Outcomes in Ixekizumab Patients Following Exposure to Secukinumab and Other Biologics in the CorEvitas Psoriasis Registry

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ABSTRACT

Introduction: The aim of this work is to describe real-world biologic-experienced psoriasis patients initiating ixekizumab by prior biologic therapy status and compare the effectiveness of ixekizumab between patients who previously failed secukinumab and those who failed other biologics. We hypothesized that (1) clinical outcomes and patient-reported outcomes would improve following a switch to IXE, and (2) there would be no differences in responses between patients who previously failed secukinumab and those who failed other biologics.

Methods: Participants (n = 419) included adult psoriasis patients enrolled in the CorEvitas Psoriasis Registry through 9/10/20 who switched to ixekizumab after discontinuing another biologic. Patients were classified by the biologic used immediately prior to ixekizumab and reason for discontinuation: prior secukinumab failure; prior secukinumab non-failure; prior other biologic failure; and prior other biologic non-failure. Discontinuations for efficacy reasons were considered failures; all others were considered non-failures. Baseline descriptive statistics were calculated. Multivariable Poisson regression models estimated the likelihood of response of other failure relative to secukinumab failure.

Results: Mean age was 51 years; 48% were women. Psoriasis disease characteristics were similar across prior biologic groups. At 6-month follow-up, disease severity improved for all who initiated ixekizumab after discontinuing another biologic. Secukinumab failure patients who switched to ixekizumab achieved BSA ≤ 1 (49%), BSA ≤ 3 (59%), PASI75 (46%), PASI ≤ 3 (64%), and IGA ≤ 1 (40%). Other failure patients achieved BSA ≤ 1 (55%), BSA ≤ 3 (72%), PASI75 (59%), PASI ≤ 3 (74%), and IGA ≤ 1 (54%). In regression modeling, we observed patients in the other biologics failure group had an increased likelihood of achieving response for BSA ≤ 1, PASI75, PASI90, PASI100, and IGA ≤ 1 compared to patients who failed secukinumab.

Conclusions: These findings suggest that patients with psoriasis who switch to ixekizumab after discontinuing another biologic demonstrate improvement in disease severity after six months. Patients who discontinued...
biologics other than secukinumab may be more likely to respond to ixekizumab compared to those who switched from secukinumab.

**Keywords:** Biologics; Ixekizumab; Psoriasis; Registries; Efficacy

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**Key Summary Points**

**Why carry out this study?**

There is little real-world data describing whether the effectiveness of ixekizumab for the treatment of psoriasis among patients for whom biologic therapy has failed differs by prior biologic status.

We compared the 6-month effectiveness of ixekizumab between patients who previously failed secukinumab and those who failed other biologics among patients in the CorEvitas Psoriasis Registry.

We hypothesized that (1) clinical outcomes and patient-reported outcomes (PROs) will improve following a switch to ixekizumab, and (2) there will be no differences in responses between patients who previously failed secukinumab and those who failed other biologics.

**What was learned from the study?**

These findings suggest that real-world patients with psoriasis who switch to ixekizumab after discontinuing another biologic demonstrate improvement in disease severity at 6-month follow-up.

Our findings that patients who switch to ixekizumab, regardless of failure or non-failure on other biologics, experience improved skin clearance, is evidence clinicians can use when treating both types of patients.

Our up-to-date research provides evidence for patient health education and confirmation that outcomes can improve following a biologic switch.

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**INTRODUCTION**

Patients with psoriasis often become resistant or refractory to biologic therapy, thus leading to more difficulty in reaching higher levels of skin clearance [1]. Newer, second-generation biologic therapies such as interleukin-17 inhibitors (IL-17i) and interleukin-23 inhibitors (IL-23i) are often used for patients in whom first-generation biologics (i.e., tumor necrosis factor inhibitors (TNFI), IL-12/23i) failed and are effective in these biologic-experienced patients [2, 3]. Further, evidence confirms that intraclass switching after failure of an IL-17i is effective in patients with moderate-to-severe psoriasis [4, 5] as previous treatment with an IL-17i may not impact the efficacy of a subsequent IL-17i inhibitor [6–10].

Ixekizumab (IXE), an IL-17A inhibitor approved for the treatment of moderate to severe psoriasis, had similar efficacy in patients with and without previous exposure to biologics in randomized clinical trials (RCTs) and real-world studies [11–16]. However, it is unclear if the effectiveness of IXE in biologic experienced patients differs depending on the prior biologic class (i.e., another IL-17i or other mechanism of action) or whether the prior therapy was deemed a treatment failure.

Although biologic switching within and between classes is common among biologic-treated patients, few studies address the reasons (both clinical and non-clinical) for switching or measure the effectiveness of such switching. To address these knowledge gaps, we utilized a real-world cohort of psoriasis patients to examine the effectiveness of switching to IXE after discontinuation of another biologics. Our objective was to compare the likelihood of achieving a 6-month response between IXE initiators who experienced failure of secukinumab (SEC), another IL-17i, and those who experienced failure of other biologics. We hypothesized that (1) clinical outcomes and patient-reported outcomes (PROs) will improve following a switch to IXE, and (2) there will be no differences in responses between patients who previously failed SEC and those who failed other biologics.
METHODS

Registry Overview

The CorEvitas Psoriasis Registry is a North American, prospective, multicenter observational disease-based registry launched in April 2015 in collaboration with the National Psoriasis Foundation, the design of which has been previously described [17]. Patients were enrolled if they met the following criteria: 18 years or older, psoriasis diagnosed by a dermatologist, and initiated or switched to an FDA approved systemic or biologic psoriasis treatment at registry enrollment or within 12 months before enrollment.

