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ORIGINAL RESEARCH

Treatment Persistence of Ixekizumab in Adults with Moderate-to-Severe Plaque Psoriasis Participating in the Canadian Patient Support Program

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ABSTRACT

Introduction: Patients with psoriasis (PsO) should adhere to and be persistent with treatment to maintain disease control. Patient support programs (PSPs) are useful to support patients with disease management. We aimed to understand the real-world patient profile and persistence of ixekizumab-initiating Canadian patients with moderate-to-severe PsO using PSP data.

Methods: This retrospective observational study was conducted utilizing a Canadian PSP database (May 2016 to March 2020). Inclusion criteria were: age ≥ 18 years with moderate-to-severe PsO, initiated ixekizumab, enrolled in the PSP for ≥ 6 months, and provided informed consent. Psoriasis Area Severity Index (PASI), body surface area (BSA) involvement, and Dermatology Life Quality Index (DLQI) were collected at PSP entry. Adherence [using the proportion of days covered (PDC)] and persistence (using Kaplan–Meier curves) were assessed after 1-year and 2-year follow-ups. Differences in persistence between biologic-naïve and biologic-experienced patients were compared using Cox proportional hazards model after adjusting baseline parameters.

Results: In total, 1891 ixekizumab-treated moderate-to-severe patients with PsO were included. The mean [standard deviation (SD)] age was 52.3 (13.3) years; 51.1% of patients were 45–65 years old and 61.4% were male. At baseline, the mean (SD) PASI score was 14.3 (8.1), the DLQI score was 16.5 (7.7), and BSA % was 17.4 (15.1). PsO lesions were commonly located on the hands (33.4%), face (28.6%), and feet (23.8%). Ixekizumab-treated patients were highly adherent [PDC ≥ 80%: 1-year (92.0%), 2-year (87.7%)] and persistent [1-year (90.4%), 2-year (85.6%)]. Biologic-naïve patients were more adherent (1-year, 94.6% versus 87.3%; 2-year, 90.3% versus 83.5%) than biologic-experienced patients. Significantly higher persistence in biologic-naïve versus biologic-experienced patients for 1-year ($p < 0.01$) and 2-year ($p = 0.010$) follow-up periods was observed after adjusting for baseline parameters.

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Conclusion: Patients with moderate-to-severe PsO overwhelmingly remained on ixekizumab treatment for more than 2 years while participating in a PSP.

Keywords: Psoriasis; Patient support program; Ixekizumab; Canada; Adherence; Persistence

Key Summary Points

Why carry out this study?

Adherence and persistence with treatment such as biologics are essential to control psoriasis (PsO)

Patient support programs (PSPs) may help in managing the disease and improving outcomes

We aimed to understand adherence and persistence to ixekizumab in Canadian patients with moderate-to-severe PsO who were enrolled in a PSP

What was learned from the study?

Ixekizumab-treated patients were highly adherent and persistent over 1 and 2 years of follow-up

A slightly higher proportion of biologic-naïve patients were adherent and persistent than biologic-experienced patients

INTRODUCTION

Psoriasis (PsO) is a chronic, immune-mediated, inflammatory skin disease with varying dermatologic manifestations [1]. Approximately 90% of the cases correspond to chronic plaque-type PsO [2]. In Canada, a population-based study reported the crude prevalence of PsO to be 2.54% [95% confidence interval (CI) 2.53–2.55%] in 2015 [3], while an expert elicitation study in 2020 reported the median prevalence to be slightly higher at 3.0% (95% credibility interval 2.7–3.3%) [4]. The distribution of PsO by sex was similar between males and females (male:female ratio 1.03) [3].

Pharmacologic systemic treatments approved in Canada for PsO include conventional non-biologics (e.g., methotrexate, cyclosporine, and acitretin), biologics [e.g., TNF inhibitors, interleukin (IL)-12/23 inhibitors, IL-17 inhibitors, and IL-23 inhibitors], and the non-conventional systemic treatment apremilast [5–7]. As PsO is a chronic disease, continuous therapy is essential; however, 18–46% of patients with PsO in real-world settings discontinue treatment in the first year of treatment [8–10], which may lead to symptom recurrence. Moreover, the rate of treatment discontinuation is lower in biologic-naïve patients versus biologic-experienced patients [11–13].

