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ORIGINAL RESEARCH

Effectiveness of Ixekizumab in Chinese Patients with Moderate-Severe Plaque Psoriasis with Special Area Involvement: Subanalysis of a Prospective, Multicenter, Observational Real-World Study

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ABSTRACT

Introduction: Ixekizumab, a monoclonal antibody against interleukin-17A, demonstrated effectiveness in the treatment of psoriasis in a Chinese real-world study that was consistent with previous randomized controlled trials. Here, we report further analyses from this study to explore the effectiveness of ixekizumab for treating patients with psoriasis and the involvement of special body areas (scalp, nail, joint, palmoplantar, or genital areas).

Methods: A multicenter, prospective, observational, single-arm, post-marketing surveillance study was conducted in patients aged ≥ 18 years with moderate-to-severe plaque psoriasis and prescribed with ixekizumab in 26 Chinese hospitals. Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) scores were compared between patients with versus without psoriasis in special

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body areas in the overall study population and across subgroups by body area.
Results: In total, 612 patients were included. At baseline, most patients (93.6%) had psoriasis involvement in at least one special body area. Overall, patients with psoriasis in special body areas reported a worse quality of life (QoL) than those without. Patients with versus without psoriasis in special body areas achieved a comparable mean reduction from baseline in PASI score (10.9 vs. 9.2 at week 2, and 16.9 vs. 14.7 at week 12, respectively) and DLQI score (6.0 vs. 4.4 at week 2, and 9.9 vs. 7.5 at week 12, respectively); a similar proportion of patients also achieved PASI 50 at week 2, and PASI 75 and PASI 90 at week 12, and a DLQI (0/1) at weeks 2 and 12. Several significantly different results were reported between subgroups, the majority of which favored patients with special body area involvement.
Conclusion: Most patients had psoriasis involvement in a special body area which was associated with worse QoL. Ixekizumab is similarly effective in reducing disease severity and improving QoL in patients with plaque psoriasis across different special body areas.

Keywords: Effectiveness; Ixekizumab; Moderate-severe plaque psoriasis; Special body areas; Quality of life

Key Summary Points

Psoriasis is a chronic, incurable inflammatory skin disease affecting over six million people in China and associated with a considerable negative impact on patient quality of life; however, there are limited real-world data to inform the treatment of psoriasis with special body area involvement, especially in the Chinese population.

In a Chinese post-marketing surveillance study, ixekizumab, a monoclonal antibody against interleukin-17A, demonstrated effectiveness in the treatment of psoriasis that was consistent with findings from previous randomized controlled trials.

This study aimed to report further analyses from the Chinese post-marketing surveillance study to explore the effectiveness of ixekizumab for treating patients with psoriasis in special body areas.

At baseline, patients with psoriasis in special body areas reported a numerically higher disease severity and significantly lower quality of life than those without.

Ixekizumab was observed to be similarly effective in reducing disease severity and improving quality of life in patients with plaque psoriasis across different locations, including special body areas.

INTRODUCTION

Psoriasis is a chronic, incurable inflammatory skin disease characterized by red, scaly plaques that can develop across different body areas as a result of complex gene-environmental-mediated epidermal hyperproliferation [1, 2]. In China, more than six million people have psoriasis [3], the majority of whom have moderate-

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to-severe plaque psoriasis [4]. Plaque psoriasis is associated with a considerable negative impact on patient quality of life (QoL), including a detrimental effect on social relationships, mental health, and occupation-related activities [5], as well as increasing the risk of cardiovascular and other comorbidities [6]. Psoriasis in special body areas often requires systemic treatment because of the increased emotional and functional impact on patients, as well as physical barriers limiting the use of alternative topical therapeutic options in these anatomical locations [7, 8]. However, there are limited real-world data to inform the treatment of psoriasis with involvement of special body areas, especially in the Chinese population.

