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ORIGINAL RESEARCH ARTICLE

The Safety of Ixekizumab in Chinese Adults with Moderate-to-Severe Plaque Psoriasis: Analyses from a Prospective, Single-Arm, Multicenter, 12-Week Observational Study

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Abstract

Introduction Ixekizumab, a monoclonal antibody against interleukin-17A, is efficacious and well tolerated for the treatment of moderate-to-severe plaque psoriasis. However, there are limited data on the real-world safety of ixekizumab in Chinese patient populations. We performed an observational study of ixekizumab for the treatment of moderate-to-severe plaque psoriasis in routine clinical practice in China. Here we present a further safety analysis of this study.

Methods In this prospective, observational, single-arm, multicenter, post-marketing safety study, adults (≥18 years) with moderate-to-severe plaque psoriasis receiving ixekizumab were enroled at dermatology departments in hospitals across China and prospectively followed for 12 weeks or until their last dose of ixekizumab. In this analysis, we evaluated adverse events (AEs) of special interest (AESIs) identified using MedDRA® search strategies. We also analyzed AEs and AESIs occurring in greater than ten patients in subgroups by age (< 65/≥ 65 years), sex, body weight (< 60/60 kg to < 80/≥ 80 kg), renal impairment, hepatic impairment, history of tuberculosis, history of HBV infection, recent or active infection, history of allergic reaction/hypersensitivity, and number (0–1/2–4/5–7) of ixekizumab 80 mg injections after baseline until day 105.

Results This analysis included 663/666 patients enrolled in the primary study. At least one AESI was reported in 224 (33.8%) patients and considered related to ixekizumab in 181 (27.3%); the most common were injection site reactions ($n = 131$, 19.8%), infections ($n = 80$, 12.1%), and allergic reactions/hypersensitivity events ($n = 59$, 8.9%). The proportion of patients with ≥ 1 AE was higher for females versus males (99/186, 53.2% versus 184/477, 38.6%, $p = 0.0006$). The proportion of patients with ≥ 1 AE increased with the number of ixekizumab injections after baseline [61/188 (32.4%) for zero to one injection, 151/338 (44.7%) for two to four injections, and 61/106 (57.5%) for five to seven injections; $p = 0.0001$].

Conclusions In this real-world study, ixekizumab was well tolerated in Chinese patients with moderate-to-severe plaque psoriasis, with no difference in safety across most patient subgroups.

Key Points

The results of this real-world study conducted in China show that ixekizumab is generally well-tolerated in patients with moderate-to-severe plaque psoriasis.

The safety profile of ixekizumab was consistent across multiple patient subgroups.

1 Introduction

Approximately 6 million people in China have psoriasis [1], an incurable, immune-mediated, chronic, recurrent inflammatory disease [2], the majority of whom have moderate-to-severe plaque psoriasis [3]. The estimated age-standardized incidence rate of psoriasis in China in 2019 was 54.0 per 100,000 people, equivalent to around 900,000 new cases per year [4]. A majority of patients with psoriasis have comorbidities at diagnosis, most commonly metabolic and cardiovascular diseases as well as other autoimmune and inflammatory conditions [5]. The presence of comorbidities usually results in a direct initiation of treatment with biologics. Biologics, including interleukin 17A (IL-17A) antagonists, have excellent efficacy and safety in the treatment of moderate-to-severe plaque psoriasis [2]. In addition,

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compared with immunomodulatory therapy with methotrexate and acitretin, biologics may have more effectiveness in reducing psoriatic itch [6]. Indeed, ixekizumab, a humanized immunoglobulin G4 monoclonal antibody that selectively inhibits IL-17A [7], was efficacious and well tolerated for the treatment of moderate-to-severe plaque psoriasis and resulted in improvements in patient quality of life in three global, randomized, phase 3 clinical trials, and a phase 3 study undertaken in China [8–10]. However, further real-world data addressing common concerns of Chinese healthcare providers and patients around the use of ixekizumab would be highly valuable. For example, a further analysis of factors associated with ixekizumab side effects and safety data in challenging patient groups such as elderly patients and those with a history of infection or allergies would help optimise and inform treatment planning.