Ixekizumab, an IL-17A inhibitor, has demonstrated efficacy and safety in the UNCOVER phase III trials [14–17] and a real-world Canadian study [18]. Moreover, ixekizumab has shown similar [12] or better adherence (i.e., the degree or extent to which a patient complies with the prescribed interval, and dose of a dosing regimen [19]) and persistence (i.e., time from initiation to discontinuation of therapy [19]), and lower risk of discontinuation compared with other biologics [20–23]. Although ixekizumab has been approved for use in Canada in adult patients with moderate-to-severe PsO since 2016 [24], data from real-world Canadian studies on ixekizumab-treated patients with PsO are still limited. Gulliver et al. [25] retrospectively analyzed clinical data of ixekizumab-treated patients with PsO at a Canadian dermatology clinic. Here, patients who remained on ixekizumab (i.e., responders) had greater total clearance than those who switched treatment (i.e., non-responders) [Psoriasis Area Severity Index (PASI) 100: 73% versus 33% and body surface area [BSA] 0: 73% versus 25%] at the end of follow-up. Mean persistence was also greater for responders versus non-responders (32 weeks versus 16 weeks).

Patient support programs (PSPs) are support programs aimed at helping patients manage their disease and medication regimens, improve adherence, and reduce costs and complications.

Evidence from the USA and Europe shows that patients' participation in PSPs results in greater adherence, lower discontinuation rate, and reduced costs compared with non-participants [26–28]. The LillyPlus PSP is one such complimentary program that helps manage the condition and treatment of ixekizumab-treated patients. This PSP offers 1-on-1 support with an optional check-in call from a patient care coordinator and educational materials to help patients manage their condition; financial support including individual attention, information, and reimbursement support; online administration training videos; and in-person or virtual administration training. The PSP records clinical measures at baseline for reimbursement purposes. It also records if the patient is still using the prescribed drug, the number of prescriptions, and any reported adverse events.

The objective of this study was to understand the real-world patient profile of ixekizumab-initiating patients with PsO and capture data on treatment persistence within Canadian clinical settings using PSPs.

METHODS

Study Design and Patient Population

This retrospective observational study was conducted using data collected in the Canadian PSP database from May 2016 to March 2020. This database is a part of the Lilly Patient Connections Platform, which captures information from PSP activities in multiple countries. Adult ($\geq$ 18 years old) patients with moderate-to-severe PsO who initiated ixekizumab were enrolled in the PSP for $\geq$ 6 months, and those who provided informed consent for research purposes were included. The start date of ixekizumab was the index date for all follow-up periods. Included patients were classified into biologic-naïve and biologic-experienced groups on the basis of whether they received any biologic therapy before enrollment in the PSP.

As only anonymized data were used, this study was exempt from institutional review board approval. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Pharmacoepidemiology Practices (GPP) and applicable laws and regulations of the country where the study was conducted, as appropriate. All patients participating in this observational study provided informed consent for their data to be used for research purposes.

Measures

The following demographic and clinical characteristics were measured at PSP entry: age; sex; location of PsO lesions from a selected list (hands, face, feet, genitals); PASI score; BSA involvement; and Dermatology Life Quality Index (DLQI) score. PASI score ranges from 0 to 72, with higher scores indicating greater severity [29]. BSA is reported as percent involvement on a scale of 0–100% and characterized as mild (0% to $<$ 3%), moderate (3–10%), or severe ($>$ 10%) on the basis of the amount of affected body surface area [30]. The DLQI is a 10-item questionnaire that covers six domains including daily activities, leisure, symptoms and feelings, personal relationships, work and school, and treatment, and inquires about experiences in the last week [31]. Responses are scored from 0 ("not at all") to 3 ("very much") for a total score of 0 to 30; higher scores indicate greater quality of life (QoL) impairment.