Psoriasis plaques can develop anywhere on the exterior surfaces of the body, with involvement in special anatomical areas, such as the scalp, nail, joint, palmoplantar, and genital regions, posing particular challenges due to visibility, sensitivity, and/or functional impairment [9–11]. The scalp is the most common site of psoriasis onset in Chinese patients (approximately 53%) [4] and is associated with a negative impact on patient QoL due to the visibility of plaques [12, 13]. In addition, the presence of hair on the scalp complicates the use of topical treatment options [7]. Notably, around half of patients with psoriasis develop nail psoriasis [14, 15], which can impair manual dexterity, negatively impacting QoL and work productivity because of pain, discomfort, and associated psychological stress [16]. Nail psoriasis is also a predictor of psoriatic arthritis [17] and is associated with enthesitis [18]. Furthermore, plaques that develop across joint lines are associated with painful fissuring [19]. Up to 40% of patients with psoriasis have involvement on their palms and soles (palmoplantar area) [20], which is associated with a significant negative effect on QoL due to physical disability [21]. During their disease course, approximately 60% of adult patients with psoriasis will develop plaques at least once in the genital area [22], which are associated with reduced QoL and sexual health [23, 24].

Ixekizumab is a humanized, immunoglobulin G4 monoclonal antibody that selectively inhibits interleukin-17A to encourage skin normalization in patients with plaque psoriasis by limiting excessive keratinocyte proliferation [25]. The efficacy and safety of ixekizumab in the treatment of moderate-to-severe plaque psoriasis were demonstrated in the global UNCOVER 1, 2, and 3 clinical trials [26–28]. The efficacy of ixekizumab treatment in psoriasis with scalp, nail, and palmoplantar involvement has also been shown during a subsequent 5-year analysis of these trials [29, 30]. To supplement clinical trial findings and further inform clinical decision-making, a post-marketing surveillance study was conducted to investigate the safety and efficacy of ixekizumab in patients with moderate-to-severe plaque psoriasis treated in routine clinical practice in China [31]. The primary results of this study showed improvements in disease severity and QoL with ixekizumab treatment. Here, we report further analyses from the Chinese post-marketing surveillance study to explore the effectiveness of ixekizumab in Chinese adults with moderate-to-severe plaque psoriasis across different special body areas.

METHODS

Study Design and Patients

The study design and primary results of this prospective, observational, single-arm, multicenter, post-marketing surveillance study have been reported previously [31].

Briefly, patients aged ≥ 18 years who were diagnosed with moderate-to-severe plaque psoriasis and prescribed ixekuzimab were recruited from the dermatology departments of hospitals across China. The recommended ixekizumab regimen for the treatment of moderate-to-severe plaque psoriasis was an initial dose of 160 mg subcutaneously (two 80 mg injections), followed by 80 mg subcutaneously every 2 weeks until week 12, and then maintenance therapy comprising 80 mg subcutaneously every 4 weeks. Patients were monitored for 12 weeks from baseline (visit 1, day 0 prior to the first dose of ixekizumab) or until their final dose of ixekizumab, whichever occurred first.

The study was conducted in compliance with Good Clinical Practice and the Declaration of Helsinki. All patients provided written, informed consent prior to participating in the study.

Assessments and Outcomes

Patient demographics and psoriasis disease characteristics were collected during the baseline visit. Skin involvement was assessed using the Psoriasis Area and Severity Index (PASI) (range 0–72 with higher scores indicating more severe disease) [32] and QoL was evaluated using the Dermatology Life Quality Index (DLQI) (range 0–30 with higher scores indicating more impairment) at baseline, 2 weeks (± 5 days), and 12 weeks (± 3 weeks) [33, 34].

The change from baseline in PASI score was evaluated at week 2 and 12. The proportions of patients achieving PASI 50 at week 2 and PASI 75 or PASI 90 at week 12, the change from baseline in DLQI score at week 2 and 12, as well as the proportions of patients achieving a DLQI score of 0/1 at week 2 and 12 were evaluated as secondary endpoints. The minimal clinically important difference (MCID) in PASI score was defined as a 75% improvement from baseline, and for DLQI was a 5-point change from baseline [35].

