Research Article

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Understanding characteristics of patients newly initiating ixekizumab: findings from the Corrona Psoriasis Registry

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Background: Real-world data on patients newly initiating ixekizumab is limited. Our study describes the characteristics of patients who initiated ixekizumab and other biologics for psoriasis treatment in North American dermatological practices. **Materials & methods:** Characteristics of patients ascertained at registry enrollment are described via means and frequencies. **Results:** Compared with other biologic initiators, ixekizumab initiators had: longer disease duration (17.1 vs 15.1 years); more were considered least severe by body surface area (33 vs 26%); moderate-to-severe by IGA (56 vs 48%); were biologic-experienced (80 vs 52%); obese (54 vs 47%); and experienced greater impact in work productivity (5.3 vs 2.9%) versus other biologic initiators. **Conclusion:** Psoriasis patients initiating ixekizumab had more severe disease, biologic experience, and worse patient-reported outcomes than those initiating other biologics.

Tweetable abstract: The use of ixekizumab among more severe PsO patients and those likely to have involvement of hard-to-treat areas aligns with the robust efficacy evidence and safety profile demonstrated by numerous clinical studies.

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Psoriasis (PsO) is a chronic relapsing and remitting inflammatory skin disorder that affects the skin and nails, and over 7.5 million adults in the US (~3.2%) suffer from the disease [1]. Individuals with PsO are at increased risk for developing other serious health issues such as psoriatic arthritis (PsA), cardiovascular disorders, metabolic syndrome or components thereof, nonalcoholic fatty liver disease, Crohn's Disease, depression, anxiety, and lymphoma [2,3]. Studies have also shown that regardless of severity, over 80% of PsO patients feel the condition has interfered with their quality of life (QoL), and affected their overall emotional well-being [4]. Moreover, severe PsO has been shown to impair work productivity [5–7] significantly.

Phase III clinical trials have shown that ixekizumab, a high-affinity humanized monoclonal antibody that selectively inhibits IL-17A, rapidly achieves and maintains high clinical response rates for patients with moderate-to-severe plaque PsO [7–12]. Further studies have shown excellent early clinical efficacy compared with etanercept with a comparable safety profile for the treatment of chronic plaque PsO [13–15]. Ixekizumab was approved by the US Food and Drug Administration (FDA) in 2016.

Whereas clinical trials have shown significant and rapid improvement among PsO patients using ixekizumab, there is limited real-world evidence describing the characteristics of PsO patients initiating ixekizumab, and assessing them against PsO patients newly initiating other biologics. Hence, the objective of our study was to describe the demographics, self-reported disease burden and treatment of PsO patients initiating ixekizumab, and assess them against the characteristics of PsO patients initiating other biologics in routine clinical practice in the US.

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Materials & methods

Study setting

The Corrona Psoriasis Registry is a prospective, multicenter observational disease-based registry launched in April 2015 in collaboration with the National Psoriasis Foundation (NPF). The registry design and patient enrollment have been previously described [16]. Briefly, patients were recruited from 119 private and academic practice sites across 35 states in the US, with 283 participating dermatologists. As of 31 October 2017, Corrona's PsO database included information on approximately 3557 patients. Data on 8136 patient visits and approximately 2594.2 patient-years of follow-up observation time had been collected, and the mean time of patient follow-up was 1.16 years (median 1.09 years).

Follow-up assessments were requested at least as often as every six months and completed during routine clinical visits. All participating investigators were required to obtain full board approval for conducting research involving human subjects. Sponsor approval and continuing review were obtained through a central IntegReview Institutional Review Board (IRB), Corrona-PSO-500. For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained from the respective governing IRBs, and documentation of approval was submitted to the Sponsor before initiating any study procedures. All registry subjects were required to provide written informed consent before participating.

Study population

Patients were enrolled in this study if they met the inclusion criteria: enrollment in the Corrona PsO Registry between 15 April 2016 and 31 October 2017; diagnosed by a dermatology healthcare provider with any type of PsO; ≥18 years of age; and had started or switched to and continued a FDA approved systemic or biologic PsO treatment within the previous 12 months. FDA approved biologic therapies for PsO (etanercept, infliximab, adalimumab, ustekinumab, secukinumab, ixekizumab, brodalumab, and guselkumab), biosimilars and non-biologic systemics (methotrexate, cyclosporine or apremilast) were allowed. Patients who initiated or switched to a biologic at registry enrollment or in the prior 12 months were included.