Adherence and persistence were evaluated for 1-year and 2-year timepoints. Adherence was measured as the proportion of days covered (PDC), calculated by dividing the total number of days on ixekizumab by the total number of days in the study duration. High adherence was defined as PDC $\geq$ 80%. Treatment persistence was defined as being on continuous treatment over time, allowing for a maximum gap of 60 days between treatment refills (where the gap period starts on the last day of treatment supply or drug exposure from the injection and ends at the next prescription refill date) [23, 32, 33].

Statistical Analysis

The baseline characteristics were analyzed descriptively. Continuous variables were reported using means and standard deviation (SD) and categorical variables were reported using counts and proportions. Persistence was assessed using Kaplan–Meier curves. Cox proportional hazards model, adjusting for age, gender, and baseline PASI scores, was used to confirm the findings. All statistical tests used a two-sided significance level of < 0.05.

RESULTS

Baseline Characteristics

A total of 1891 ixekizumab-treated patients with moderate-to-severe PsO were included in this study. Overall, the mean (SD) age of the patients was 52.3 (13.3) years, and 51.1% of them were 45–65 years old. The majority of the patients were male (61.4%). At baseline, the mean (SD) PASI score, BSA%, and DLQI score were 14.3 (8.1), 17.4 (15.1), and 16.5 (7.7), respectively. Among the evaluated sites, PsO lesions were present the most on the hands (33.4%), followed by the face (28.6%), feet (23.8%), and genitals (21.7%). The biologic-naïve and biologic-experienced groups had similar baseline characteristics (Table 1).

Treatment Adherence

Overall, patients were highly adherent to ixekizumab treatment (PDC $\geq$ 80%) over 1 year (92.0%) and 2 years (87.7%). Although the majority of the patients in both biologic-naïve and biologic-experienced groups were adherent over the follow-up periods, a greater proportion of biologic-naïve patients were adherent compared with biologic-experienced patients (1 year, 94.6% versus 87.3%; 2 year, 90.3% versus 83.5%; Table 2).

Treatment Persistence

Overall, ixekizumab-treated patients were highly persistent (90.4% after 1 year and 85.6% after 2 years of follow-ups). The results showed a higher persistent rate in biologic-naïve versus biologic-experienced patients after 1 year (93.4% versus 85.0%) (Fig. 1A) and 2 years (88.5% versus 80.7%) of follow-up (Fig. 1B). Adjusting for age, gender, and baseline PASI showed significantly higher persistence in biologic-naïve versus biologic-experienced patients for 1-year ($p < 0.01$) and 2-year ($p = 0.010$) follow-up periods.

DISCUSSION

This is the first study to utilize a PSP to understand the adherence and persistence of ixekizumab-treated Canadian patients with moderate-to-severe PsO. Most of the patients adhered (87.7%) and persisted (85.6%) with ixekizumab even after 2 years, with biologic-naïve patients being more adherent and persistent than biologic-experienced patients.

Drug adherence and persistence are important measures of real-world treatment effectiveness among patients with PsO, as they represent an overall interpretation of drug efficacy, drug safety, and patient satisfaction [34]. As the Canadian healthcare system shifts toward a greater emphasis on value-based healthcare, it becomes even more essential to improve average QoL and life expectancy and reduce health outcome inequality [35], especially in chronic diseases. The use of PSPs is one strategy that has demonstrated value in improving the quality of care and QoL by enhancing drug adherence and persistence [26–28], as well as by reducing healthcare costs [26, 27] in patients receiving biologics. In other indications, biologic-treated Canadian patients participating in PSPs have demonstrated greater adherence and persistence [36, 37] and increased disease control [38, 39] than non-PSP patients. Argenziano et al. [28] have reported the benefits of PSP participation in secukinumab-treated Italian patients with PsO who participated in the PSP PSOLife CARE. Similar to