Subgroup Analyses

PASI and DLQI scores were compared across the following patient subgroups: with versus without psoriasis in any special body areas (defined as any of these areas, i.e., overall, or either scalp, nail, joint, palmoplantar, and/or genital area involvement).

Statistical Analyses

The effectiveness analysis was performed in patients who had received at least one dose of ixekizumab and with at least one post-baseline observation (efficacy population). Baseline characteristics and effectiveness outcomes were summarized using descriptive statistics. Analysis of variance (ANOVA) was used to analyze differences in the mean PASI and DLQI scores at baseline across patient subgroups. Analysis of covariance (ANCOVA) was used to analyze the mean differences in the change from baseline in PASI score or DLQI at week 2 and 12, with the baseline value as the covariate. Pearson's chi-square test or Fisher's exact test was used to compare differences in the proportions of patients achieving PASI 50, PASI 75, PASI 90, and DLQI score of 0/1 in different subgroups.

All statistical analyses were performed using SAS v9.4. There were no imputations for missing values and no adjustments for multiplicity. A two-sided p value $< 5\%$ was considered statistically significant.

RESULTS

Patients

The efficacy population comprised 612 of the 666 patients enrolled in the study at 26 hospitals across China. Baseline demographics and disease characteristics for the overall population have been reported previously [31]. Briefly, the mean (standard deviation [SD]) age of patients was 40.0 (13.0) years, 71.9% were male, the mean (SD) duration of disease was 9.2 (9.5) years, and 86.4% of patients had received previous treatment.

Psoriasis locations and severity at baseline are detailed in Table 1. Most patients had psoriasis involvement in at least one special body area at baseline (573/612; 93.6%), with the majority of patients reporting scalp involvement (506/612; 82.7%). Patients with versus psoriasis involvement in special body areas had a numerically higher PASI score at baseline than those without, reaching statistical significance in patients with nail, joint, palmoplantar, or genital area involvement (Table 1). Overall, patients with versus psoriasis involvement in special body areas reported a significantly higher DLQI score at baseline than those without (12.8 vs. 9.9; $p = 0.0140$), a trend also observed in the palmoplantar and genital subgroups (Table 1).

Table 1 Baseline patient characteristic and disease severity

Parameter		Efficacy analysis population (N = 612)	
Special body area of plaque psoriasis at baseline, *n* (%)			
Scalp		506 (82.7)	
Nails		206 (33.7)	
Joint area		219 (35.8)	
Palmoplantar area		184 (30.1)	
Genital area		72 (11.8)	
Number of special body areas, *n* (%)			
0		39 (6.4)	
1		215 (35.1)	
2		183 (29.9)	
3		109 (17.8)	
4		51 (8.3)	
5		15 (2.5)	
Total		612 (100.0)	
Baseline PASI score, mean (SD)			
Special body area	With special body area	Without special body area	*P* value
Overall[a]	18.4 (13.1)	15.4 (8.1)	0.1744
Scalp	18.6 (13.0)	15.9 (11.8)	0.0534
Nails	22.2 (15.9)	16.1 (10.4)	< 0.0001
Joint area	20.0 (12.6)	17.1 (12.9)	0.0081
Palmoplantar area	23.3 (16.1)	15.9 (10.4)	< 0.0001
Genital area	21.6 (18.1)	17.7 (11.9)	0.0181
Baseline DLQI, mean (SD)			
Special body area	With special body area	Without special body area	*P* value
Overall	12.8 (7.2)	9.9 (6.4)	0.0140
Scalp	12.8 (7.2)	11.7(6.9)	0.1876
Nails	13.0 (7.6)	12.4 (7.0)	0.3607
Joint area	13.2 (7.2)	12.2 (7.1)	0.1218
Palmoplantar area	14.0 (7.9)	12.0 (6.8)	0.0016
Genital area	14.8 (8.1)	12.3 (7.0)	0.0051