Although real-world data on the use of ixekizumab have been reported in western patient populations [11], there are limited data available regarding the use of ixekizumab in Chinese patients in a real-world setting. Therefore, we conducted a study to investigate the safety and effectiveness of ixekizumab for the treatment of moderate-to-severe plaque psoriasis in routine clinical practice in China [12]. The primary results of this study showed that ixekizumab is effective for the treatment of moderate-to-severe plaque psoriasis in Chinese adults; after 12 weeks' treatment, 93.2%, 77.4%, and 45.1% of patients who received ixekizumab had achieved at least a 75%, 90%, or 100% improvement in Psoriasis Area and Severity Index (PASI) score, respectively [12]. The safety findings of this study showed that ixekizumab was well tolerated in Chinese adults with moderate-to-severe plaque psoriasis [12], with a safety profile consistent to that reported in international phase 3 trials conducted in predominantly Caucasian populations and a phase 3 study undertaken in China [9, 10, 13]. The primary analysis of this real-world study also revealed that at least one adverse event (AE) was reported in 42.7% of patients, 85.5% of which were mild in intensity. Three patients reported a serious AE (SAE), two of which were considered related to study treatment (hypersensitivity and pustular psoriasis); no deaths were reported. Five patients discontinued treatment due to an AE [12].

In this paper, we report further safety data from the above real-world study of ixekizumab for the treatment of moderate-to-severe plaque psoriasis conducted in Chinese adults, focusing on AEs of special interest (AESIs) and an analysis of safety data by patient subgroups.

2 Methods

2.1 Study Design and Patients

A prospective, observational, single-arm, multicenter, post-marketing safety study was undertaken in China to investigate the safety and effectiveness of ixekizumab for the treatment of moderate-to-severe plaque psoriasis in routine clinical practice. The study design and the primary results of this study have been reported previously [12].

Briefly, adults (≥ 18 years of age) diagnosed with moderate-to-severe plaque psoriasis who had initiated ixekizumab treatment were enrolled at dermatology departments in hospitals across China. Patients were prospectively followed for 12 weeks from baseline (visit 1, day 0 prior to the first dose of ixekizumab) or until their last dose of ixekizumab, whichever occurred first. The recommended regimen for the treatment of moderate-to-severe plaque psoriasis is an initial dose of ixekizumab 160 mg subcutaneously (two 80 mg injections), followed by 80 mg subcutaneously every 2 weeks until week 12 and then maintenance therapy with 80 mg subcutaneously every 4 weeks.

The study was conducted in compliance with Good Clinical Practice and the principles outlined in the Declaration of Helsinki and its amendments. The study protocol and its amendments were approved by Independent Ethics Committees at each study site. All patients provided written, informed consent prior to participating in the study.

2.2 Assessments and Outcomes

The primary outcome of the study was the safety of ixekizumab over 12 weeks in routine clinical practice, assessed based on the incidence of AEs and SAEs.

During the baseline visit, data regarding patient demographics, medical history, and concomitant medications were collected.

Safety was assessed during follow-up visits 2 weeks (± 5 days) and 12 weeks (± 3 weeks) after the first dose of ixekizumab and on the telephone 6 weeks (± 5 days) after the first dose of ixekizumab. Patients were instructed to inform the investigator about any AEs that occurred between the visits. All AEs were recorded, irrespective of any potentially causal relationship with ixekizumab. AEs were evaluated by severity (mild, moderate, and severe [14]) and causality (yes or no [15]) based on the investigator's opinion. All AE terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA®) v25.0. Any AE meeting the definition of "serious" [14] was reported as an SAE. The World Health Organization (WHO) Drug Dictionary (version GLOBALB3MAR2022) was used to classify concomitant medications.

We evaluated the proportions of patients in whom AESIs were reported over 12 weeks of treatment. AESIs included injection site reactions (ISRs, plural), referring to the high-level grouping of different preferred terms (PT) used to describe various injection-site reactions, hepatic events, defined as hepatic adverse events and abnormal hepatic tests, cytopenias, allergic reactions/hypersensitivity, infections, major adverse cardiovascular events (MACE), malignancies,

inflammatory bowel disease (IBD), and interstitial lung disease. AESIs were identified using MedDRA® query search strategies.

An evaluation of Drug-Induced Serious Hepatotoxicity (eDISH) was used to clearly identify any cases of drug induced liver injury that met Hy's law [defined as an alanine transaminase (ALT) or aspartate aminotransferase (AST) > 3× the upper limit of normal (ULN), total bilirubin > 2 × ULN, absence of initial findings of cholestasis (i.e., absence of elevation of alkaline phosphatase to > 2 × ULN), and no other reason can be found to explain the combination of increased ALT and total bilirubin, such as viral hepatitis A through E, other preexisting or acute liver disease, or another drug capable of causing the observed injury [16]].