Data is collected from dermatologists and patients during routine clinical visits occurring at approximately 6-month intervals. All participating investigators were required to obtain full board approval for conducting research involving human subjects. All registry subjects were required to provide written informed consent prior to participating.

Study Population

The current study included patients who switched to IXE after discontinuing another biologic therapy at or after enrollment into the registry (baseline visit) between March 2016 and September 2020, provided a reason for discontinuing their prior biologic therapy, and had a corresponding 6-month follow-up visit (5–9-month window) following IXE initiation. Patients who had experience with non-IL-17i biologics (TNFi, IL-12/23i, IL-23i) were excluded if they also had a history of IL-17i exposure.

Variables

Prior Biologic Status

Dermatologists record the patient’s entire psoriasis treatment history, current medications, and any drugs prescribed during enrollment in CorEvitas’ registry. Changes to their treatments are recorded at all follow-up visits, including changes to dose and frequency. The reasons for discontinuations (efficacy, safety, insurance, or other) are also collected.

Patients in the current study were classified into four mutually exclusive groups based on the biologic used immediately prior to IXE and the reason for its discontinuation. Efficacy reasons for discontinuation were considered failures (inadequate initial response, failure to maintain initial response), and all safety and other reasons were considered non-failures. The four groups included: (1) SEC failure, (2) SEC non-failure, (3) other biologic (TNFi, IL-12/23i, IL-23i) failure, and (4) other biologic non-failure (other non-failure).

Outcomes

Disease Activity Measures

Body surface area (BSA) [18], Psoriasis Area Severity Index (PASI) [19], and Investigator’s Global Assessment (IGA) [20] were ascertained at the IXE initiation and the 6-month follow-up visit. At the 6-month follow-up, the proportions of patients achieving BSA ≤ 3% (among those with baseline BSA > 3%) and BSA ≤ 1% (among those with baseline BSA > 1%), and percent change in PASI from IXE initiation to the 6-month follow-up visit were calculated. The proportions of patients achieving PASI75, PASI90, PASI100, achieving PASI ≤ 3 (among those with baseline PASI > 3) and achieving IGA 0/1 (among those with baseline IGA > 1) at 6 months was also determined.

Patient-reported Outcomes (PROs)

At IXE initiation and the 6-month follow-up visit, patient itch, fatigue, skin pain, as well as the Patient Global Assessment (PGA) for psoriasis and the patient health state today (EQ-5D-3L) were measured using a Visual Analog Scale (VAS, 0–100) [21]. Lower scores indicate better health for patient itch, fatigue, and skin pain; higher scores indicate better health for the EQ-5D-3L health state. Measures from the Work Productivity Activity Impairment (WPAI) questionnaire were ascertained at IXE initiation and the 6-month follow-up visit. The WPAI measures for absenteeism (work hours missed), presenteeism (impairment at work/reduced on-the-job effectiveness), work productivity loss (overall work impairment) were collected in...
those currently employed, and daily activity impairment was ascertained for all patients. The WPAI measures are scored as percentages of impairment, with higher numbers indicating more significant impairment and less productivity [22]. For all VAS and WPAI measures, the mean absolute difference from IXE initiation to the 6-month follow-up visit was calculated. Dermatology Life Quality Index (DLQI) [23] measures were collected, and the proportion of patients achieving 0/1 (among those with baseline DLQI ≥ 1) at six months was determined.

Other Variables
Baseline visit variables included were sociodemographics, lifestyle characteristics, history of comorbidities, psoriasis disease characteristics, psoriasis-specific measures, and the Psoriasis Epidemiology Screening Tool (PEST). Medications included past and concomitant psoriasis therapies (non-biologic systemics (apremilast, methotrexate (MTX), cyclosporine, acitretin), phototherapy and topical agents; previous biologic therapies, including the number of prior biologics (categorized as 0, 1, or ≥ 2); and the specific biologic treatment used prior to IXE initiation (class, drug).

Statistical Analysis

Patient Characteristics at IXE Initiation
Patient demographics, clinical characteristics, and primary outcome measures at the baseline visit were summarized using descriptive statistics separately for each of the four prior biologic groups. Categorical variables were summarized using frequency counts and percentages. Continuous variables were summarized by the number of observations, mean, standard deviation, medians, and 25th and 75th percentiles.

Six-month Outcomes Among Prior Biologic Groups
Separately for each of the four prior biologic groups, mean absolute differences with 95% confidence intervals (CI) for continuous outcomes were calculated, and paired t tests were conducted to determine whether the changes from baseline to six months was statistically significant within each group. For binary outcomes, the proportions of patients achieving response were calculated. For patients who discontinued IXE prior to their 6-month follow-up visit without evidence of starting a new therapy, observations at their follow-up visit were used to calculate response. For patients who discontinued IXE and started a new therapy prior to their 6-month follow-up visit, the last observation prior to discontinuation was used for continuous response measures, and for binary response measures these patients were classified as non-responders. Proportions of patients who discontinued IXE over follow-up and their corresponding reasons were calculated.

Likelihood of Response in Other Biologic Failure vs. SEC Failure
Among patients who had a prior biologic failure, the association failure group (SEC vs. other biologics) and response was calculated using relative risks (RR) for binary outcomes and mean change from baseline for continuous outcomes. Multivariable Poisson regression models with robust standard errors were fit to estimate the likelihood (RR) of response of other biologic failure relative to SEC failure [24], and multivariable linear regression models were conducted for continuous outcomes.

Covariates were selected a priori to adjust for known confounders. Models were adjusted for age, gender, race, disease duration, psoriatic arthritis, line of therapy, and the respective baseline value of the response variable. In exploratory analyses, we replicated the analysis to compare all prior SEC patients (failure and non-failure) and all prior other biologic patients (failure and non-failure).