DLQI Dermatology Life Quality Index, *PASI* Psoriasis Area and Severity Index, *SD* standard deviation
[a]"Overall" represents all patients who had ≥ 1 psoriasis plaque in a special body location

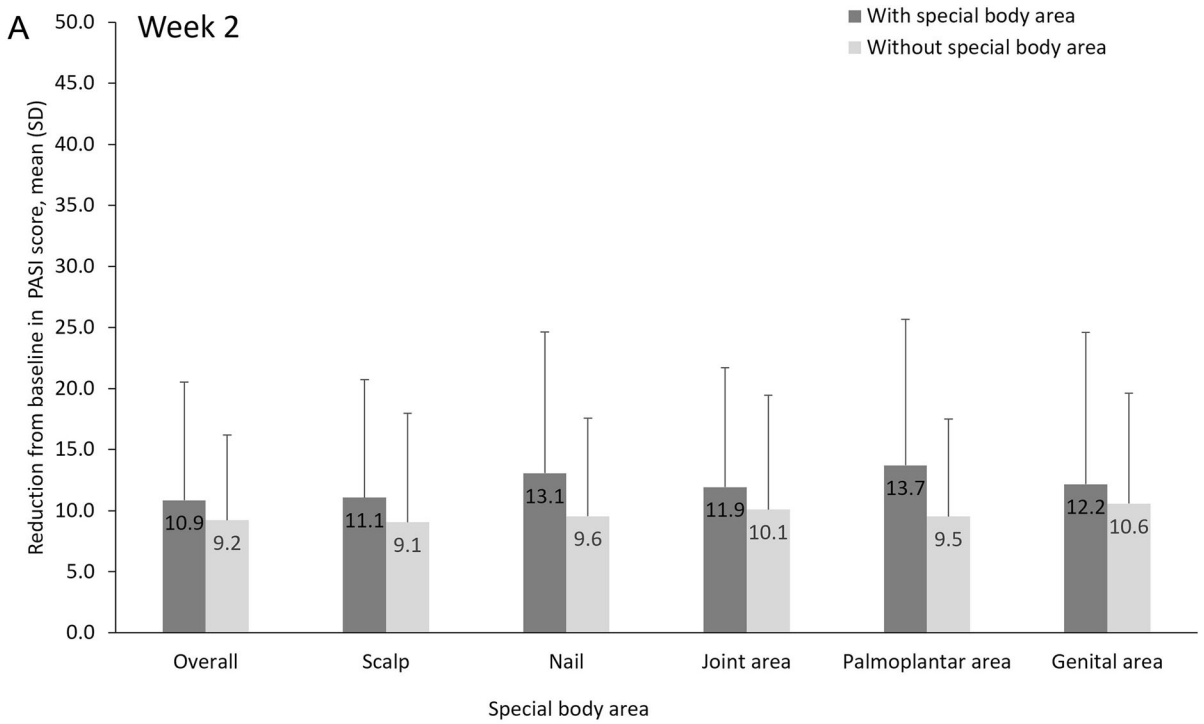
SUBGROUP EFFECTIVENESS

PASI Score

Mean PASI score decreased over time (at baseline vs. week 2 vs. week 12) in both patients with and without special body area involvement (Supplemental Fig. 1). There were no significant differences in the mean reduction in PASI score from baseline at week 2 or 12 between patients with versus without psoriasis involvement in any of the specified special body areas (Fig. 1). The proportions of patients achieving PASI 50, PASI 75, or PASI 90 were generally similar across subgroups (Supplemental Fig. 2A–C). However, PASI 50 at week 2 was achieved by significantly more patients with scalp involvement than those without (65.4% vs. 53.8%; $p = 0.0461$).