Patients were grouped into therapy cohorts: patients using ixekizumab who enrolled in the Corrona PsO Registry on ixekizumab as the eligible therapy and patients using other biologics (non-ixekizumab) such as etanercept, infliximab, adalimumab, ustekinumab or secukinumab as the eligible therapy. There were no exclusion criteria.

Descriptive characteristics

Data were collected on sociodemographics, history of comorbidities, history of PsO morphology, and PsO and PsA disease duration. Measures of disease activity include the Psoriasis Area and Severity Index (PASI), body surface area (BSA), and Investigator Global Assessment (IGA). The PASI is measured on a scale 0–72 where a higher score indicates more severity. The PASI takes into account the percentage of the affected area and the severity of redness, thickness, and scaling of the skin [17]. The BSA is reported as a percent involvement on a scale of 0–100% and characterized as mild (0 to <3), moderate (3–10), or severe (>10) as defined by the NPF according to the amount of BSA affected [18]. The IGA is a 5-point tool used to measure disease severity on a scale of 0–4, where 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, and 4 = severe [19].

Patient-reported outcomes

Several patient-reported outcomes (PROs) including Work Productivity and Activity Impairment (WPAI), Dermatology Life Quality Index (DLQI), Euro-QoL 5-Dimensional 3 Level (EQ-5D-3L), as well as patient skin pain, fatigue, and overall itch on a visual analog scale (VAS) of 0–100 were collected. The WPAI is a validated self-administered questionnaire to assess the impact of PsO on productivity in the workplace and personal daily activities and includes four domains: percent work time missed; percent impairment while working; percent overall work impairment; and percent daily activity impairment. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating more significant impairment and less productivity [20].

The DLQI is a composite measure ranging from 0 to 30 evaluating the effect of the disease on health-relate QoL. Ten questions refer to how the patient's disease impacted his or her life in the previous week. The questions cover symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sexual difficulties, and treatment. The higher the score, the more QoL is impaired [21]. The EQ-5D-3L is a standardized instrument used to measure overall health status and applies to a wide range of health conditions and treatments. The EQ-5D-3L covers five dimensions: mobility, self-care, usual activities, pain/discomfort, and

anxiety/depression. There are three levels within each dimension: no problems, some problems, and extreme problems [22]. Patient fatigue, skin pain, and overall itch over the past week were separately assessed using a VAS of 0–100. Higher scores indicate better health [23]. Data were also collected on history and current medication (biologic and non-biologic systemic use).

Statistical analysis

Descriptive analyses of sociodemographics, disease characteristics and clinical features, PROs, and biologic and non-biologic systemic use history were examined for patients initiating ixekizumab and those initiating other biologics (tumor necrosis factor inhibitors [TNFis] and non-TNFis). Categorical variables were summarized using frequency counts and percentages; the median, 25th and 75th percentiles, and the interquartile range were included when applicable. Continuous variables were summarized by the number of observations, mean, standard deviation, median, 25th and 75th percentiles, and the interquartile range. Analysis of variance or *t*-tests for means and or Mann–Whitney U tests for medians were employed for continuous covariates and Chi-square tests of association for categorical covariates.

Results

Table 1 presents patient demographics and comorbidities at enrollment for patients initiating ixekizumab and those initiating other biologics. Our study included 2963 patients, of which 388 were ixekizumab initiators. The mean age for patients initiating ixekizumab was similar to patients initiating other biologics (50.3 vs 49.2 years). The proportion of males in both groups (ixekizumab vs other biologics) was similar, 54 versus 52%, respectively. The distribution of body mass index (BMI) differed with more patients who were ixekizumab initiators in the overweight group (31 vs 30%) and obese group (54 vs 47%) than patients initiating other biologics ($p = 0.006$). More patients initiating ixekizumab had private health insurance (83 vs 76%) than those initiating other biologics ($p = 0.004$).