We also analyzed safety (AEs and AESIs) in subgroups of patients by age (< 65/≥ 65 years), sex (male/female), body weight (< 60/60 to < 80/≥ 80 kg), renal impairment (yes/no at baseline), hepatic impairment (yes/no at baseline), history of tuberculosis (TB, yes/no), history of hepatitis B virus (HBV) infection (yes/no), recent or active infection (yes/no at baseline), history of allergic reaction/hypersensitivity (yes/no), and number (0–1/2–4/5–7) of ixekizumab 80 mg injections after baseline until day 105. Subgroup data were collected by the investigators at baseline. Subgroup analyses of AESIs were only undertaken for AESIs occurring in greater than ten patients.

2.3 Statistical Analyses

Safety was analyzed in all patients who had received at least one dose of ixekizumab (safety population).

All analyses were descriptive. The difference in incidences of AEs/AESIs between/among patients within categories of each subgroup were analyzed using the Pearson's chi-squared test or Fisher's exact test. A two-sided significance level of 5% was used for all statistical analyses. There were no imputations for missing data and no adjustments for multiplicity. All statistical analyses were performed using SAS v9.4.

3 Results

3.1 General

The safety population included 663 of the 666 patients enrolled in the study across 26 hospitals in China. Three patients were excluded from the safety population because the data to confirm whether they had received at least one dose of ixekizumab were not available.

A total of 75/663 (11.3%) patients discontinued from the study after 12 weeks. The most common reasons for discontinuation were patient decision (35 patients, 5.3%), loss to follow-up (19 patients, 2.9%), and poor compliance (11 patients, 1.7%). Five patients discontinued due to an AE; the events included pustular psoriasis, dermatitis atopic, erythema, psoriasis, oedema, hypersensitivity, and hypoproteinemia (Note that > 1 AE could lead to discontinuation in a single patient) [12].

More than one-half of the patients (55.4%) were using ≥ 1 concomitant medication. The most commonly received concomitant medications were dermatologicals (35.0%) at an anatomical level. The dermatologicals used by at least 10% of the population were emollients and protectives (14.0%), corticosteroids, dermatological preparations (12.2%), and antipruritics, including antihistamines and anesthetics (11.6%).

3.2 AESIs

A summary of AESIs is shown in Table 1. At least one AESI was reported in 224 (33.8%) patients, and in 181 (27.3%) patients AESIs were considered related to ixekizumab. The most commonly reported AESI was ISRs (131 patients, 19.8%). No MACE or cases of interstitial lung disease were reported. One case of lung neoplasm (causality was determined as "no") and one case of ulcerative colitis (causality was determined as "yes") was reported. The three AESIs reported by the highest proportions of patients in addition to hepatic events are detailed below.

Table 1 Summary of AESIs (safety analysis population, $n = 663$)

	Number of events	Incidence of event	
		All, *n* (%)	Related to study drug[a], *n* (%)
≥ 1 AESI	520	224 (33.8)	181 (27.3)
ISRs	349	131 (19.8)	128 (19.3)
Infections	92	80 (12.1)	42 (6.3)
Allergic reactions/hypersensitivities	70	59 (8.9)	38 (5.7)
Hepatic events	6	6 (0.9)	1 (0.2)
Cytopenias	1	1 (0.2)	0
IBD	1	1 (0.2)	1 (0.2)
Malignancy	1	1 (0.2)	0
Interstitial lung disease	0	–	0
MACE	0	–	0

[a]Based on the opinion of the investigator

AESI adverse event of special interest, *ISRs* injection site reactions, *CI* confidence interval, *IBD* inflammatory bowel disease, *MACE* major adverse cardiovascular event

3.2.1 ISRs

In total, 131 (19.8%) patients reported 349 ISRs, 335 (96.0%) of which were mild; no severe or serious events were reported. The most commonly reported ISRs were erythema (64 patients, 9.7%), swelling (62 patients, 9.4%), and pain (31 patients, 4.7%). It should be noted that patients may have experienced multiple ISRs that were recorded as separate events.