DLQI

The mean reductions in DLQI score from baseline to week 2 or 12 were generally similar across subgroups (Fig. 2). At week 2, patients with scalp involvement reported a significantly greater reduction in mean DLQI score from baseline compared with those without scalp involvement (6.1 vs. 4.6; $p = 0.0416$) (Fig. 2a). At week 12, patients with nail involvement reported a significantly smaller reduction in mean DLQI from baseline than those without



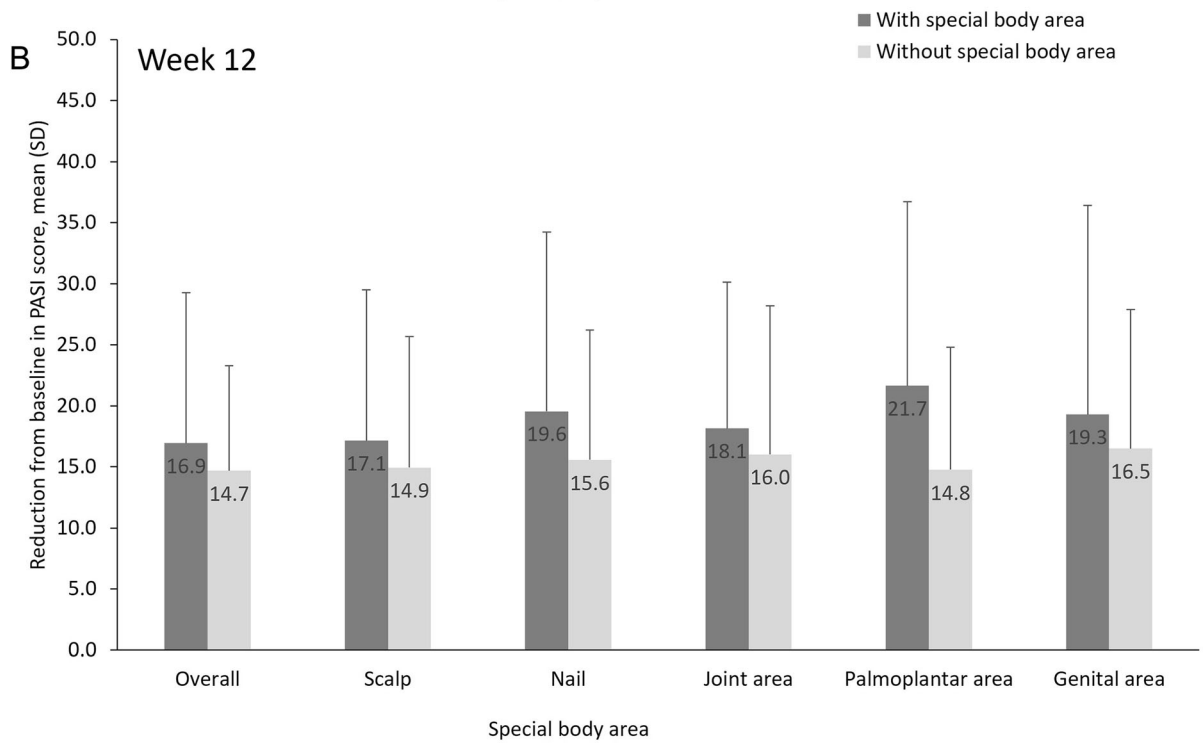


Fig. 1 Reduction from baseline in PASI score in patients with versus without psoriasis in special body areas at week 2 **a** and week 12 **b**. There were no significant differences found between patients with and without psoriasis involvement in any special body area. *PASI* Psoriasis Area and Severity Index, *SD* standard deviation

(9.3 vs. 10.0; $p = 0.0462$) (Fig. 2b). The proportions of patients achieving a DLQI score of 0/1 were generally similar across the subgroups (Supplemental Fig. 3A, B). A DLQI of 0/1 was achieved by significantly more patients with palmoplantar involvement at week 2 than those without (25.0% vs. 17.6%; $p = 0.0464$) (Supplemental Fig. 3A), and significantly fewer patients with joint (53.0% vs. 64.0%; $p = 0.0235$) or palmoplantar area (52.3% vs. 63.1%; $p = 0.0350$) involvement at week 12 than those without (Supplemental Fig. 3B).