Table 1 Baseline characteristics

Parameter	Overall (n = 1891)	Biologic-naïve (n = 1208)	Biologic-experienced (n = 683)
Age in years, mean (SD)	52.3 (13.3)	51.4 (13.5)	53.9 (12.7)
Age categories, n (%)			
< 45	562 (29.7)	394 (32.6)	168 (24.6)
45–65	966 (51.1)	602 (49.8)	364 (53.3)
≥ 65	363 (19.2)	212 (17.6)	151 (22.1)
Sex, n (%)			
Female	717 (37.9)	450 (37.3)	267 (39.1)
Male	1161 (61.4)	749 (62.0)	412 (60.3)
PASI score, mean (SD)	14.3 (8.1)	14.8 (7.8)	13.5 (8.6)
BSA %, mean (SD)	17.4 (15.1)	18.1 (14.9)	16.1 (15.4)
DLQI score, mean (SD)	16.5 (7.7)	17.1 (7.7)	15.5 (7.4)
Psoriasis location, n (%)[a]			
Face	540 (28.6)	360 (29.8)	180 (26.4)
Hand	631 (33.4)	390 (32.3)	241 (35.3)
Feet	450 (23.8)	272 (22.5)	178 (26.1)
Genitals	411 (21.7)	263 (21.8)	148 (21.7)

Sex was not recorded in 13 patients. Patients can have psoriasis in multiple locations; thus, the total percentage is > 100%
BSA body surface area, *DLQI* Dermatology Life Quality Index, *PASI* Psoriasis Area Severity Index, *SD* standard deviation
[a]These are a non-exhaustive list of body sites involved. These particular anatomical sites were of special interest and patients could have psoriatic lesions on any other part of the body

Table 2 Adherence to ixekizumab treatment

PDC ≥ 80%, n (%)	Overall	Biologic-naïve	Biologic-experienced
1-year follow-up	n = 1596	n = 1023	n = 573
Yes	1468 (92.0)	968 (94.6)	500 (87.3)
No	128 (8.0)	55 (5.4)	73 (12.7)
2-year follow-up	n = 962	n = 599	n = 363
Yes	844 (87.7)	541 (90.3)	303 (83.5)
No	118 (12.3)	58 (9.7)	60 (16.5)

PDC proportion of days covered

our results, these patients reported high medication adherence.

As PSPs provide additional support to patients, the observed persistence in such programs may be higher than other data sources

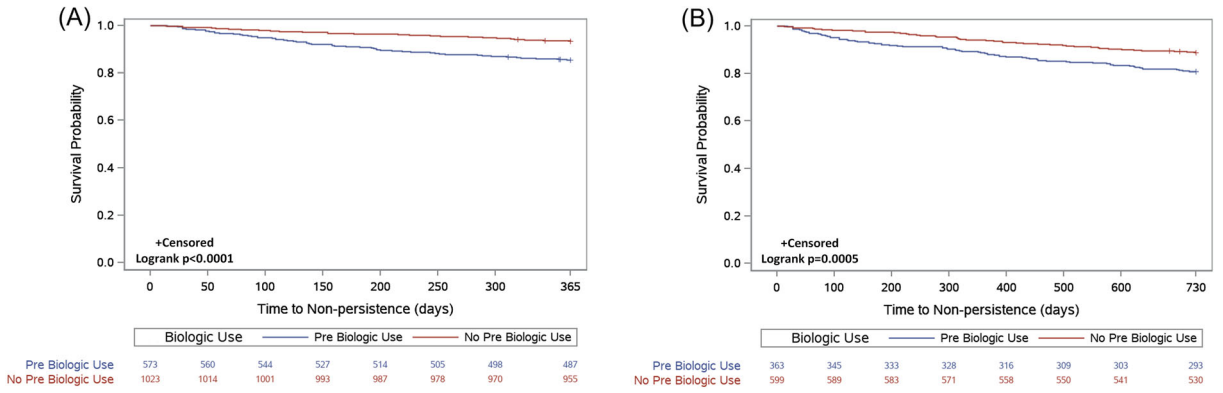

Fig. 1 Ixekizumab treatment persistence by prior biologic therapy status. **A** Treatment persistence at 1-year follow-up, **B** treatment persistence at 2-year follow-up. Persistent rate was significantly greater in biologic-naïve versus biologic-experienced patients after 1 year (93.4% versus 85.0%) and 2 years (88.5% versus 80.7%) of follow-up. $p < 0.01$ (Cox model) for 1-year follow-up and $p = 0.010$ (Cox model) for 2-year follow-up after adjusting for age, gender, and baseline PASI