3.2.2 Infections

In total, 80 patients (12.1%) reported 92 infections. Most infections were mild in intensity (80 of 92 events, 87.0%); no severe infection or SAE of infection was reported. Infections reported in > 1% of patients were upper respiratory tract infection (23 patients, 3.5%), nasopharyngitis (12 patients, 1.8%), pharyngitis (8 patients, 1.2%), and tinea pedis (8 patients, 1.2%). Two patients reported herpes simplex and herpes virus infection separately. No patient reported an opportunistic infection in a narrow search. No cases of TB, HBV infection, or candidiasis were reported.

3.2.3 Allergic Reactions/Hypersensitivity Events

There were 70 allergic reactions/hypersensitivity events reported in 59 (8.9%) patients, all of which were considered not potentially anaphylactic in nature. The majority of nonanaphylactic allergic reactions/hypersensitivity events were mild (58 of 70 events, 82.9%), occurring in 48 (81.4%) patients, with no severe events reported. One patient had moderate hypersensitivity, which was classified as an SAE (considered medically significant). Events reported by > 1% of patients were urticaria (22 patients, 3.3%), dermatitis (12 patients, 1.8%), hypersensitivity (8 patients, 1.2%), and eczema (7 patients, 1.1%).

3.2.4 Hepatic Events

All six hepatic events reported in six patients (0.9%) were mild in intensity. Abnormal liver function test results were reported in three patients, and three patients had conditions related to liver damage (hepatic steatosis or liver disorder). eDISH illustrated that most patients had liver function test results within the normal range and no patient had results that met Hy's law (Fig. 1).

3.3 Subgroup Analyses

3.3.1 AEs

No significant differences in the incidence of AEs or AEs considered related to study drug by the investigators were observed over 12 weeks across the majority of the subgroups analyzed including age and weight, with the exception of sex and number of ixekizumab injections after baseline (Table 2). A higher proportion of female patients had at least one AE over 12 weeks compared with male patients (99/186, 53.2% versus 184/477, 38.6%, $p = 0.0006$). The proportion of patients with at least one AE increased with an increasing number of ixekizumab injections after baseline [61/188 (32.4%) of those who received zero to one injection, 151/338 (44.7%) for two to four injections, and 61/106 (57.5%) for five to seven injections; $p = 0.0001$].

3.3.2 AESIs

Only data for the most common AESIs (ISRs, infections, and allergic reaction/hypersensitivity) were analyzed by subgroup (Table 3) due to small numbers of patients ($n \leq 10$) for the other AESIs.

ISRs A higher proportion of female patients than male patients had ISRs [47/186 (25.3%) versus 84/477 (17.6%); $p = 0.0261$]. In addition, the proportions of patients with ISRs increased as the number of ixekizumab injections increased. ISRs were reported in 23/188 (12.2%) patients who received zero to one ixekizumab injections, 67/338 (19.8%) who received two to four injections, and 36/106 (34.0%) who received five to seven ixekizumab injections ($p < 0.0001$). No significant differences were observed over 12 weeks in patients who reported ISRs across the other subgroups analyzed.

Infections The proportions of patients with infections increased as the number of ixekizumab injections increased. Infections were reported in 14/188 (7.4%) patients who received zero to one ixekizumab injections, 46/338 (13.6%) who received two to four injections, and 18/106 (17.0%) who received five to seven injections ($p = 0.0338$). In addition, a higher proportion of patients with a history of allergic reactions/hypersensitivity had an infection (8/23, 34.8%) compared with those without a history of allergic reactions/hypersensitivity (72/640, 11.3%; $p = 0.0034$). No significant differences were observed across the other subgroups analyzed.

Allergic reactions/hypersensitivity events A higher proportion of female patients than male patients had allergic reactions/hypersensitivity events [26/186 (14.0%) versus 33/477 (6.9%); $p = 0.0041$]. There were no significant differences across the other subgroups analyzed. Patient's history of allergic reaction/hypersensitivity was not significantly correlated with the occurrence of allergic reactions AESI ($p = 0.1394$).