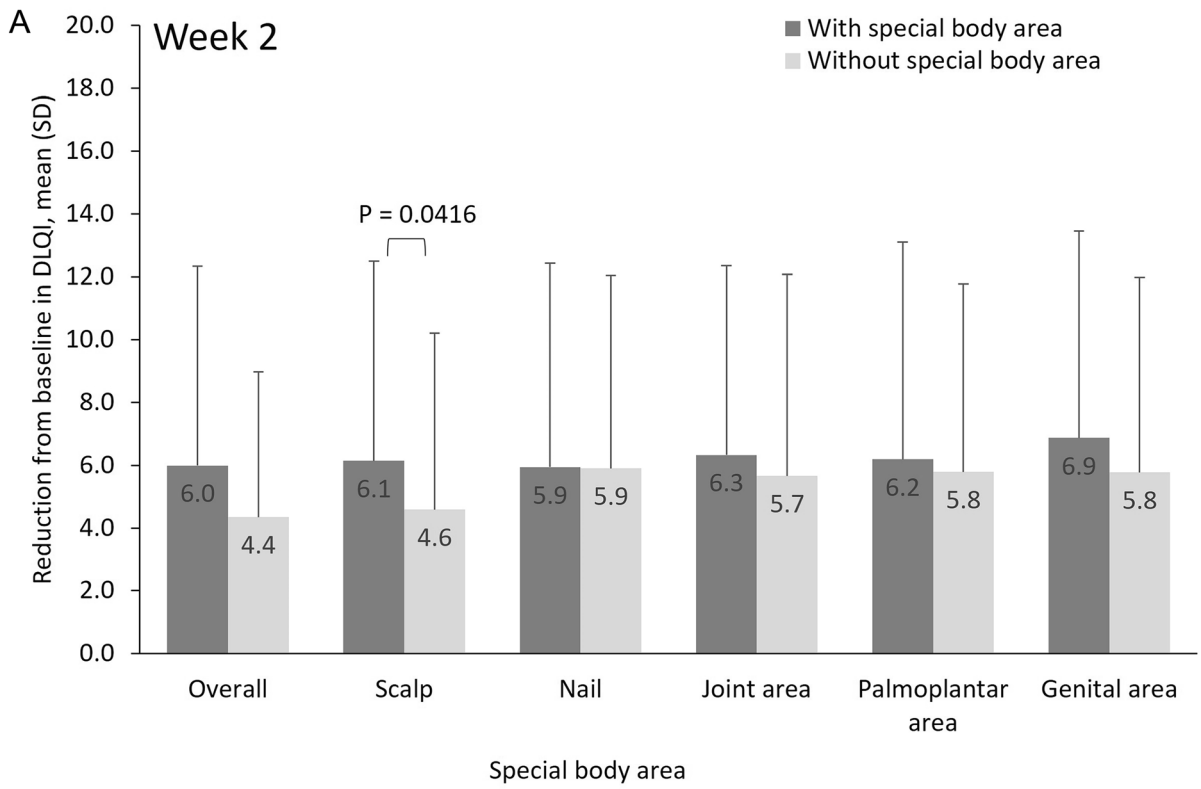
DISCUSSION

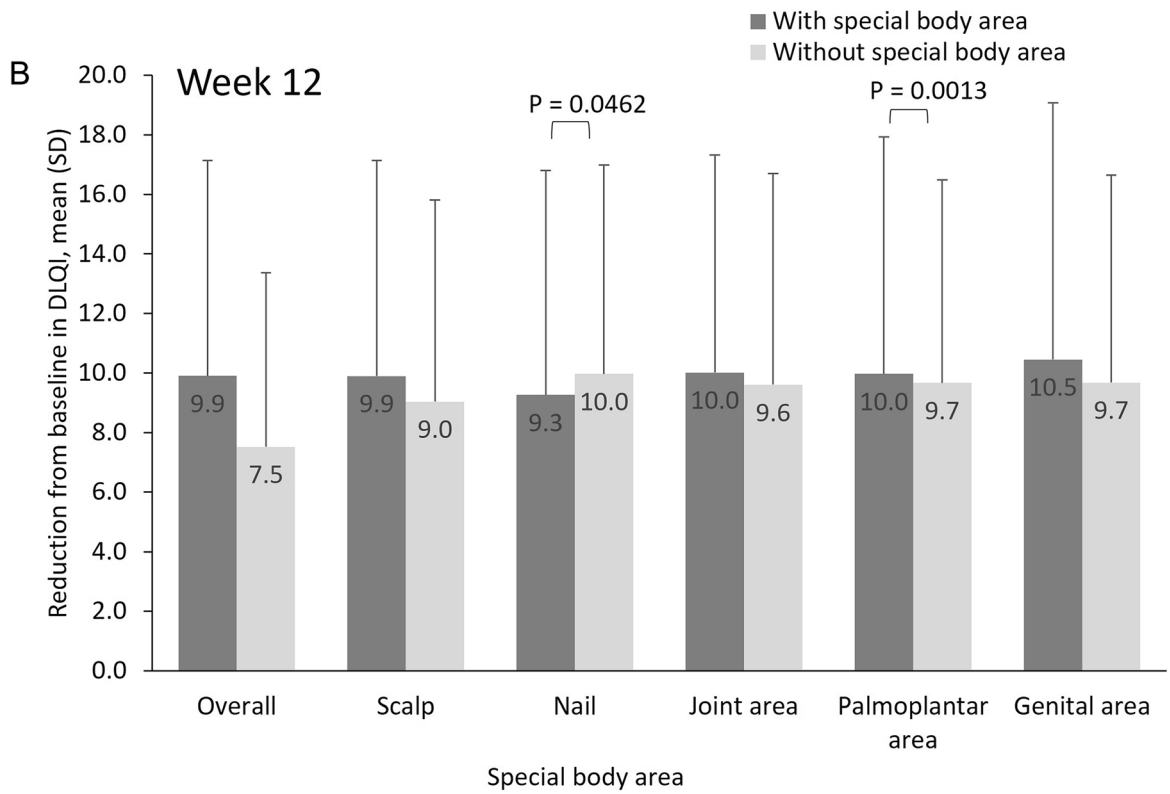
Plaque psoriasis that develops in special body areas is associated with a significant negative impact on patient health and QoL [9–11]. Findings from this subanalysis of a real-world, observational study conducted in Chinese adults with moderate-to-severe plaque psoriasis showed that treatment with ixekizumab was similarly effective in reducing disease severity and improving QoL across different disease locations including scalp, nail, as well as joint, palmoplantar, and genital regions. Therefore, these results indicate that ixekizumab is effective in treating patients with moderate-to-severe plaque psoriasis even in those with involvement of special body areas that are considered difficult to treat [36]. Our observations are consistent with analyses from global phase 3 clinical studies showing that ixekizumab is effective for the treatment of moderate-to-severe plaque psoriasis with scalp [37], nail [38–40], or non-pustular palmoplantar [41] involvement.

In our subgroup analyses, significant differences were observed for a small number of endpoints. For instance, significantly better outcomes were observed for patients with scalp involvement in achievement of PASI 50 and change from baseline in DLQI score at week 2 than for those without, and for patients with palmoplantar involvement in achievement of DLQI of 0/1 at week 2 than for those without. It is possible that the high visibility of scalp involvement influenced the negative effect on DLQI, in line with a previous cross-sectional study performed to describe the QoL in patients with scalp psoriasis [42]. However, as these apparent differences were not consistent across the PASI and DLQI endpoints or timepoints, it is challenging to draw a meaningful interpretation of these findings.