Ethics
The study was performed following Good Pharmacoepidemiology Practice. All participating investigators were required to obtain full board approval for conducting noninterventional research involving human subjects with a limited dataset. Sponsor approval and continuing review was obtained through a central Institutional Review Board (IRB), the New
England Independent Review Board (NEIRB; no. 120160610). 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 CorEvitas, LLC prior to the initiation of any study procedures. All patients in the registry were required to provide written informed consent and authorization prior to participating.

RESULTS

As of September 10, 2020, among the 12,175 patients enrolled in the registry, there were 1596 initiations of IXE, of which 1228 were among biologic-experienced patients. Among these initiations, 937 patients had a corresponding baseline visit, of which 843 provided a reason for the discontinuation of their prior biologic. Our study only included the 468 patients who provided a reason for discontinuation and had a baseline and a 6-month follow-up visit. However, 49 patients were excluded due to having a history of IL-17i exposure ($n = 42$) or missing covariates ($n = 7$). Therefore, 419 patients were included in the analysis, with 108 (25.8%) in the SEC failure group, 28 (6.7%) in the SEC non-failure group, 200 (47.7%) in the other failure group, and 83 (19.8%) in the other non-failure group (Fig. 1).

Patient Characteristics at IXE Initiation

The mean age of all study patients at baseline was 51 years, 48% were women, 82% were White, 79% were using private insurance, and 65% were working full time. Sociodemographics, lifestyle characteristics, and history of comorbidities were similar across the prior biologic groups, although the other non-failure

Fig. 1 Patient attrition flow chart
**Table 1** Patient sociodemographics, lifestyle, clinical characteristics, and disease activity measures at enrollment among psoriasis patients who initiated ixekizumab after switching from another biologic, by prior biologic status

|                     | Secukinumab | Other Biologic | Overall |
|---------------------|-------------|----------------|---------|
|                     | Total       | Prior SEC failure | Prior SEC non-failure | Total | Prior other BIO failure | Prior other BIO non-failure | Total |
|                     | N = 136     | n = 108         | n = 28     | N = 283 | n = 200            | n = 83              | N = 419 |
| Age in years        |             |                 |            |           |                   |                   |         |
| Mean (SD)           | 50.4 (12.6) | 50.1 (13.1)    | 51.6 (10.7) | 51.6 (13.1) | 50.8 (13.1)     | 53.4 (13.0)       | 51.2 (12.9) |
| Gender—Female       |             |                 |            |           |                   |                   |         |
| Female              | 64/136      | 52/108          | 12/28      | 139/283   | 99/200            | 40/83             | 203/419 |
|                     | (47.1%)     | (48.1%)         | (42.9%)    | (49.1%)   | (49.5%)           | (48.2%)           | (48.4%) |
| Race—White          |             |                 |            |           |                   |                   |         |
| White               | 106/136     | 83/108          | 23/28      | 237/283   | 168/200           | 69/83             | 343/419 |
|                     | (77.9%)     | (62.0%)         | (82.1%)    | (83.7%)   | (84.0%)           | (83.1%)           | (81.9%) |
| Type of health insurance plan\(^a\) |             |                 |            |           |                   |                   |         |
| Private, n (%)      |             |                 |            |           |                   |                   |         |
|                     | 103/135     | 83/107          | 20/28      | 223/277   | 158/195           | 65/82             | 326/412 |
|                     | (76.3%)     | (77.6%)         | (71.4%)    | (80.5%)   | (81.0%)           | (79.3%)           | (79.1%) |
| Medicare, n (%)     |             |                 |            |           |                   |                   |         |
|                     | 23/135      | 18/107          | 5/28       | 46/277    | 25/195            | 21/82             | 69/412  |
|                     | (17.0%)     | (16.8%)         | (17.9%)    | (16.6%)   | (12.8%)           | (25.6%)           | (16.7%) |
| Education           |             |                 |            |           |                   |                   |         |
| No college, n (%)   |             |                 |            |           |                   |                   |         |
|                     | 86/136      | 67/108          | 19/28      | 165/283   | 118/200           | 47/83             | 251/419 |
|                     | (63.2%)     | (62.0%)         | (67.9%)    | (58.3%)   | (59.0%)           | (56.6%)           | (59.9%) |
| College graduate or higher, n (%) | 50/136 | 41/108          | 9/28       | 118/283   | 82/200            | 36/83             | 168/419 |
|                     | (36.8%)     | (38.0%)         | (32.1%)    | (41.7%)   | (41.0%)           | (43.4%)           | (40.1%) |
| Lifestyle characteristics |         |                 |            |           |                   |                   |         |
| Smoking history     |             |                 |            |           |                   |                   |         |
| Never smoker, n (%) |             |                 |            |           |                   |                   |         |
|                     | 56/136      | 46/108          | 10/28      | 127/281   | 89/198            | 38/83             | 183/417 |
|                     | (41.2%)     | (42.6%)         | (35.7%)    | (45.2%)   | (44.9%)           | (45.8%)           | (43.9%) |
| Former smoker, n (%)|             |                 |            |           |                   |                   |         |
|                     | 53/136      | 40/108          | 13/28      | 106/281   | 70/198            | 36/83             | 159/417 |
|                     | (39.0%)     | (37.0%)         | (46.4%)    | (37.7%)   | (35.4%)           | (43.4%)           | (38.1%) |
| Current smoker, n (%)|            |                 |            |           |                   |                   |         |
|                     | 27/136      | 22/108          | 5/28       | 48/281    | 39/198            | 9/83 (10.8%)      | 75/417  |
|                     | (19.9%)     | (20.4%)         | (17.9%)    | (17.1%)   | (19.7%)           | (18.0%)           | (18.0%) |
| BMI (body mass index) in kg/m\(^2\) | n = 136 | n = 108 | n = 28 | n = 283 | n = 197 | n = 83 | n = 416 |
| Mean (SD)           | 33.8 (8.4)  | 33.3 (7.7)     | 35.7 (10.6) | 32.3 (8.0) | 32.6 (8.5)  | 31.5 (6.7) | 32.8 (8.2) |

