
Drug survival of secukinumab and ixekizumab for moderate-to-severe plaque psoriasis



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Background: Biologics targeting interleukin 17 are increasingly being used for treatment of moderate-to-severe psoriasis, but data on drug survival for these therapies remain scarce.

Objectives: To investigate the drug survival of secukinumab and ixekizumab in a nationwide cohort of patients with psoriasis in Denmark.

Methods: Using DERMBIO, we examined Danish patients receiving treatment with secukinumab or ixekizumab according to the standard in-label dosing. Kaplan-Meier plots were used to present survival curves.

Results: In all, 368 and 62 patients received treatment with secukinumab and ixekizumab, respectively. In total, 40.7% and 12.9% of secukinumab- and ixekizumab-treated patients were bionative. Ixekizumab-treated patients had received significantly more previous treatments. Over 12 months, 23.5% and 0.0% of bionative secukinumab- and ixekizumab-treated patients discontinued therapy, respectively. Drug survival for bionative and non-naive patients was lower for secukinumab than for ixekizumab. During the maximum 3 years of follow-up, secukinumab drug survival was lowest for patients who had previously been treated with 2 or more biologics, followed by patients treated with secukinumab as their second-ever biologic.

Limitations: The total number of patients and follow-up time were modest.

Conclusions: Drug survival was higher for ixekizumab even though secukinumab-treated patients had been treated with significantly fewer biologics before starting this drug. (J Am Acad Dermatol 2019;81:173-8.)

Key words: biologics; drug survival; IL-17; ixekizumab; psoriasis; secukinumab.

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Dr Egeberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, as well as for the study concept, design and drafting of the article, and statistical analysis. Drs Egeberg, Bryld, and Skov all take responsibility for acquisition, analysis, and interpretation of the data, as well as for critical revision of the article for important intellectual content. Drs Egeberg and Skov take responsibility for administrative, technical, or material support, as well as for study supervision.

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In recent years, a number of novel biologic therapies have been developed for treatment of inflammatory diseases, including moderate-to-severe plaque psoriasis. Notably, drugs targeting interleukin 17 (IL-17) or IL-23 have shown impressive efficacy in phase 3 clinical trials compared with older biologics targeting tumor necrosis factor- α .¹⁻³

However, real-world studies from Europe and North America have reported that drug survival (ie, the probability that patients will continue taking a given drug) was lower than expected for the IL-17 inhibitor secukinumab, suggesting that its efficacy in real life may differ from what has been observed in clinical trials. Before the present study, several potential explanations for these differences had been put forward, including the argument that patients treated with secukinumab in real life may represent the harder-to-treat patients who have already failed therapy with several other biologics.

So far, very few data have been published on the real-life performance of IL-17 inhibitors; in recent years, however, secukinumab has been placed at the top of the biologic treatment algorithm in Denmark, enabling analysis of data on a relatively large pool of bionative patients treated with secukinumab in Denmark. Similarly, very few real-world data has so far been published for the IL-17 inhibitor ixekizumab. We therefore investigated the efficacy and drug survival of secukinumab and ixekizumab in a nationwide cohort of patients with psoriasis in Denmark.

MATERIALS AND METHODS

Data sources and study population

DERMBIO^{4,5} is a national quality assurance database that contains information on all patients in Denmark who have been treated with biologics for moderate-to-severe plaque psoriasis. Data are prospectively collected, and registration is mandatory for all Danish dermatologists when using biologics for psoriasis. In Denmark, national guidelines describe the order in which the approved biologics should be used for patients initiating treatment with a biologic or switching biologics. On a national level, it is required that at least 80% of all patients be treated according to these guidelines, thus enabling physicians to decide which therapy to use in the remaining 20% of patients

(eg, for patients with a particular risk profile, in which case a specific biologic may be particularly beneficial [or advised against]). Denmark is a formulary tender market, and during the majority of the study period the Danish guidelines required physicians to prescribe secukinumab as the first-line biologic because it had a lower price than ixekizumab did.