Initiators of ixekizumab had a higher prevalence of hypertension (42 vs 36%; $p = 0.014$) and hyperlipidemia (31 vs 26%; $p = 0.062$) than initiators of other biologics. On medical history at enrollment, there were no significant differences in rates of prior tuberculosis (3 vs 4%), cardiovascular disease (4 vs 5%), lymphoma/malignancy (4 vs 4%), anxiety (18 vs 19%), and depression (19 vs 19%) between ixekizumab initiators and other biologics initiators.

Table 2 displays patient disease characteristics at enrollment for patients initiating ixekizumab and those initiating other biologics. Patients initiating ixekizumab had more inverse/intertriginous (10 vs 7%; $p = 0.018$), nail (19 vs 14%; $p = 0.007$), and palmoplantar (12 vs 9%; $p = 0.051$) morphologies than patients initiating other biologics. Psoriasis duration and PsA duration (among those with a history of PsA) were longer for initiators of ixekizumab than for initiators of other biologics (17.1 vs 15.1 years; $p = 0.007$) and (8.6 vs 6.9 years; $p = 0.016$), respectively. Patients initiating ixekizumab had a greater distribution of patients with IGA moderate and severe (56 vs 48%; $p < 0.0001$), and significantly higher mean PASI scores than patients initiating other biologics (7.5 vs 5.7; $p < 0.0001$), respectively. Likewise, ixekizumab initiators had a significantly higher proportion of patients with PASI greater than 10 (28 vs 19%, respectively; $p < 0.0001$), and also a greater proportion of patients were in the severe and very severe BSA categories (33 vs 26%; $p = 0.009$), respectively.

Table 3 presents PROs at enrollment for patients initiating ixekizumab and those initiating other biologics. Ixekizumab initiators and other biologics initiators experienced similar mean VAS scores for skin pain (23.6 vs 23.6) and fatigue (30.1 vs 30.7), respectively. Likewise, both groups reported similar health-related QoL as measured by the DLQI (7.0 vs 6.8) and DLQI 'Effect on Life', with more than 44% in both groups experiencing a moderate or very large impact on their lives. Slightly more patients initiating ixekizumab were currently employed than those initiating other biologics (73 vs 69%). Both patient groups were similar for percent of impairment while working due to PsO (12.5 vs 11.9%) and percent of daily activities impaired by PsO (19.6 vs 18.1%). However, patients initiating ixekizumab had significantly higher percent mean work hour missed compared with those initiating other biologics (5.3 vs 2.9%; $p = 0.005$).

Table 4 displays treatment status and medication histories at enrollment for patients initiating ixekizumab and those starting other biologics. A significantly lower proportion of patients initiating ixekizumab were biologic-naive than that of patients initiating other biologics (20 vs 52%; $p < 0.0001$), and a significantly greater proportion of patients initiating ixekizumab had used at least two or more prior biologics than those initiating other biologics (70 vs 49%; $p < 0.0001$). A significantly lower proportion of ixekizumab initiators were naive to non-biologics than that of other biologics initiators (43 vs 52%; $p = 0.0006$), and among those with prior non-biologic use, a

Table 1. Patient sociodemographics and comorbidities at enrollment for ixekizumab and other biologics initiators.