\(^a\) Adis
Table 1  continued

|                          | Secukinumab | Other Biologic | Overall |
|--------------------------|-------------|----------------|---------|
|                          | Total       | Prior SEC failure | Prior SEC non-failure | Total | Prior other BIO failure | Prior other BIO non-failure | Total |
|                          | N = 136     | N = 108         | N = 28    | N = 283 | N = 200              | N = 83                      | N = 419 |
| History of comorbidities<sup>a</sup> |             |                 |           |          |                      |                            |        |
| Cardiovascular disease<sup>b</sup>, n (%) | 11/136 (8.1%) | 10/108 (9.3%) | 1/28 (3.6%) | 35/283 (12.4%) | 24/200 (12.0%) | 11/83 (13.3%) | 46/419 (11.0%) |
| Hypertension, n (%)      | 59/136 (43.4%) | 48/108 (44.4%) | 11/28 (39.3%) | 125/283 (44.2%) | 89/200 (44.5%) | 36/83 (43.9%) | 184/419 (43.9%) |
| Hyperlipidemia, n (%)    | 46/36 (33.8%) | 39/108 (36.1%) | 7/28 (25.0%) | 93/283 (32.9%) | 63/200 (31.5%) | 30/83 (33.2%) | 13/4199 (33.2%) |
| Diabetes mellitus, n (%) | 25/136 (18.4%) | 21/108 (19.4%) | 4/28 (14.3%) | 54/283 (19.1%) | 33/200 (16.5%) | 21/83 (25.3%) | 79/419 (18.9%) |
| Disease characteristics  |             |                 |           |          |                      |                            |        |
| Psoriasis morphology<sup>a</sup> |             |                 |           |          |                      |                            |        |
| Plaque, n (%)            | 135/136 (99.3%) | 108/108 (100.0%) | 27/28 (96.4%) | 275/283 (97.2%) | 194/200 (97.0%) | 81/83 (97.6%) | 410/419 (97.9%) |
| Palmoplantar, n (%)      | 16/136 (11.8%) | 13/108 (12.0%) | 3/28 (10.7%) | 41/283 (14.5%) | 29/200 (14.5%) | 12/83 (14.5%) | 57/419 (13.6%) |
| Inverse/intertriginous, n (%) | 19 (14.0%) | 15/108 (13.9%) | 4/28 (14.3%) | 24 (8.5%) | 19/200 (9.5%) | 5/83 (6.0%) | 43/419 (10.3%) |
| Scalp, n (%)             | 56/136 (41.2%) | 44/108 (40.7%) | 12/28 (42.9%) | 99/283 (35.0%) | 66/200 (33.0%) | 33/83 (39.8%) | 155/419 (37.0%) |
| Nail, n (%)              | 38/136 (27.9%) | 31/108 (28.7%) | 7/28 (25.0%) | 150/283 (53.0%) | 36/200 (18.0%) | 17/83 (20.5%) | 91/419 (21.7%) |
| Duration of psoriasis disease in years | n = 136 | n = 108 | n = 28 | n = 283 | n = 200 | n = 83 | n = 419 |
| Mean (SD)                | 19.2 (12.5) | 19.6 (12.8) | 17.5 (11.4) | 18.4 (12.6) | 18.5 (13.0) | 18.4 (11.8) | 18.7 (12.6) |
| Psoriatic arthritis, n (%) | 75/136 (55.1%) | 62/108 (57.4%) | 13/28 (46.4%) | 150/283 (53.0%) | 104/200 (52.0%) | 46/83 (55.4%) | 225/419 (53.7%) |
| Psoriasis-specific measures |             |                 |           |          |                      |                            |        |
| BSA (% involvement)      | n = 136 | n = 108 | n = 28 | n = 283 | n = 200 | n = 83 | n = 419 |
| Mean (SD)                | 10.4 (11.0) | 9.4 (8.6) | 13.9 (17.3) | 11.6 (14.2) | 11.8 (14.7) | 11.3 (12.8) | 11.2 (13.2) |

<sup>a</sup>Adis
group had a lower proportion of current smokers (11%). Psoriasis disease characteristics were similar across prior biologic groups, though patients who previously discontinued SEC had a higher proportion of patients with history of nail psoriasis (SEC failure: 29%; SEC non-failure 25%) than patients who discontinued other biologics (other failure: 18%; other non-failure 21%), and the SEC failure group had the lowest baseline mean [SD] BSA (9.4 [8.6]) compared to the other groups (SEC non-failure: 13.9 [17.3]; other failure: 11.8 [14.7]; other non-failure: 11.3 [12.8]) (Table 1). For psoriasis treatment characteristics, the prior SEC groups had higher