such as claims databases or patient registries. Indeed, 1-year persistence with ixekizumab was higher in the current study (90.4%) than in a claims database study in the USA (56.4%)[23] and an Austrian PsO registry study (86.0%) [12]. Similar results were observed for 2-year persistence versus an American claims database study (85.6% versus 37.2%) [22]. In addition, in a retrospective study of 38 ixekizumab-treated patients with PsO at a Canadian dermatology clinic, 84% of the patient cohort were still on the drug at the end of the observational period (mean 32 weeks) [25]. However, additional factors such as varying healthcare systems in different countries, varying clinical practices (e.g., up-titration of biologics by many Canadian dermatologists before switching), number of treatment alternatives, different study time periods, the requirement of the minimum follow-up period, inherent differences between the data sources, and the definition of drug survival in the studies may also result in the observed persistence rates.

As drug survival and adherence are influenced by the line of therapy, we also stratified the analyses by biologic use status. We observed greater persistence in ixekizumab-treated biologic-naïve versus biologic-experienced patients after 1 year (93.4% versus 85.0%) and 2 years (88.5% versus 80.7%) of follow-up in our study. This was expected owing to a higher likelihood of treatment failure in the more refractory biologic-experienced patient population. Our results are consistent with Lockshin et al. [11] who analyzed data from the Corrona patient registry (comprising American and Canadian patients) and reported greater 1-year (81% versus 65%) and 2-year (68% versus 46%) persistence for ixekizumab-treated biologic-naïve patients compared with biologic-experienced patients [11]. Other biologics have also demonstrated greater persistence in biologic-naïve versus biologic-experienced patients [40].

This study mainly focused on supporting the patient experience, helping patients manage their disease and medication regimens, improve adherence, and reduce costs and complications within the PSP. Dermatologists had a limited opportunity to report clinical measures or record other outcomes. Thus, we were unable to conclude the impact of additional factors such as drug tolerability, rapidity of response, and extent of skin clearance based on PASI response (PASI75, PASI90, or PASI100) on persistence and adherence of ixekizumab and differences between biologic-naïve or biologic-experienced patients in the current article.

Limitations

Several limitations should be considered when interpreting the results of this study. As participation in the PSP was voluntary, differences may exist in the characteristics and behavior of patients who chose to participate and those who did not. Therefore, the results may not be generalizable to all ixekizumab-treated patients. As the findings relied on the accuracy of self-report only rather than confirmation of medical records, a difference may be observed if a similar study is conducted in the future using accurate documentation. In addition, we did not evaluate health outcomes and safety over time, as our focus was on treatment persistence and adherence. Future research is needed to assess the relationship between treatment persistence and adherence and changes in health outcomes within PSP participants.

CONCLUSIONS

This report on the real-world persistence of ixekizumab across a large nationwide Canadian population with moderate-to-severe PsO shows that the vast majority of patients enrolled in a PSP remained on ixekizumab treatment for more than 2 years. Biologic-naïve patients treated with ixekizumab demonstrated greater adherence and persistence than biologic-experienced patients.

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Compliance with Ethics Guidelines. As only anonymized data were used, this study was exempt from institutional review board approval. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Pharmacoepidemiology Practices and applicable laws and regulations of the country where the study was conducted, as appropriate. All patients participating in this observational study provided informed consent.

Data Availability. The datasets generated and/or analyzed during the current study are available at Eli Lilly and Company upon reasonable request.

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