Characteristics	Total (all biologics) n = 2963	Ixekizumab initiators n = 388	Other biologics initiations† (non-ixekizumab) n = 2575	p-value†
Age (years), n	n = 2963	n = 388	n = 2575	0.1785
mean (SD)	49.4 (14.3)	50.3 (13.2)	49.2 (14.5)	
Sex, male, n (%)	1553 (52%)	210 (54%)	1343 (52%)	0.4692
Race, white, n (%)	2338 (79%)	290 (75%)	2048 (80%)	0.1845
BMI categorical, n (%)	n = 2940	n = 386	n = 2554	0.0057
– Normal/underweight (<25)	632 (21%)	60 (16%)	572 (22%)	
– Overweight (25.0 – <30)	891 (30%)	118 (31%)	773 (30%)	
– Obese (≥30)	1417 (48%)	208 (54%)	1209 (47%)	
Insurance type, n *(%)*				
– Private	2282 (77%)	321 (83%)	1961 (76%)	0.0041
– Medicare	462 (16%)	54 (14%)	408 (16%)	0.3293
– Medicaid	305 (10%)	31 (8%)	274 (11%)	0.1092
– No insurance	90 (3%)	7 (2%)	83 (3%)	0.1289
Education, n (%)	n = 2960	n = 387	n = 2573	0.0458
– 12th grade or less	182 (6%)	17 (4%)	165 (6%)	
– High school graduate/GED	645 (22%)	99 (26%)	546 (21%)	
– Some college/Assoc. degree	940 (32%)	107 (28%)	833 (32%)	
– College graduate or higher	1193 (40%)	164 (42%)	1029 (40%)	
Work status, n (%)	n = 2961	n = 388	n = 2573	0.1815
– Full time	1811 (61%)	251 (65%)	1560 (61%)	
– Part time	239 (8%)	34 (9%)	205 (8%)	
– Work at home	182 (6%)	18 (5%)	164 (6%)	
– Student	90 (3%)	5 (1%)	85 (3%)	
– Disabled	215 (7%)	26 (7%)	189 (7%)	
– Retired	424 (14%)	54 (14%)	370 (14%)	
History of comorbidities‡, n (%)				
– TB, n	119 (4%)	11 (3%)	108 (4%)	0.2028
– CVD, n (%)	156 (5%)	16 (4%)	140 (5%)	0.2782
– Hypertension, n (%)	1078 (36%)	163 (42%)	915 (36%)	0.0141
– Hyperlipidemia, n (%)	792 (27%)	119 (31%)	673 (26%)	0.0618
– Diabetes mellitus, n (%)	445 (15%)	61 (16%)	384 (15%)	0.6842
– Lymphoma/malignancy, n (%)	124 (4%)	16 (4%)	108 (4%)	0.9449
– Metabolic syndrome, n (%)	32 (1%)	2 (1%)	30 (1%)	0.2478
– Depression, n (%)	572 (19%)	73 (19%)	499 (19%)	0.7849
– Anxiety, n (%)	568 (19%)	70 (18%)	498 (19%)	0.5379

†Other biologics–TNFi's include adalimumab, etanercept, infliximab; IL-17 secukinumab, and IL-12/23 ustekinumab listed by name due to singular drug in class. P-values compare ixekizumab vs other biologics (non-ixekizumab) with significance level $\alpha = 0.05$.
‡Past comorbidities. CVD: Revascularization procedures (CABG, stent, angioplasty), ventricular arrhythmia, cardiac arrest, acute coronary syndrome, coronary artery disease, transient ischemic attack, hemorrhage with/without hospitalization (serious bleed), deep vein thrombosis, Peripheral arterial disease, pulmonary embolism, carotid artery disease. Malignancy: breast, lung, skin (excluding non-melanoma skin cancer) & other.
BMI: Body mass index; CVD: Cardiovascular disease; GED: General equivalency diploma; TB: Tuberculosis.

significantly higher proportion of ixekizumab initiators group had used at least two or more non-biologics than that of other biologics initiators (41 vs 26%; $p < 0.0001$). Approximately 12% of patients in both therapy groups had concomitant use of non-biologic therapy a biologic initiation (data not shown).

Discussion

In our study, we found patients newly initiating ixekizumab were more likely to have involvement of hard-to-treat areas (inverse/intertriginous, nail, and palmoplantar). They had a longer duration with PsO and PsA, as well as more severe disease than those newly initiating other biologics, based on three disease severity measures (PASI, BSA,

Table 2. Disease characteristics at enrollment for ixekizumab and other biologics initiators.

