studies, our analysis may be susceptible to various biases, including selection bias and unmeasured confounding factors. Second, the study cohort only included Chinese patients, which limits the generalizability of the results. Third, although a follow-up period of 6 months offers notable findings on early responses to treatment, it does not provide information on the long-term efficacy of systemic therapy or the potential effects of disease duration on outcomes such as comorbidities. Therefore, extended longitudinal follow-up is necessary to evaluate these crucial aspects.

## Conclusion

Our research findings demonstrate that the short-term efficacy of systemic therapy is consistent across different disease durations, supporting the “step-up” treatment strategy in psoriasis management. This multicenter evidence adds new insights by comparing traditional agents and biologics, showing that disease duration does not alter systemic therapy response. However, emerging evidence suggests that early systemic therapy may provide long-term benefits in preventing psoriatic arthritis and major cardiovascular events. Future long-term prospective studies are needed to determine whether early systemic interventions have a protective effect on comorbidities and to refine personalized treatment plans to balance the benefits for skin and quality of life with the prevention of systemic comorbidities.

## Data Sharing Statement

The dataset supporting this research can be obtained from the corresponding author upon reasonable request.

## Ethics Statement

This study was approved by the medical ethics committees of the following institutions: Shanghai Skin Disease Hospital (approval No. 2020-36), Shanghai Sixth People’s Hospital (approval No.2020-KY-047K), Shanghai Changzheng Hospital (approval No.2020-27), and Shanghai Tenth People’s Hospital (approval No.20KT110). All participants provided written informed consent for the publication of their clinical data. The study was conducted in accordance with the principles of the Declaration of Helsinki.

## Author Contributions

Min Dai, Yuxiong Jiang, Yujing Xi and Lezhen Xu are co-first authors. All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no conflicts of interest.

## References

- Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. *Lancet*. 2021;397(10281):1301–1315. doi:10.1016/S0140-6736(20)32549-6
- Ma LF. Inflammatory memory in psoriasis: from remission to recurrence. *J Allergy Clin Immunol*. 2024;154(1):1.
- Gisoni P, Del Giglio M, Girolomoni G. Treatment Approaches to Moderate to Severe Psoriasis. *Int J Mol Sci*. 2017;18(11):2427. doi:10.3390/ijms18112427
- Chinese Society of Dermatology, China Dermatologist Association, Dermatology & Venereology Specialized Committee of Chinese Association of Integrative Medicine. Guidelines for the treatment of psoriasis with biologics and small-molecule drugs in China (2024). *Chin J Dermatol*. 2024;57(11):976–997.
- Sugumaran D, Yong ACH, Stanslas J. Advances in psoriasis research: from pathogenesis to therapeutics. *Life Sci*. 2024;355:122991. doi:10.1016/j.lfs.2024.122991
- Lebwohl M. Advances in biologic therapy of psoriasis. *J Eur Acad Dermatol Venereol*. 2023;37(9):1689–1690. doi:10.1111/jdv.19287
- Lee HJ, Kim M. Challenges and Future Trends in the Treatment of Psoriasis. *Int J Mol Sci*. 2023;24(17):13313. doi:10.3390/ijms241713313
- Alabas OA, Mason KJ, Yiu ZZN, et al. Effectiveness and survival of methotrexate versus Adalimumab in patients with moderate-to-severe psoriasis: a cohort study from the British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR). *Br J Dermatol*. 2023;189(3):271–278. doi:10.1093/bjd/ljad179
- Armstrong AW, Pathophysiology RC. Clinical Presentation, and Treatment of Psoriasis: a Review. *JAMA*. 2020;323(19):1945–1960. doi:10.1001/jama.2020.4006
- Huang D, Zhong X, Jiang Y, et al. Insulin resistance impairs biologic agent response in moderate-to-severe plaque psoriasis: insights from a prospective cohort study in China. *Br J Dermatol*. 2024;191(4):616–623. doi:10.1093/bjd/ljae147
- Jiang Y, Liu X, Ma R, et al. The Impact of Family History on Clinical Presentation and Biologic Treatment Response in Patients with Psoriasis: a Multicenter Prospective Cohort Study. *Am J Clin Dermatol*. 2025;26(2):291–300. doi:10.1007/s40257-025-00918-y
- Jiang Y, Chen Y, Yu Q, Shi Y. Biologic and Small-Molecule Therapies for Moderate-to-Severe Psoriasis: focus on Psoriasis Comorbidities. *BioDrugs*. 2023;37(1):35–55. doi:10.1007/s40259-022-00569-z
- Deane KD, Holers VM. Rheumatoid Arthritis Pathogenesis, Prediction, and Prevention: an Emerging Paradigm Shift. *Arthritis Rheumatol*. 2021;73(2):181–193. doi:10.1002/art.41417
- Berg DR, Colombel JF, Ungaro R. The Role of Early Biologic Therapy in Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2019;25(12):1896–1905. doi:10.1093/ibd/izz059
- Yu N, Peng C, Zhou J, et al. Measurement properties of the patient global assessment numerical rating scale in moderate-to-severe psoriasis. *Br J Dermatol*. 2023;189(4):437–446. doi:10.1093/bjd/ljad188
- Iskandar IYK, Ashcroft DM, Warren RB, et al. Demographics and disease characteristics of patients with psoriasis enrolled in the British Association of Dermatologists Biologic Interventions Register. *Br J Dermatol*. 2015;173(2):510–518. doi:10.1111/bjd.13908
- Antoniou C, Dessinioti C, Stratigos A, Avgerinou G, Stavropoulos P, Katsambas A. Etanercept in severe, recalcitrant psoriasis: clinical response, safety profile and predictors of response based on a single institution's experience. *J Eur Acad Dermatol Venereol*. 2009;23(8):979–982. doi:10.1111/j.1468-3083.2009.03093.x
- Hung YT, Lin YJ, Chiu HY, Huang YH. Impact of previous biologic use and body weight on the effectiveness of guselkumab in moderate-to-severe plaque psoriasis: a real-world practice. *Ther Adv Chronic Dis*. 2021;12:20406223211046685. doi:10.1177/20406223211046685
- Diels J, Thilakarathne P, Cameron C, McElligott S, Schubert A, Puig L. Adjusted treatment COMPARisons between guselkumab and ustekinumab for treatment of moderate-to-severe plaque psoriasis: the COMPASS analysis. *Br J Dermatol*. 2020;183(2):276–284. doi:10.1111/bjd.18634
- Hjort G, Schwarz CW, Skov L, et al. Clinical characteristics associated with response to biologics in the treatment of psoriasis: a meta-analysis. *JAMA Dermatol*. 2024;160(8):830–837. doi:10.1001/jamadermatol.2024.1677
- Warren RB, Smith CH, Yiu ZZN, et al. Effectiveness and persistence of Acitretin, ciclosporin, fumaric acid esters and methotrexate for patients with moderate-to-severe psoriasis: a cohort study from BADBIR. *Br J Dermatol*. 2015;172(2):337–346. doi:10.1111/bjd.13225
- Iskandar IYK, Ashcroft DM, Warren RB, et al. Persistence and effectiveness of nonbiologic systemic therapies for moderate-to-severe psoriasis in adults: a systematic review. *Br J Dermatol*. 2016;174(3):606–617.
- Tabolli S, Giannantoni P, Paradisi A, Abeni D. The ‘switcher’ patient profile in psoriasis treatment: from traditional to biological and from biological to traditional systemic drugs. *Br J Dermatol*. 2015;173(1):256–258. doi:10.1111/bjd.13560
- Piaserico S, Cazzaniga S, Gisoni P, et al. “Full-naïve” patients: the impact of previous methotrexate, cyclosporine, and Acitretin on first-line biologics response in the treatment of moderate-to-severe psoriasis—a monocentric retrospective study. *J Eur Acad Dermatol Venereol*. 2021;35(5):e327–e330.
- Gisoni P, Bellinato F, Targher G, Idolazzi L, Girolomoni G. Biological disease-modifying antirheumatic drugs may mitigate the risk of psoriatic arthritis in patients with chronic plaque psoriasis. *Ann Rheum Dis*. 2022;81(1):68–73. doi:10.1136/annrheumdis-2021-219961