For the present study, patients were included if they received treatment with either secukinumab or ixekizumab according to the standard in-label dosing. We excluded patients who were treated with these drugs as part of a clinical trial.

Outcomes

The primary outcome was the 12-month drug survival for secukinumab and ixekizumab. The secondary outcome was the 3-year drug survival of secukinumab. The earliest possible day of study entry was

April 1, 2015, and database lock was on August 1, 2018.

Statistical analysis

We present patient characteristics as frequencies with percentages for categorical variables and means with standard deviations for continuous variables. Kaplan-Meier plots were used to present descriptive (unadjusted) survival curves. Data in DERMBIO are set up as treatment series (ie, sequences of continuous treatment with the same biologic drug). If treatment with 1 drug is discontinued, a new treatment series will commence when treatment with another biologic is started. For both secukinumab and ixekizumab, treatment sequences were merged if the same drug was used in 2 consecutive series and the discontinuation lasted less than 2 months. For descriptive purposes, data in Kaplan-Meier plots were stratified into data on bionative patients (ie, first-ever treatment series) and data on non-naive patients. All analyses were performed using SAS software (version 9.4, SAS Institute Inc, Cary, NC) and Stata software (version 13.0, StataCorp, College Station, TX).

RESULTS

Population characteristics are shown in [Table I](#). Briefly, 368 and 62 patients received treatment with secukinumab and ixekizumab, respectively. Generally, patient characteristics were comparable

CAPSULE SUMMARY

- Efficacy of biologics for psoriasis differs between clinical trials and real-world studies. Secukinumab has shown lower drug survival than older biologics in some studies.
- Drug survival was lower for secukinumab than ixekizumab, albeit that performance was higher for bio-naïve patients with both drugs. Ixekizumab may be a suitable option especially in patients who have previously failed on other biologics, whereas secukinumab may be most useful for bio-naïve patients.

Abbreviations used:

IL: interleukin
SD: standard deviation

between patients starting treatment with secukinumab and ixekizumab; however, a markedly higher number of patients treated with secukinumab were bionative (Fig 1). The mean numbers of previous biologic treatments before initiation of secukinumab and ixekizumab were 1.3 (standard deviation [SD], 1.6) and 3.6 (SD, 2.4), respectively ($P < .0001$). Among non-naïve patients the mean number of previous treatments were 2.3 (SD, 1.4) and 4.1 (SD, 2.1) for secukinumab and ixekizumab, respectively ($P < .0001$). For secukinumab, the majority of patients were switched from ustekinumab (41.2%), followed by adalimumab (27.8%), whereas only 2 patients were switched from ixekizumab. For ixekizumab, the most common biologics from which patients were switched were ustekinumab (60.0%) and etanercept (16.7%); only 2 patients were switched from secukinumab directly to ixekizumab. Throughout the study, the main reason for discontinuation of secukinumab and for discontinuation of ixekizumab was lack of efficacy, followed by adverse events. Over the first 12 months of treatment, 23.5% of bionative secukinumab-treated patients (16 of 68 noncensored patients) discontinued therapy, of whom 68.8% had already discontinued therapy within the first 6 months. The Kaplan-Meier survival curve is shown in Fig 2. No bionative patients discontinued ixekizumab during follow-up ($P = .136$ vs secukinumab). In total, 58 secukinumab-treated patients and 8 ixekizumab-treated patients discontinued therapy in the first 12 months ($P = .075$), with 33 and 5 discontinuations, respectively, occurring within the first 6 months ($P = .001$). The 3-year drug survival for secukinumab was lowest for patients who had previously been treated with 2 or more biologics, followed by patients treated with secukinumab as their second-ever biologic (as seen in Fig 3). Baseline Psoriasis Area Severity Index was somewhat lower for ixekizumab because most patient were switch patients on account of previous failure of other treatment with biologics, yet treatment with both secukinumab and ixekizumab yielded noticeable reductions in Psoriasis Area Severity Index over 52 weeks of therapy (Fig 4).