The vast majority (> 90%) of patients in this study had psoriasis in at least one special body area at baseline, demonstrating the considerable disease burden in a real-world Chinese population with moderate-to-severe plaque psoriasis. This finding is similar to data from the UNCOVER 1, 2, and 3 trials, in which the majority (> 80%) of patients reported scalp or nail involvement [41]. This observation from our study also suggests a preference among Chinese doctors for using ixekizumab in patients with psoriasis in special body areas. Furthermore, our results revealed that the majority (> 80%) of patients had scalp psoriasis, which is consistent with a previous survey reporting that the scalp was the most common site of onset in Chinese patients with psoriasis [4]. The presence of plaque psoriasis in special body areas was associated with worse disease severity at baseline, particularly in patients with nail, joint, palmoplantar, or genital involvement. For patients across all subgroups, mean baseline DLQI scores were > 11, indicating that their disease had a very large negative effect on QoL [35]. At baseline, the greatest difference in QoL was observed between patients with palmoplantar or genital involvement and those without. These results are in line with those reported from a USA-based study that found psoriasis with special area involvement was linked to adverse life consequences, including poor QoL and depression [43]. Interestingly, however, a recent systematic review of worldwide data concluded that the anatomic location of psoriasis involvement did not differentially effect patient QoL [44], indicating potential regional differences that require further investigation.

Key limitations of this study include those inherent to all single-arm observational studies such as a lack of a comparator arm and the risk of selection bias. Moreover, this study was primarily designed to assess safety, and did not use questionnaires specifically designed to assess


A
Week 2
With special body area
Without special body area
Reduction from baseline in DLQI, mean (SD)
20.0
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
P = 0.0416
6.0
4.4
6.1
4.6
5.9
5.9
6.3
5.7
6.2
5.8
6.9
5.8
Overall
Scalp
Nail
Joint area
Palmoplantar area
Genital area
Special body area


B
Week 12
With special body area
Without special body area
Reduction from baseline in DLQI, mean (SD)
20.0
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
P = 0.0462
P = 0.0013
9.9
7.5
9.9
9.0
9.3
10.0
10.0
9.6
10.0
9.7
10.5
9.7
Overall
Scalp
Nail
Joint area
Palmoplantar area
Genital area
Special body area

◀**Fig. 2** Reduction from baseline in DLQI in patients with versus without psoriasis involvement in special body areas at week 2 **a** and week 12 **b**. There were no significant differences found between patients with and without psoriasis involvement across the different special body areas except for where indicated. *DLQI* Dermatology Life Quality Index, *SD* standard deviation

disease extent and severity in special body areas, such as the Nail Psoriasis Severity Index (NAPSI) and the Psoriasis Scalp Severity Index (PSSI), which may limit the conclusions that can be drawn regarding treatment effectiveness. In addition, only a small proportion of patients in this study (approximately 6%) did not have involvement of a challenging body area and many patients within the specific subgroups had psoriasis plaques in more than one special body area, which may have confounded the results of the subgroup analyses. Therefore, the current findings should be interpreted with caution and further studies are required to investigate the relationship between QoL and plaque psoriasis in particular body regions in isolation.

CONCLUSIONS

Ixekizumab treatment reduced disease severity and improved QoL in a real-world population of Chinese adults with moderate-to-severe plaque psoriasis, with similar effectiveness across different disease locations including special body areas.

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Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available for this database had been registered on the Human Genetic Resource Administration of China; due to related regulations of genetic resource and information protection, this database cannot be published or re-analyzed.

Declarations

Conflict of Interest. Lu Yi, Chen Rong, Li Jinnan, and Dou Guanshen are employees of Eli Lilly. Other authors have no conflicts of interest.

Ethics Approval. The study was conducted in compliance with Good Clinical Practice and the Declaration of Helsinki. All patients provided written, informed consent prior to participating in the study.

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