26. Felquer MLA, LoGiudice L, Galimberti ML, Rosa J, Mazzuoccolo L, Soriano ER. Treating the skin with biologics in patients with psoriasis decreases the incidence of psoriatic arthritis. *Ann Rheumatic Dis.* 2022;81(1):74–79. doi:10.1136/annrheumdis-2021-220865
27. Rosenthal YS, Schwartz N, Sagy I, Pavlovsky L. Incidence of Psoriatic Arthritis Among Patients Receiving Biologic Treatments for Psoriasis: a Nested Case–Control Study. *Arthritis Rheumatol.* 2022;74(2):237–243. doi:10.1002/art.41946
28. Song WJ, Oh S, Yoon HS. Association between biologic and nonbiologic systemic therapy for psoriasis and psoriatic arthritis and the risk of new-onset and recurrent major adverse cardiovascular events: a retrospective cohort study. *J Am Acad Dermatol.* 2025;93(1):S0190–9622(25)00524–9. doi:10.1016/j.jaad.2025.03.055
29. Reich K, Griffiths CEM, Gordon KB, et al. Maintenance of clinical response and consistent safety profile with up to 3 years of continuous treatment with guselkumab: results from the VOYAGE 1 and VOYAGE 2 trials. *J Am Acad Dermatol.* 2020;82(4):936–945. doi:10.1016/j.jaad.2019.11.040
30. 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(5):1004–1016. doi:10.1111/jdv.18846
31. Schäkel K, Reich K, Asadullah K, et al. Early disease intervention with guselkumab in psoriasis leads to a higher rate of stable complete skin clearance (‘clinical super response’): week 28 results from the ongoing phase IIIb randomized, double-blind, parallel-group, GUIDE study. *J Eur Acad Dermatol Venereol.* 2023;37(10):2016–2027. doi:10.1111/jdv.19236
32. Committee on Psoriasis. Chinese Society of Dermatology. Guideline for the diagnosis and treatment of psoriasis in China (2023 edition). *Chin JI of Dermatology.* 2023;56(7):573–625.

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