DISCUSSION

In this nationwide study, we present up to 3 years of real-life data on the use and drug survival of patients treated with secukinumab and preliminary

Table I. Characteristics of the study population at initiation of therapy

Characteristic	Secukinumab (n = 368)	Ixekizumab (n = 62)
Men, n (%)	225 (61.1)	37 (59.7)
Mean age, y (SD)	47.1 (14.0)	49.8 (13.7)
Mean PASI (SD)	9.0 (7.1)	6.6 (6.1)
For non-naïve patients	7.5 (6.4)	6.9 (6.3)
Mean DLQI (SD)	9.9 (7.3)	9.6 (6.6)
Psoriatic arthritis, n (%)	115 (31.3)	19 (30.6)
Mean duration of psoriasis, y (SD)	23.1 (11.7)	23.7 (11.6)
Mean age at first biologic, y (SD)	43.7 (13.6)	43.5 (13.9)
Mean weight, kg (SD)	94.1 (25.3)	100.4 (27.8)
Mean body mass index, kg/m ² (SD)	30.6 (7.3)	32.6 (7.3)

DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index; SD, standard deviation.

(12-month) data on treatment with ixekizumab in Denmark. Patients treated with secukinumab had been exposed to significantly fewer previous biologic treatments than patients receiving ixekizumab. Although the absolute number of patients is modest, to our knowledge these data represent the largest cohorts to date of patients with psoriasis treated with secukinumab and ixekizumab in a real-world setting.

Previously, analyses of data from DERMBIO showed that secukinumab had lower drug survival than did older biologics such as adalimumab and ustekinumab.⁵ Although the present study was restricted to secukinumab and ixekizumab, the findings of a low drug survival with secukinumab remained consistent in the present findings. Generally, the performance of secukinumab was better among bionative patients than among non-naïve patients in the current study. The performance of secukinumab in the present study is comparable to that in previously published studies from European⁶ as well as North American cohorts,^{7,8} suggesting that treatment with secukinumab yields somewhat lower efficacy in real life than in clinical trials.²

So far, data on the real-life performance of ixekizumab have been scarce. Diotallevi et al reported data on 15 ixekizumab-treated patients,⁹ whereas Georgakopoulos et al presented data on 60 patients receiving ixekizumab.⁸ However, although these studies reported that ixekizumab appeared to be efficacious in real-life settings, both were limited to 12 weeks of follow-up, thereby limiting interpretation. Although our data support the aforementioned findings, the present study expands the current literature considerably by