**Table 1 continued**

|                | Secukinumab Total | Prior SEC failure | Prior SEC non-failure | Other Biologic Total | Prior other BIO failure | Prior other BIO non-failure | Overall Total |
|----------------|-------------------|------------------|----------------------|----------------------|------------------------|-----------------------------|--------------|
|                | N = 136 (20.6%)   | N = 108 (18.5%)  | N = 28 (28.6%)       | N = 283 (20.1%)      | N = 200 (21.0%)        | N = 83 (18.1%)              | N = 419      |
| Mild disease [0, 3] | 28/136 (20.6%)   | 20/108 (18.5%)   | 8/28 (28.6%)         | 57/283 (20.1%)       | 42/200 (21.0%)         | 15/83 (18.1%)               | 85/419       |
| Moderate disease [3, 10] | 67/136 (49.3%)   | 59/108 (54.6%)   | 8/28 (28.6%)         | 133/283 (47.0%)      | 92/200 (46.0%)         | 41/83 (49.4%)               | 200/419      |
| Severe disease [0, 100] | 41/136 (31.0%)   | 29/108 (26.9%)   | 12/28 (42.9%)        | 93/283 (32.9%)       | 66/200 (33.0%)         | 27/83 (32.5%)               | 134/419      |
| PASI (score: 0–72) | n = 136          | n = 108          | n = 28               | n = 136              | n = 200                | n = 83                     | n = 419      |
| Mean (SD)       | 7.6 (6.5)        | 7.5 (5.8)        | 7.9 (9.0)            | 7.6 (6.5)            | 7.7 (7.5)              | 7.7 (6.5)                  | 7.7 (7.0)    |
| PASI—categorical |                  |                  |                      |                      |                        |                            |              |
| PASI ≤ 10, n (%)| 101/136 (74.3%)  | 81/108 (75.0%)   | 20/28 (71.4%)        | 201/283 (71.0%)      | 140/200 (70.0%)        | 61/83 (73.5%)               | 302/419      |
| PASI > 10, n (%)| 35/136 (25.7%)   | 27 (25.0%)       | 8 (28.6%)            | 82/283 (29.0%)       | 60 (30.0%)             | 22 (26.5%)                 | 117          |
| IGA (score: 0–5) | n = 136          | n = 108          | n = 28               | n = 136              | n = 200                | n = 83                     | n = 419      |
| Mean (SD)       | 3.9 (0.7)        | 4.0 (0.7)        | 3.8 (0.8)            | 3.8 (0.9)            | 3.8 (0.8)              | 3.8 (1.0)                  | 3.8 (0.8)    |
| PEST, n (%)     |                  |                  |                      |                      |                        |                            |              |
| Negative screen (< 3) | 80/133 (60.2%)   | 63/105 (60.9%)   | 17/28 (60.7%)        | 171/274 (62.4%)      | 120/195 (61.5%)        | 51/79 (64.6%)              | 251/407      |
| Positive screen (≥ 3) | 53/133 (39.8%)   | 42/105 (40.0%)   | 11/28 (39.3%)        | 103/274 (37.6%)      | 75/195 (38.5%)         | 28/79 (35.4%)              | 156/407      |

SEC secukinumab, BIO biologic, BSA body surface area, PASI Psoriasis Area and Severity Index, IGA Investigator’s Global Assessment, PEST Psoriasis Epidemiology Screening Tool

aNot mutually exclusive

bCardiovascular disease includes cardiac revascularization procedure, ventricular arrhythmia, cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, coronary artery disease, congestive heart failure, and cerebrovascular disease (stroke, transient ischemic attack (TIA)), peripheral vascular disease, peripheral arterial disease
Table 2  Patient treatment history and patient-reported outcomes among psoriasis patients who initiated ixekizumab after switching from another biologic, by prior biologic status

| Treatment characteristics | Secukinumab | Other Biologic | Overall |
|----------------------------|-------------|----------------|---------|
| **Total**                  | 136         | 283            | 419     |
| **Prior SEC failure**      | 108         | 200            | 419     |
| **Prior SEC non-failure**  | 28          | 83             | 419     |

### Treatment characteristics

#### Concomitant therapies

| Non-biologic systemics, n (%) | 10/108 (9.3%) | 27/283 (9.5%) | 9/83 (10.8%) | 39/419 (9.3%) |
| Phototherapy, n (%)           | 3/108 (2.8%)  | 6/283 (2.1%)  | 2/83 (2.4%)  | 9/419 (2.1%)  |
| Topical agents, n (%)         | 38/108 (35.2%) | 134/283 (47.3%) | 35/83 (42.2%) | 181/419 (43.2%) |

### Specific previous biologic therapies received

| TNFi, n (%) | 87/108 (80.6%) | 253/283 (89.4%) | 72/83 (86.7%) | 360/419 (85.9%) |
| IL-17, n (%)  | 108/108 (100.0%) | 0 (0.0%) | 0 (0.0%) | 136/419 (32.5%) |
| IL-12/23, n (%) | 51/108 (47.2%) | 131/283 (46.3%) | 31/83 (37.3%) | 196/419 (46.8%) |
| IL-23, n (%)  | 0 (0.0%) | 12/283 (4.2%) | 10/200 (5.0%) | 12/419 (2.9%) |

### Previous non-biologic systemic therapies, n (%)

| 0  | 41/136 (30.1%) | 111/283 (39.2%) | 35/83 (42.2%) | 152/419 (36.3%) |
| 1  | 56/136 (41.2%) | 117/283 (41.3%) | 33/83 (39.8%) | 173/419 (41.3%) |
| 2+ | 39/136 (28.7%) | 55/283 (19.4%) | 15/83 (18.1%) | 94/419 (22.4%) |

### Patient-reported outcomes

| DLQI (score: 0–30) | n = 136 | n = 108 | n = 28 | n = 283 | n = 200 | n = 83 | n = 419 |
|---------------------|---------|---------|--------|---------|---------|--------|--------|
| Mean (SD)            | 7.7 (6.3) | 7.4 (5.8) | 8.8 (7.8) | 7.5 (6.2) | 7.1 (5.8) | 8.4 (7.1) | 7.6 (6.2) |