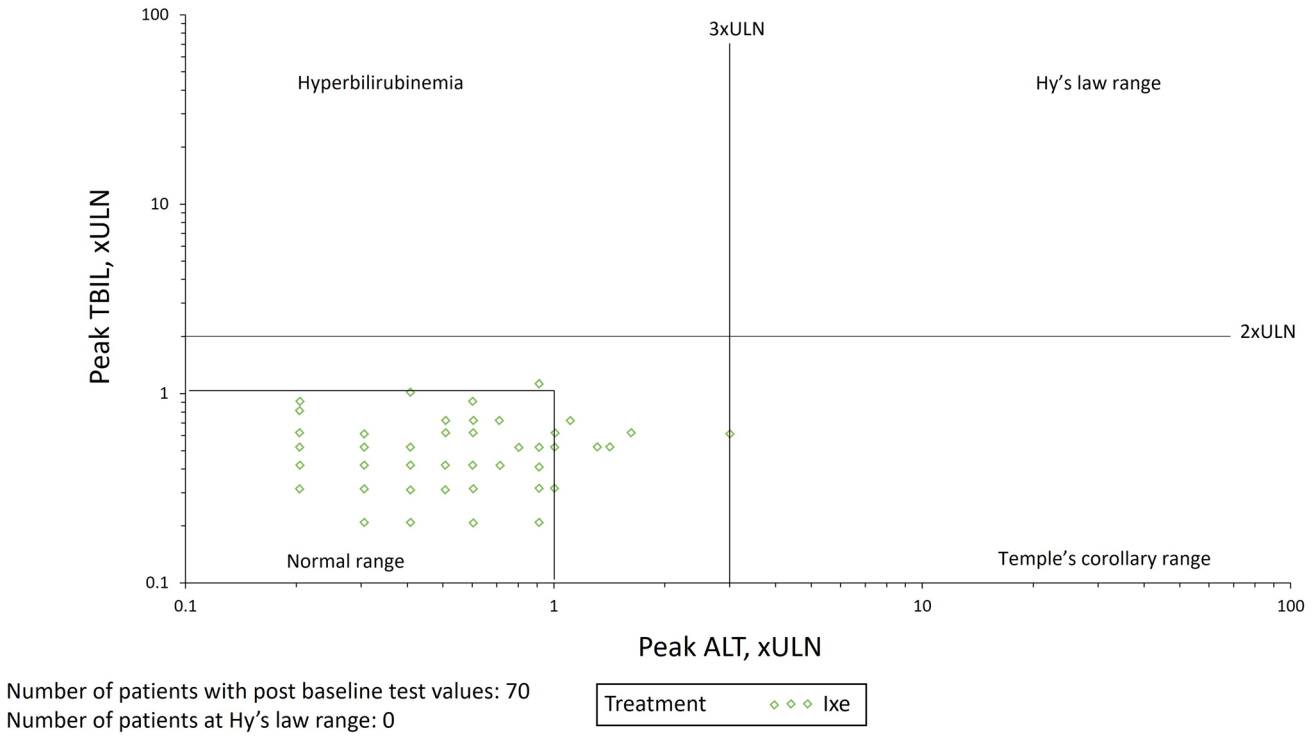

Fig. 1 Evaluation of drug-induced serious hepatotoxicity (eDISH) with ixekizumab. *ALT* alanine aminotransferase, *Ixe* ixekizumab, *TBIL* total bilirubin, *ULN* upper limit of normal.

4 Discussion

Ixekizumab was well tolerated in Chinese patients with moderate-to-severe plaque psoriasis in this real-world study. Over the 12-week treatment period, the proportion of Chinese patients in whom the AESI 'ISRs' was reported (19.8%) was slightly higher than reported in the international phase 3 studies, which included a predominantly Caucasian population (15.9–17.3%) [8, 9], and a phase 3 study undertaken in China (14.2%) [10]. In contrast, the AESI "infections" were reported in a smaller proportion of Chinese patients in the current study (12.1%) than in the international phase 3 studies (25.9–28.6%) [8, 9] and the phase 3 study undertaken in China (34.7%) [10], which could be attributed to the under-reporting of mild infections, such as upper respiratory tract infection (15.9% versus 3.5%), nasopharyngitis (4.5% versus 1.8%), or tinea pedis (5.1% versus 1.2%) [10], in a real-world setting.