Disease characteristics	Total (all biologics) n = 2963	Ixekizumab initiators n = 388	Other biologics initiators (non-ixekizumab) n = 2575	p-value†
History of PsO morphology, n (%)				
– Plaque	2868 (97%)	374 (96%)	2494 (97%)	0.6297
– Guttate	175 (6%)	24 (6%)	151 (6%)	0.8023
– Erythrodermic	92 (3%)	14 (4%)	78 (3%)	0.5398
– Pustular (localized)	30 (1%)	9 (2%)	21 (1%)	0.0058
– Pustular (generalized)	22 (1%)	4 (1%)	18 (1%)	0.4479
– Inverse/intertriginous	206 (7%)	38 (10%)	168 (7%)	0.0182
– Scalp	965 (33%)	136 (35%)	829 (32%)	0.2629
– Nail	438 (15%)	75 (19%)	363 (14%)	0.0068
– Palmoplantar	279 (9%)	47 (12%)	232 (9%)	0.0510
Years since diagnosis				
Psoriasis duration (years), n	n = 2960	n = 388	n = 2572	
– Mean (SD)	15.3 (13.7)	17.1 (13.7)	15.1 (13.6)	0.0074
Psoriatic arthritis, n *(%)*	n = 2963	n = 388	n = 2575	0.5616
	1182 (40%)	160 (41%)	1022 (40%)	
Psoriatic arthritis duration (years), n	n = 1178	n = 160	n = 1018	
– Mean (SD)	7.1 (8.4)	8.6 (8.5)	6.9 (8.3)	0.0163
IGA, n	n = 2958	n = 388	n = 2570	
– Mean (SD)	2.2 (1.2)	2.3 (1.3)	2.2 (1.2)	0.1510
IGA categorical, n *(%)*	n = 2958	n = 388	n = 2570	<0.0001
– 0: Clear	373 (13%)	65 (17%)	308 (12%)	
– 1: Almost clear	445 (15%)	40 (10%)	405 (16%)	
– 2: Mild	684 (23%)	66 (17%)	618 (24%)	
– 3: Moderate	1131 (38%)	155 (40%)	976 (38%)	
– 4: Severe	325 (11%)	62 (16%)	263 (10%)	
BSA (% involvement), n	n = 2956	n = 388	n = 2568	
Mean (SD)	10.3 (14.9)	11.6 (15.9)	10.1 (14.8)	0.0708
BSA categorical % involvement, n (%)	n = 2956	n = 388	n = 2568	0.0085
– Mild disease (0, 3)	1029 (35%)	135 (35%)	894 (35%)	
– Moderate disease (3,10)	1140 (39%)	125 (32%)	1015 (40%)	
– Severe disease (10, 20)	312 (11%)	53 (14%)	259 (10%)	
– Very severe disease (20,100)	475 (16%)	75 (19%)	400 (16%)	
PASI (score: 0–72), n	n = 2956	n = 388	n = 2568	
Mean (SD)	6.0 (7.3)	7.5 (9.0)	5.7 (7.0)	<0.0001
PASI>10, n *(%)*	587 (20%)	110 (28%)	477 (19%)	<0.0001

†Other biologics–TNFi's include adalimumab, entanercept, infliximab; IL-17 secukinumab and IL-12/23 ustekinumab, listed by name due to singular drug in class. P-values compare ixekizumab vs other biologics (non-ixekizumab) with significance level $\alpha = 0.05$.
BSA: Body surface area; IGA: Investigator Global Assessment; PASI: Psoriasis Area and Severity Index.

and IGA). Likewise, initiators of ixekizumab had more significant proportions of patients with higher overall itch and percent mean work hours missed than initiators of other biologics. In addition to observing that more patients initiating ixekizumab were biologic experienced, these clinical characteristics demonstrate that in the real-world, ixekizumab is predominantly being used by patients with more severe PsO and as a later line of therapy.

The observation that more patients initiating ixekizumab had more severe PsO (56% IGA moderate and severe or 33% BSA severe and very severe) and that most of them had used two or more biologic therapies previously (70%) than those initiating other biologics, may imply that patients prescribed ixekizumab are more severe PsO patients and or are likely to be resistant to other treatments. The use of ixekizumab among more severe PsO patients and its higher use among patients likely to have involvement of hard-to-treat areas could be attributed to the robust efficacy evidence and safety profile demonstrated by numerous clinical studies [8,11–13,24].

Table 3. Patient-reported outcomes at enrollment for ixekizumab and other biologics initiators.