### WPAI summary scores

| Currently employed, n (%) | 92/136 (67.6%) | 209/283 (73.9%) | 59/83 (71.1%) | 301/419 (71.8%) |
### Table 2 continued

|                      | Secukinumab | Other Biologic | Overall |
|----------------------|-------------|---------------|---------|
|                      | Total       | Prior SEC failure | Total       | Prior other BIO failure | Total       | Prior other BIO non-failure | Total       | Prior SEC non-failure | Total       | Prior SEC failure | Total       | N = 136 | N = 108 | N = 28 | N = 283 | N = 200 | N = 83 | N = 419 |
| Absenteeism<sup>b</sup> | n = 88      | n = 70         | n = 18     | n = 190 | n = 138 | n = 52     | n = 278 |
| Mean (SD)            | 1.7 (2.7)   | 1.4 (1.7)      | 2.9 (4.7) | 2.5 (4.1) | 2.4 (4.0) | 2.7 (4.6) | 2.3 (3.7) |
| Presenteeism<sup>b</sup> | n = 88    | n = 70         | n = 18     | n = 189 | n = 136 | n = 53     | n = 277 |
| Mean (SD)            | 8.5 (9.2)   | 8.2 (8.8)      | 9.9 (10.5) | 8.9 (10.4) | 8.3 (9.8) | 10.5 (11.8) | 8.8 (10.0) |
| Work productivity loss<sup>b</sup> | n = 88 | n = 70         | n = 18     | n = 186 | n = 135 | n = 51     | n = 274 |
| Mean (SD)            | 10.4 (11.8) | 9.8 (10.9)     | 12.7 (14.8) | 11.1 (13.5) | 10.3 (12.8) | 13.4 (15.1) | 10.9 (12.9) |
| Activity impairment  | n = 135     | n = 107        | n = 28     | n = 280 | n = 198 | n = 82     | n = 415 |
| Mean (SD)            | 16.3 (14.9) | 15.4 (14.7)    | 20.0 (15.1) | 15.3 (15.1) | 15.0 (14.7) | 16.0 (16.1) | 15.7 (15.0) |
| Patient global assessment | n = 135 | n = 107        | n = 28     | n = 283 | n = 200 | n = 83     | n = 418 |
| Mean (SD)            | 47.9 (27.6) | 48.4 (26.5)    | 46.1 (32.3) | 47.8 (28.7) | 45.4 (27.4) | 53.8 (31.0) | 47.9 (28.3) |
| Patient overall itch/pruritis (VAS range 0–100) | n = 135 | n = 107        | n = 28     | n = 283 | n = 200 | n = 83     | n = 418 |
| Mean (SD)            | 51.7 (33.1) | 52.6 (32.7)    | 48.2 (35.0) | 48.6 (33.7) | 47.1 (32.4) | 52.1 (36.8) | 49.6 (33.5) |
| Patient overall fatigue (VAS range 0–100) | n = 135 | n = 107        | n = 28     | n = 283 | n = 200 | n = 83     | n = 418 |
| Mean (SD)            | 40.9 (31.4) | 40.7 (31.6)    | 41.5 (31.1) | 37.7 (29.3) | 35.0 (27.9) | 44.1 (31.9) | 38.7 (30.0) |
| Patient overall skin pain (VAS range 0–100) | n = 135 | n = 107        | n = 28     | n = 283 | n = 200 | n = 83     | n = 418 |
| Mean (SD)            | 38.3 (32.9) | 38.8 (31.9)    | 36.1 (36.9) | 30.8 (31.1) | 29.4 (29.0) | 34.3 (35.6) | 33.2 (31.8) |
| Patient health state today (EQ-5D-3L VAS range 0–100) | n = 136 | n = 108        | n = 28     | n = 282 | n = 199 | n = 83     | n = 418 |
| Mean (SD)            | 70.8 (21.2) | 71.9 (20.4)    | 66.5 (23.9) | 68.5 (21.5) | 69.5 (19.8) | 66.2 (25.2) | 69.3 (21.4) |

SEC secukinumab, BIO biologic, SD standard deviation, DLQI Dermatology Life Quality Index, WPAI Work Productivity Activity Impairment Questionnaire (Absenteeism—% work missed; Presenteeism—% impairment at work; Work productivity lost—% work hours affected; Activity impairment—% daily activities impaired), EQ-5D-3L EuroQoL 5D-3L Health Questionnaire, VAS Visual Analogue Scale

<sup>a</sup>Not mutually exclusive

<sup>b</sup>Among those currently employed

△ Adis
proportions of patients with a history of 2+ biologics (SEC failure: 86%, SEC non-failure 79%) compared to the prior other biologic groups (other failure: 59%; other non-failure: 49%) (Table 2).

**Six-month Outcomes Among Prior Biologic Groups**

In unadjusted models, there was significant improvement in disease severity and PROs after switching to IXE for all the prior biologic groups. Patients who previously discontinued other biologics had higher proportions of patients who achieved response at six months following IXE treatment for most dichotomous disease severity outcomes (BSA \( \leq 3 \), PASI90, PASI100, PASI \( \leq 3 \), IGA \( \leq 1 \)) and PROs (DLQI 0/1) compared to those who discontinued SEC (Fig. 2). For PASI, BSA, IGA, and DLQI, patients in all four prior biologic groups had statistically significant improvements in outcomes over six months of IXE treatment and these changes were similar among the prior biologic groups (Fig. 3).