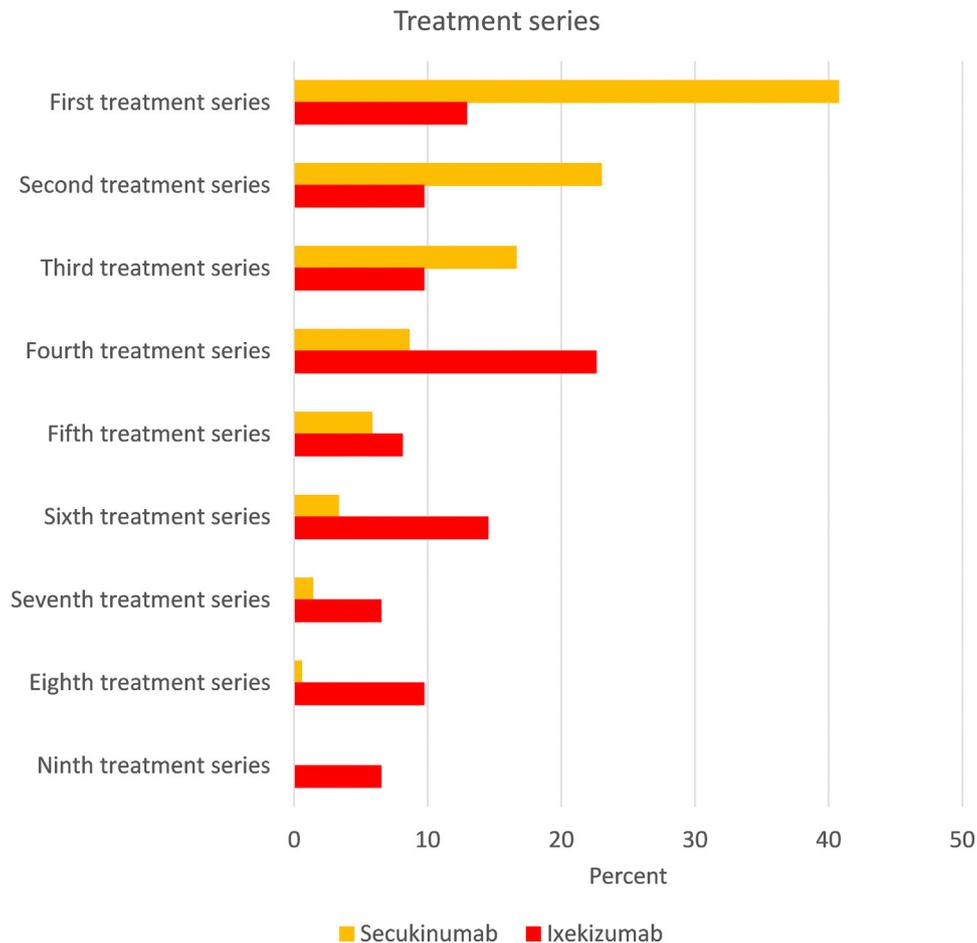


Fig 1. Overview of the treatment series when secukinumab and ixekizumab therapy is initiated. This chart shows the order in which patients receive secukinumab and ixekizumab. Bionative patients are patients receiving the drug as their first treatment series, whereas patients previously treated with 1 biologic are currently in their second treatment series, and so on. Some patients may have had more than 1 treatment series with the same drug.

adding up to 52 weeks of follow-up for ixekizumab-treated patients.

We found that during a maximum of 52 weeks of therapy, ixekizumab showed a higher drug survival than did secukinumab in Danish patients with psoriasis. Although the reasons remain unclear, differences in their binding affinity to IL-17 may at least in part explain these findings.

In the phase 3 clinical trial, IXORA-S, 124 of 136 patients (91.2%) continued therapy with ixekizumab at week 52.¹⁰ For comparison, 8 of 62 patients discontinued ixekizumab therapy within the first year (ie, 87.1% of patients continued therapy during follow-up).

Our study was limited by the relatively low number of patients, especially for ixekizumab, and by the short follow-up. Although we presented up to 3 years of data on secukinumab, it remains unclear whether the performance and drug survival of ixekizumab will

continue in a linear trend beyond the initial 12 months for which we have presented data in this study. Indeed, the small number of patients may limit interpretation of whether differences in performance between the 2 drugs were significant and clinically relevant. Over time, as larger cohorts with longer follow-up are created, these may enable such analysis. Nevertheless, to our knowledge, this study represents the largest published cohort to date of patients treated with secukinumab and ixekizumab in a real-world setting. Moreover, the fact that there was a notable difference between the number of patients who received secukinumab and the number of those who received ixekizumab in our study may affect interpretation of the findings. Numerically, the difference between the proportions of patients discontinuing secukinumab and those discontinuing ixekizumab at 6 and 12 months was small. However, one should be careful when comparing raw numbers