Some statistically significant differences were observed in the analyses of safety by patient subgroups. For example, a higher proportion of women had AEs versus men (53.2% versus 38.6%), which was consistent with the higher proportion of women who had the AESIs "ISRs" (25.3% versus 17.6%) or allergic reaction/hypersensitivity (14.0% versus 6.9%). In addition, during the 12-week study, the proportion of patients with at least one AE increased with an increasing number of ixekizumab injections, mainly manifested as a higher proportion of patients with the AESI "ISRs" and "infections." It seems probable that patients with greater exposure to ixekizumab would have a higher risk of developing an ISR or mild infection. However, long-term safety data for ixekizumab collected over a 5-year period suggest the incidence of ISRs actually decreases significantly with exposure [17]. There was no increase in the proportion of patients with an allergic reaction/hypersensitivity with an increasing number of injections. Of note, a revised, citrate-free formulation of ixekizumab has been approved for use in the European Union (EU) [18] and USA [19] to replace the initial commercial formulation. The citrate-free formulation improves product tolerability and patient comfort by reducing the incidence or severity of injection site pain or both. Finally, we observed that a higher proportion of patients with a history of allergic reactions/hypersensitivity (8/23, 34.8%) had infections versus those without a history of allergic reactions/hypersensitivity (72/640, 11.3%). This finding is difficult to explain but may be due to the large difference in patient numbers between the two subgroups (23 versus 640 patients).

As this was an observational study that included many confounding factors, and due to high variability in ixekizumab exposure, few conclusions can be made regarding safety differences within the subgroups investigated.

Table 2 Analysis of the incidence of AEs over 12 weeks across patient subgroups

Subgroup	Patients, *n*	Patients with ≥ 1 AE		Patients with ≥ 1 AE related to study drug[a]	
		n (%)	*p*-value	*n* (%)	*p*-value
Age			0.1303		0.0807
< 65 years	627	272 (43.4)		210 (33.5)	
≥ 65 years	36	11 (30.6)		7 (19.4)	
Sex			0.0006		0.0053
Male	477	184 (38.6)		141 (29.6)	
Female	186	99 (53.2)		76 (40.9)	
Body weight			0.1854		0.0828
< 60 kg	144	71 (49.3)		58 (40.3)	
60 to < 80 kg	320	133 (41.6)		101 (31.6)	
≥ 80 kg	198	79 (39.9)		58 (29.3)	
Renal impairment			0.5086		1.000[b]
Yes	12	4 (33.3)		4 (33.3)	[b]
No	651	279 (42.9)		213 (32.7)	
Hepatic impairment			0.5344		0.3507
Yes	42	16 (38.1)		11 (26.2)	
No	621	267 (43.0)		206 (33.2)	
History of TB			0.3492		0.0809
Yes	16	5 (31.3)		2 (12.5)	
No	647	278 (43.0)		215 (33.2)	
History of HBV			0.6400		0.4889
Yes	57	26 (45.6)		21 (36.8)	
No	606	257 (42.4)		196 (32.3)	
Recent or active infection			0.8053		0.8261
Yes	20	8 (40.0)		7 (35.0)	
No	643	275 (42.8)		210 (32.7)	
History of allergic reaction/hypersensitivity			0.1721		0.5055
Yes	23	13 (56.5)		9 (39.1)	
No	640	270 (42.2)		208 (32.5)	
Ixekizumab injections after baseline[c]			0.0001		0.0059
0–1	188	61 (32.4)		51 (27.1)	
2–4	338	151 (44.7)		109 (32.2)	
5–7	106	61 (57.5)		48 (45.3)	

P values are based on Pearson's chi-squared test unless stated otherwise

[a]Based on the opinion of the investigator

[b]Fisher's exact test

[c]To day 105

AE adverse event, *HBV* hepatitis B virus, *TB* tuberculosis

Generally, no notable influence on the incidence of AEs was observed for the following factors: age, body weight, renal/hepatic impairment, history of TB, history of HBV infection, recent or active infection, or history of allergic reaction/hypersensitivity. Notably, the small sample size and limited follow-up duration (12 weeks) precluded the evaluation of rare events or events that require a longer latency period, such as malignancy. Additional limitations of this study include the small sample sizes in some of the patient subgroups, and the lack of an active comparator to allow the safety of ixekizumab to be assessed relative to other agents. The AEs observed in this study were consistent with the known safety profile of ixekizumab.