Patients who discontinued IXE at six months included 22 (20%) SEC failures, 5 (18%) SEC non-failures, 45 (23%) other failures, and 20 (24%) other non-failures; among these, 22, 4, 42, and 19 patients, respectively, reported a reason for discontinuation. Though proportions were based on small numbers of patients, the other non-failure group had the lowest proportion of patients who discontinued due to efficacy (11%) vs. 64% SEC failure, 50% SEC non-failure, and 48% other failure, respectively; and the highest proportion who discontinued due to insurance (21%) vs. 9% SEC failure, 0% SEC non-failure, and 7% other failure (Table 3).

![Fig. 2 Unadjusted proportion of patients achieving disease activity and patient-reported outcomes at six months among psoriasis patients who initiated IXE after switching from another biologic, by prior biologic](image_url)
Likelihood of Response in Other Biologic Failure vs. SEC Failure

In unadjusted Poisson regression models, patients in the other failure group had an increased likelihood of achieving PASI75 (crude relative risk [RR] = 1.28, 95% CI: 1.01, 1.62), PASI90 (1.57, 95% CI: 1.10, 2.26), PASI100 (2.03, 95% CI: 1.23, 3.35), and IGA 0/1 (1.37, 95% CI: 1.05, 1.80) compared to the SEC failure group; adjustment for covariates yielded similar results (Fig. 4). In the adjusted models, there were statistically significant differences between groups with the prior other failure group being more likely to achieve BSA ≤ 3% (1.3, 95% CI: 1.06, 1.61). There were no statistically significant differences in achievement of BSA ≤ 1%, PASI ≤ 3, and DLQI 0/1 (Fig. 4).

Difference in mean change in continuous outcomes at six months between the other failure and SEC failure groups, summarized by linear regression coefficients, were small and not statistically significant in both unadjusted and adjusted analyses (Table 4).

In the exploratory analysis comparing all prior SEC patients vs. all prior other biologic patients, a higher proportion of patients in the prior other biologic group achieved PASI75, PASI90, PASI100, and IGA 0/1 compared to the prior SEC group in both unadjusted models and models adjusted for age, gender, race, disease duration, psoriatic arthritis, line of therapy, and baseline outcome value (Supplementary Materials, Table S1).
DISCUSSION

At the 6-month visit following a switch from a biologic to IXE, improvements in disease severity occurred across all patients, while patients who switched after non-IL-17i failure achieved better response compared to those switching from SEC failure. Our study provides evidence that a meaningful proportion of patients who switch to IXE from another biologic will respond after switching to IXE regardless of the prior biologic therapy or reason for the switch.

When patients with moderate to severe psoriasis do not achieve an adequate primary response to biologic therapy, experience secondary failure due to loss of efficacy over time, or undergo an adverse event, switching is often employed to achieve the goal of complete skin clearance [25]. Non-clinical factors such as lack of health insurance and adherence to formulary design changes (i.e., a repositioning of therapy on the copay tier, leading to increases in copayment/out-of-pocket costs, or required switches from one therapy to another due to loss in formulary coverage in the current therapy) may also prompt patients to switch biologic therapy [26]. Studies indicate that biologic switching to a different class or within the same class is common [27, 28] with many studies reporting that initiating a subsequent biologic can be advantageous [4, 29–35]. Moreover, in a recent systematic review and meta-analysis (14 publications and 655 patients), Loft et al. determined that previous IL-17i use does not appear to impact subsequent IL-17i effectiveness in the treatment of psoriasis [5]. Our finding that IXE is effective in patients with

Table 3 Treatment patterns and reasons for discontinuation at six months among psoriasis patients who initiated IXE after switching from another biologic, by prior biologic status

| Prior SEC failure | Prior SEC non-failure | Prior other BIO failure | Prior other BIO non-failure | Total |
|------------------|----------------------|------------------------|---------------------------|-------|
| Discontinued IXE at time of follow-up visit | n = 108 | n = 28 | n = 200 | n = 83 | n = 419 |
| n (%) | 22 (20.4%) | 5 (17.9%) | 45 (22.5%) | 20 (24.1%) | 92 (22.0%) |
| Primary reason for discontinuation | n = 22 | n = 4 | n = 42 | n = 19 | n = 87 |
| Efficacy | 14 (63.6%) | 2 (50.0%) | 20 (47.6%) | 2 (10.5%) | 38 (43.7%) |
| Safety | 1 (4.5%) | 0 (0.0%) | 8 (19.0%) | 3 (15.8%) | 12 (13.8%) |
| Insurance | 2 (9.1%) | 0 (0.0%) | 3 (7.1%) | 4 (21.1%) | 9 (10.3%) |
| Active disease | 0 (0.0%) | 1 (25.0%) | 0 (0.0%) | 2 (10.5%) | 3 (3.4%) |
| Other reasons | 5 (22.7%) | 1 (25.0%) | 11 (26.2%) | 8 (42.1%) | 25 (28.7%) |

*Efficacy reasons: inadequate initial response, failure to maintain initial response
Safety reasons: serious side effect, minor side effect
Other reasons: fear of future side effect, temporary interruption, patient preference, to improve compliance, to improve tolerability, frequency of administration, route of administration, alternate mechanism of action, other
Insurance reasons: co-pay/patient cost, denied by the insurance, active disease (for starts or increasing dose), patient doing well
moderate to severe disease psoriasis patients who have previously failed other biologics or SEC is consistent with studies that evaluated treatment outcomes between 12 and 24 weeks but had limited sample sizes [1, 6, 8, 9, 14, 36, 37].