Characteristics	Total (all biologics) n = 2963	Ixekizumab initiators n = 388	Other biologics initiators (non-ixekizumab) n = 2575	p-value[†]
WPAI[‡] summary scores	n = 2957	n = 388	n = 2569	0.1014
Currently employed, n (%)	2059 (70%)	284 (73%)	1775 (69%)	
% Work hours missed due to PsO, n	n = 1867	n = 253	n = 1614	
Mean (SD)	3.2 (12.4)	5.3 (17.1)	2.9 (11.4)	0.0047
% Impairment while working due to PsO, n	n = 1854	n = 248	n = 1606	
Mean (SD)	11.9 (20.9)	12.5 (23.1)	11.9 (20.5)	0.6348
Overall % work hours affected by PsO, n	n = 1851	n = 248	n = 1603	
Mean (SD)	13.4 (22.3)	14.6 (25.4)	13.2 (21.8)	0.3507
% of daily activities impaired by PsO, n	n = 2942	n = 386	n = 2556	
Mean (SD)	18.3 (26.2)	19.6 (27.6)	18.1 (26.0)	0.2870
Patient health state today (EQ-5D VAS 0–100), n	n = 2957	n = 388	n = 2569	
Mean (SD)	73.2 (21.5)	72.1 (22.6)	73.3 (21.4)	0.2842
DLQI (Score: 0–30), n[§]	n = 2956	n = 388	n = 2568	
Mean (SD)	6.8 (6.2)	7.0 (6.2)	6.8 (6.2)	0.6377
DLQI 'Effect on life', n *(%)*	n = 2956	n = 388	n = 2568	0.8295
– 0–1: none	703 (24%)	94 (24%)	609 (24%)	
– 2–5: small	835 (28%)	100 (26%)	735 (29%)	
– 6–10: moderate	652 (22%)	90 (23%)	562 (22%)	
– 11–20: very large	641 (22%)	88 (23%)	553 (22%)	
– 21–30: extremely large	125 (4%)	16 (4%)	109 (4%)	
Overall fatigue (VAS range 0–100), n	n = 2959	n = 388	n = 2571	
Mean (SD)	30.6 (28.7)	30.1 (28.5)	30.7 (28.8)	0.7308
Overall skin pain (VAS range 0–100), n	n = 2958	n = 388	n = 2570	
Mean (SD)	23.6 (30.1)	23.6 (30.8)	23.6 (30.0)	0.9965
Overall itch (VAS range 0–100), n	n = 2960	n = 388	n = 2572	
Mean (SD)	37.0 (34.6)	38.7 (36.2)	36.7 (34.4)	0.2912
EQ-5D-3L[¶] categorical domains				
Walking, n (%)	n = 2931	n = 385	n = 2546	0.5138
– No problems	2282 (78%)	306 (79%)	1976 (78%)	
– Some problems	644 (22%)	79 (21%)	565 (22%)	
– Bed ridden	5 (0%)	0 (0%)	5 (0%)	
Self-care, n (%)	n = 2914	n = 382	n = 2532	0.5719
– No problems	2711 (93%)	352 (92%)	2359 (93%)	
– Some problems	200 (7%)	30 (8%)	170 (7%)	
– Unable to do	3 (0%)	0 (0%)	3 (0%)	
Usual activities, n (%)	n = 2923	n = 383	n = 2540	0.6103
– No problems	2129 (73%)	277 (72%)	1852 (73%)	
– Some problems	748 (26%)	102 (27%)	646 (25%)	
– Unable to do	46 (2%)	4 (1%)	42 (2%)	
Pain & discomfort, n (%)	n = 2926	n = 385	n = 2541	0.2778
– No problems	1510 (52%)	213 (55%)	1297 (51%)	
– Some problems	1278 (44%)	154 (40%)	1124 (44%)	
– Extreme problems	138 (5%)	18 (5%)	120 (5%)	
Anxiety & depression, n (%)	n = 2914	n = 383	n = 2531	0.2327
– No problems	2145 (74%)	286 (75%)	1859 (73%)	
– Some problems	714 (25%)	94 (25%)	620 (24%)	
– Extreme problems	55 (2%)	3 (1%)	52 (2%)	

[†]Other biologics–TNFi's include adalimumab, entanercept, infliximab; IL-17 secukinumab and IL-12/23 ustekinumab, listed by name due to singular drug in class. P-values compare ixekizumab vs other biologics (non-ixekizumab) with significance level $\alpha = 0.05$.
[‡]WPAI: Work Productivity & Activity Impairment Questionnaire (Scoring: www.reillyassociates.net/WPAI_Scoring.html).
[§]DLQI: Dermatology Life Quality Index (Scoring: http://sites.cardiff.ac.uk/dermatology/quality-of-life/dermatology-quality-of-life-index-dlqi/dlqi-instructions-for-use-and-scoring/).
[¶]EQ-5D-3L: Self-completed measure of health status (Scoring: www.euroqol.org/about-eq-5d/how-to-use-eq-5d.html).
EQ-5D-3L: Euro-QoL 5-Dimensional 3 Level; VAS: Visual analog scale.