5 Conclusions

In conclusion, the most commonly reported AESI for ixekizumab in real word was ISRs, followed by infections. There was no difference in safety across most of

Table 3 Analysis of the incidence of the AESIs "ISRs," infections, and allergic reaction/hypersensitivity events over 12 weeks across patient subgroups

Subgroup	Patients, *n*	Patients with ≥ 1 ISRs		Patients with ≥ 1 infections		Patients with ≥1 allergic reaction/hypersensitivity event	
		n (%)	*p*-value	*n* (%)	*p*-value	*n* (%)	*p*-value
Age			0.0767		1.0000[a]		0.3585[a]
< 65 years	627	128 (20.4)		76 (12.1)		58 (9.3)	
≥ 65 years	36	3 (8.3)		4 (11.1)		1 (2.8)	
Sex			0.0261		0.1403		0.0041
Male	477	84 (17.6)		52 (10.9)		33 (6.9)	
Female	186	47 (25.3)		28 (15.1)		26 (14.0)	
Body weight			0.1805		0.5887		0.1080
< 60 kg	144	36 (25.0)		19 (13.2)		19 (13.2)	
60 to < 80 kg	320	61 (19.1)		41 (12.8)		23 (7.2)	
≥ 80 kg	198	34 (17.2)		20 (10.1)		17 (8.6)	
Renal impairment			0.7128		1.0000[a]		1.0000[a]
Yes	12	3 (25.0)		1 (8.3)		1 (8.3)	
No	651	128 (19.7)		79 (12.1)		58 (8.9)	
Hepatic impairment			0.1866		0.6482		0.7819[a]
Yes	42	5 (11.9)		6 (14.3)		4 (9.5)	
No	621	126 (20.3)		74 (11.9)		55 (8.9)	
History of TB			0.0518[a]		1.0000[a]		1.0000[a]
Yes	16	0		2 (12.5)		1 (6.3)	
No	647	131 (20.2)		78 (12.1)		58 (9.0)	
History of HBV			0.4312		0.9586		0.3483
Yes	57	9 (15.8)		7 (12.3)		7 (12.3)	
No	606	122 (20.1)		73 (12.0)		52 (8.6)	
Recent or active infection			0.7785[a]		0.2865[a]		1.0000[a]
Yes	20	3 (15.0)		4 (20.0)		1 (5.0)	
No	643	128 (19.9)		76 (11.8)		58 (9.0)	
History of allergic reaction/hypersensitivity			1.0000[a]		0.0034[a]		0.1394[a]
Yes	23	4 (17.4)		8 (34.8)		4 (17.4)	
No	640	127 (19.8)		72 (11.3)		55 (8.6)	
Ixekizumab injections after baseline[b]			< 0.0001		0.0338		0.7049
0–1	188	23 (12.2)		14 (7.4)		15 (8.0)	
2–4	338	67 (19.8)		46 (13.6)		34 (10.1)	
5–7	106	36 (34.0)		18 (17.0)		9 (8.5)	

P values are based on Pearson's chi-squared test unless stated otherwise

[a]Fisher's exact test

[b]To day 105

AESI adverse event of special interest, *ISRs* injection site reactions, *HBV* hepatitis B virus, *TB* tuberculosis

the subgroup analyses. Ixekizumab was well tolerated in Chinese patients with moderate-to-severe plaque psoriasis in this real-world study.

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Declarations

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Conflicts of Interest R.C. and J.L. are employees of Eli Lilly China. The other authors have no conflicts of interest to declare.

Ethics Approval This study was conducted with respect for the individual participants according to the protocol, the World Medical Association Declaration of Helsinki, the ICH-GCP guideline, and applicable local regulatory requirements of each participating region. The study was approved by Independent Ethics Committees at each study center (see electronic supplementary material, Table 1).

Consent to Participate All patients provided written, informed consent prior to participating in the study.

Consent for Publication Not applicable.

Availability of Data and Material Data can be made available from the corresponding author on reasonable request.

Code Availability Not applicable.

Author Contributions L.Y. and D.L. contributed to design of the work, acquisition of data for the work, interpretation of data for the work and critical revision of the work for important intellectual content. S.Y.L. contributed to conception of the work, acquisition of data for the work, interpretation of data for the work and critical revision of the work for important intellectual content. L.Y.S., L.Y.H., L.C.Z., L.B.J., T.J., Y.N., D.Y., W.H.P., K.X.J., and Q.H. contributed to acquisition of data for the work and critical revision of the work for important intellectual content. C.R. and L.J.N. contributed to interpretation of data for the work and critical revision of the work for important intellectual content. All authors read and approved the final version.

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