We observed patients switching from the other non-IL-17i biologics failure group had an increased likelihood of achieving response for several skin clearance outcomes and quality-of-life measures compared to patients who failed SEC. The SEC group, on average, had used a higher number of prior biologics, suggesting that these patients may have more difficult-to-treat disease and, therefore, less likely to respond to a new therapy or may not respond as quickly within six months post-switch. Yet, we did adjust our models for line of therapy, and we still found significant differences between the prior SEC and prior other biologics groups. Nevertheless, patients who switched to IXE from SEC still demonstrated improvement in both disease activity and quality-of-life outcomes.

Limitations in our study included a limited sample size in the non-failure groups leading us to only focus on the failure groups in the regression analyses. Small patient numbers impeded our ability to conduct analyses on specific types of failure (e.g., primary vs. secondary) and non-failure switches. We were also unable to investigate whether our observed 6-month findings would hold over longer-term follow-up. Finally, the generalizability of our findings is limited to patients being seen in clinical practice in the US and Canada.

Conversely, our study has many strengths. CorEvitas’ registry patients are varied and

Fig. 4 Unadjusted and adjusted* relative risks (RR) estimating the likelihood of achievement of disease activity measures and patient-reported outcomes at six months among psoriasis patients who initiated IXE in patients who failed on and switched from other biologics vs. those who switched from SEC.
heterogeneous in terms of baseline characteristics and previous treatments. The registry collects study data from both academic and private practice dermatologists across the US and Canada, and these patients likely reflect a typical real-world psoriasis patient population. Unlike the recent real-world studies investigating the switching of biologics, we did not rely on claims data which lacks essential outcomes such as clinical characteristics, PROs, and reasons for switching. Most importantly, our present study has one of the largest real-world samples to date, thus allowing us to differentiate between failure and non-failure.

### Clinical Implications

Living with the burden of psoriasis is more than just having a skin disease to patients. Patients desire effective treatment and individualized health education to strengthen their knowledge and self-management skills [38]. However, many patients taking effective biologic treatments may harbor insecurities regarding the discontinuation of biologics and are reluctant to discuss this with their healthcare provider [39], leading to undertreatment. Both concepts offer an example of the dichotomy clinicians face when treating patients. Our findings that patients who switch to IXE, regardless of failure or non-failure on other biologics, experience improved skin clearance, is evidence clinicians can use when treating both types of patients.

### Table 4
Unadjusted and adjusted linear regression models assessing the difference in mean change in patient-reported outcomes by 6-month follow-up visit, comparing other biologic failure to prior secukinumab failure (reference group)

| Outcome                        | Unadjusted | Adjusted * | Unadjusted | Adjusted * |
|--------------------------------|------------|------------|------------|------------|
|                                | β (95% CI) | p valueb   | β (95% CI) | p valueb   |
| Patient-reported outcomes      |            |            |            |            |
| Itch                           | -1.10 (-9.76, 7.56) | 0.804 | -4.34 (-11.59, 2.91) | 0.241 |
| Fatigue                        | -2.72 (-9.69, 4.25) | 0.445 | -5.00 (-11.00, 1.01) | 0.104 |
| Pain                           | -1.10 (-9.76, 7.56) | 0.804 | -5.17 (-13.83, 3.48) | 0.242 |
| Patient Global Assessment      | -1.80 (-9.62, 6.01) | 0.652 | -2.77 (-9.31, 3.78) | 0.408 |
| EQ-5D-3L VAS                    | 2.08 (-2.48, 6.65) | 0.372 | -0.01 (-3.89, 3.88) | 0.998 |
| WPAl                           |            |            |            |            |
| Absenteeismc                   | -0.24 (-1.47, 0.99) | 0.702 | 0.08 (-0.11, 1.88) | 0.084 |
| Presenteeismc                  | -1.49 (-4.25, 1.28) | 0.294 | -1.06 (-3.02, 0.91) | 0.294 |
| Work productivity lossc        | -2.09 (-5.80, 1.63) | 0.272 | -1.13 (-3.97, 1.71) | 0.437 |
| Activity impairment            | -2.36 (-5.56, 0.85) | 0.150 | -2.15 (-4.58, 0.29) | 0.085 |

β: beta coefficient from regression model—represents difference in mean change at the 6-month follow-up visit of biologic failure relative to secukinumab failure, PRO: patient-reported outcome, CI: confidence interval, EQ-5D-3L: EuroQoL Questionnaire, VAS: Visual Analog Scale, WPAl: Work Productivity and Activity Impairment Questionnaire

*Adjusted for age, gender, race, disease duration, psoriatic arthritis, line of therapy, and baseline outcome value

b: p value for beta coefficient for biologic failure vs. secukinumab failure
c: Among those patients currently working
Our up-to-date research provides evidence for patient health education and confirmation that outcomes can improve following a biologic switch.

CONCLUSIONS

These findings suggest real-world psoriasis patients who switch from other biologics to IXE due to lack of effectiveness or non-effectiveness reasons can see improvement in disease severity. Patients who discontinued biologics other than SEC due to efficacy reasons (i.e., biologic failure) were more likely to achieve a response for several disease severity measures compared to patients who discontinued SEC. More long-term real-world data are needed to determine the persistence of IXE response after switching from other biologics.

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Compliance with Ethics Guidelines. The study was performed following Good Phar- macoepidemiology Practice. All participating investigators were required to obtain full board approval for conducting noninterventional research involving human subjects with a limited dataset. Sponsor approval and continuing review was obtained through a central Institutional Review Board (IRB), the New England Independent Review Board (NEIRB; no. 120160610). 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 CorEvitas, LLC.
prior to the initiation of any study procedures. All patients in the registry were required to provide written informed consent and authorization prior to participating.

**Data Availability.** Data are available from CorEvitas, LLC through a commercial subscription agreement and are not publicly available. No additional data are available from the authors.

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