Table 4. Treatment status and histories at enrollment for ixekizumab and other biologics initiators.

Medication history (prior to registry enrollment)	Total (all biologics) n = 2963	Ixekizumab initiators n = 388	Other biologics initiators (non-ixekizumab) n = 2575	p-value†
Biologic naive, n (%)	n = 2963	n = 388	n = 2575	<0.0001
	1320 (45%)	79 (20%)	1241 (48%)	
Prior biologic usage count‡				
Count of patients: n	n = 1643	n = 309	n = 1334	
Count of drugs: median (IQR)	2.0 (1.0,2.0)	2.0 (1.0,3.0)	1.0 (1.0,2.0)	
Prior biologic counts given prior usage‡, n (%)	n = 1643§	n = 309	n = 1334	<0.0001
– 1	765 (47%)	92 (30%)	673 (50%)	
– 2	470 (29%)	94 (30%)	376 (28%)	
– 3	239 (15%)	53 (17%)	186 (14%)	
– 4	120 (7%)	46 (15%)	74 (6%)	
– 5 or more	49 (3%)	24 (8%)	25 (2%)	
Non-biologic naive, n (%)	n = 2963	n = 388	n = 2575	0.0006
	1502 (51%)	165 (43%)	1337 (52%)	
Prior non-biologic usage count¶,				
Count of patients: n	n = 1461#	n = 223	n = 1238	
Count of drugs: median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	
Prior nonbiologic counts given prior usage§, n (%)	n = 1461	n = 223	n = 1238	<0.0001
– 1	1046 (72%)	132 (59%)	914 (74%)	
– 2	316 (22%)	64 (29%)	252 (20%)	
– 3 or more	99 (7%)	27 (12%)	72 (6%)	

†Other biologics–TNFi's include adalimumab, entanercept, infliximab; IL-17 secukinumab and IL-12/23 ustekinumab listed by name due to singular drug in class. P-values compare ixekizumab vs other biologics (non-ixekizumab) with significance level $\alpha = 0.05$.
‡Prior biologics include: adalimumab, alefacept, certolizumab pegol, efalizumab, entanercept, golimumab, infliximab, secukinumab, ustekinumab, ixekizumab, investigational drugs and other biologics.
§Patients with prior biologic usage.
¶Prior non-biologics include: acitretin, apremilast, cyclosporine, hydroxyurea, methotrexate, mycophenolate mofetil, sulfasalazine, tofacitinib, 6-thioguanine and other non-biologics.
#Patients with prior non-biologic usage.

In head-to-head trials, ixekizumab has been shown to have superior efficacy compared with eternacept (UNCOVER-2 and UNCOVER-3) [25], ustekinumab (IXORAS-S) [26], and guselkumab [27]. Further, ixekizumab has been associated with rapid improvement in health-related QoL and itch [28], work productivity [29], and both nail [30] and scalp [31] PsO. While the evidence on the high efficacy of ixekizumab among patients who are potentially resistant to other biologics may support using it as a later line therapy, a recent study has shown that ixekizumab is highly efficacious among biologic-naive patients similarly to biologic-experienced patients [32].

Our findings that most patients initiating ixekizumab were biologic-experienced, and had used at least two prior biologics, could, in part, be explained by limitations to access. Some insurance policy plans have incorporated restrictions on treatment choice, such as step-therapy policies that require payer preferred medications before being prescribed newer biologics [33]. These policies can impede providers from prescribing drugs in the sequence and order that they feel will result in the best outcomes for their patients.

The argument for access restriction policies is improved quality and economic benefit [34]. However, a recent study that compared treatment effectiveness among rheumatoid arthritis and PsA patients with and without plan-level access restrictions to biologic disease modifying antirheumatic drugs (DMARDs) or targeted synthetic DMARDs (tsDMARDs), found patients in plans without access restrictions or with prior authorization only, rheumatoid arthritis and PsA patients in insurance plans with step therapy had lower odds of treatment effectiveness [35]. Moreover, the Institute for Clinical and Economic Review (ICER) concluded in a recent review that IL-17 inhibitors were highly efficacious, had reasonable economic value, and were reasonable first-line targeted treatments [35,36].

Limitations to access and patient and provider preferences may, at least in part, explain the different use of ixekizumab among biologic-naive patients. Factors that play a role in the decision-making process for both the provider and patient, including provider clinical inertia, defined as the failure of healthcare providers to initiate

or intensify therapy when indicated [37] and or a patient's unwillingness to switch therapies due to fear of side effects [38], could potentially lead to delays in realizing treatment benefits among these patients. Studies have shown that poor results and reduced patient satisfaction has been attributed to the lack of confidence many physicians exhibit when prescribing systemic drugs, especially biologics [39].

While our study has several integral strengths, including the use of data from an extensive national disease registry with patients from academic and private practice dermatologists who are likely to reflect a typical real-world patient population in the US, as with any observational registry, it is not without limitations. The results may not be generalizable to others outside of the US because the data are from a US registry. Information bias may have been introduced because measures were assessed and collected by multiple providers; however, we strived to reduce this bias by using validated data collection instruments where possible. Selection bias could have been introduced by the voluntary participation of dermatologists and patients. To minimize the selection bias leading to highly correlated characteristics due to lack of adjustments, we only present descriptive findings.

Future studies should evaluate longitudinal effectiveness, QoL outcomes, safety, and treatment patterns among users of ixekizumab in the real-world. Likewise, comparative effectiveness studies comparing results of ixekizumab users to users of other biologics by line of therapy would provide valuable insights for treatment choice. Similarly, studies evaluating the impact of barriers to treatment access on treatment outcomes and treatment choice would be informative.

Conclusion

In this real-world study from routine clinical practice data, we found that patients' newly initiating ixekizumab were more likely to be obese, biologic-experienced, and have involvement in hard-to-treat areas. These patients had more severe PsO, and most reported a more substantial impact on work productivity and worse QoL than patients initiating other biologics. The use of ixekizumab predominantly among more severe and biologic-experienced PsO patients may be attributed, in part, to its proven efficacy and safety profile, as well as possible formulary management restrictions.

Future perspective

Clinical effectiveness information and scientific knowledge are essential for the effective and safe use of the increasingly complex and diverse treatment options for physicians and patients in psoriatic diseases. As more innovative PsO treatment options grow, a robust paradigm to guide clinical decision making in clinical practices in necessary.

Summary points

- Our study is one of the first real-world studies to characterize newly initiating ixekizumab patients in a real-world clinical setting.
- Our patients were recruited from academic and private practice dermatology clinics across North America.
- Our study found that ixekizumab initiators were Investigator Global Assessment moderate and severe and had significantly higher mean Psoriasis Area and Severity Index scores than patients initiating other biologics.
- Patients initiating ixekizumab in our study had significantly higher percent mean work hour missed compared with those initiating other biologics.
- Clinical characteristic findings in our study demonstrate that in the real-world, ixekizumab is predominantly being used by patients with more severe PsO and as a later line of therapy.
- Our findings that most patients initiating ixekizumab were biologic-experienced, and had used at least two prior biologics, could, in part, be explained by limitations to access.
- Limitations to access and patient and provider preferences may, at least in part, explain the different use of ixekizumab among biologic-naive patients.
- Comparative effectiveness studies comparing results of ixekizumab users to users of other biologics by line of therapy would provide valuable insights for treatment choice.

Author contributions

Each author listed participated sufficiently in the work to take responsibility for the content, and all those who qualify are listed.

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Ethical conduct of research

All participating investigators were required to obtain full board approval for conducting research involving human subjects. Study approval and continuing review was obtained through a central IRB (IntegReview, Protocol number is Corrona-PSO-500). All registry subjects were required to provide written informed consent prior to participating.

Data sharing statement

The Corrona dataset is based on a large US North American multicenter study adhering to a number of institutional review boards, with complex logistics. Patients did not provide consent to raw data sharing during the data collection for this purpose, and the Corrona data sharing policies do not permit raw data sharing for this purpose. An aggregated limited dataset from the current analyses is available to qualified investigators with an approved protocol. Data requests may be sent to Corrona, represented by JD Greenberg, NYU School of Medicine, New York, NY, e-mail jgreenberg@corrona.org.

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