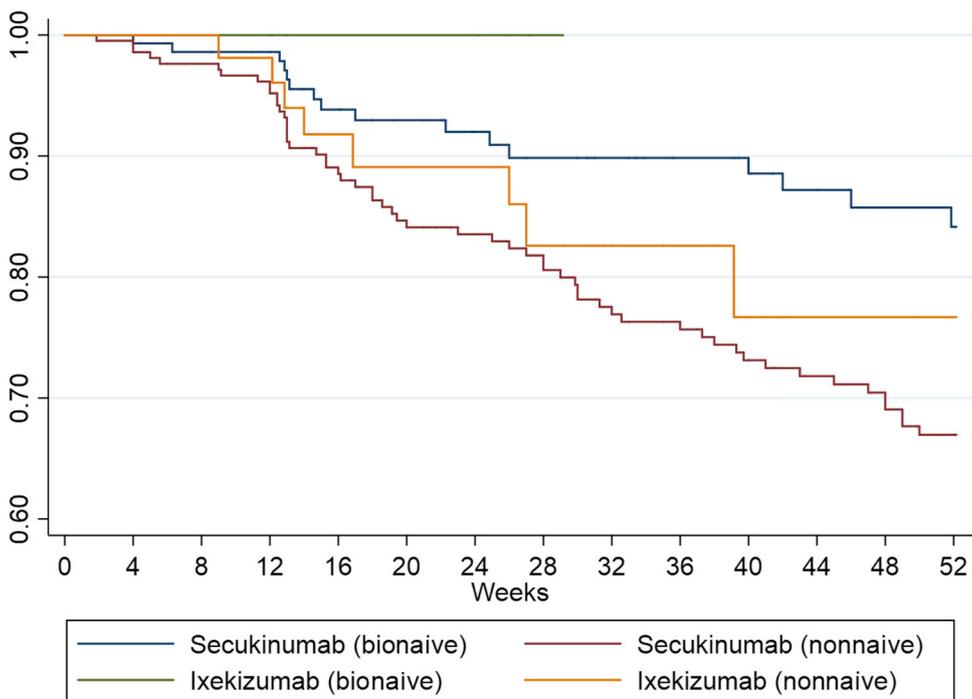


Fig 2. Kaplan-Meier plot of drug survival for secukinumab and ixekizumab over 52 weeks.

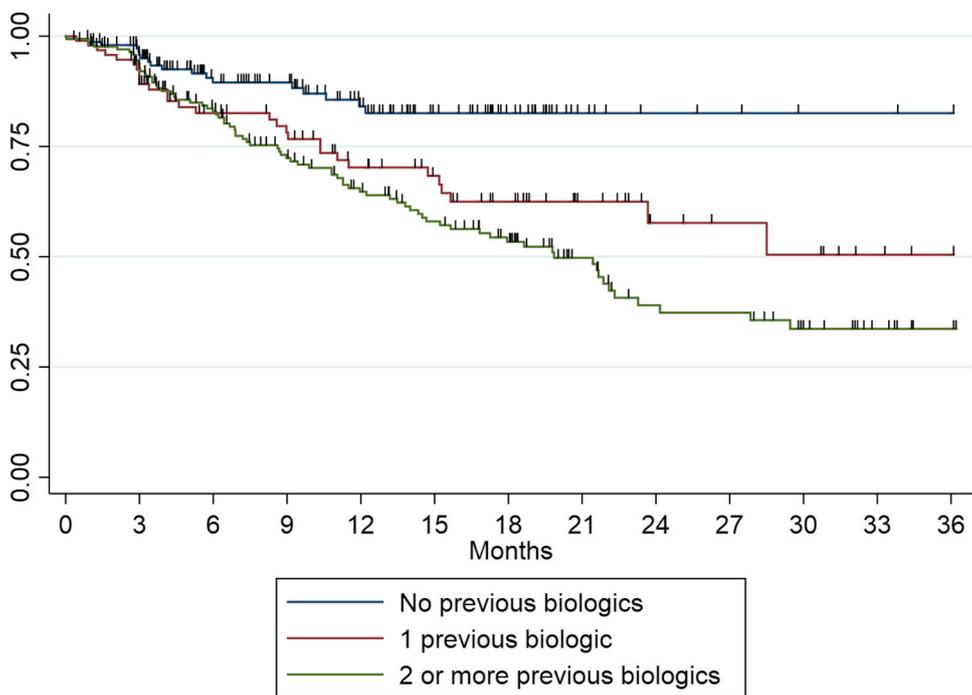


Fig 3. Kaplan-Meier plot of drug survival for secukinumab over 3 years.

or proportions in studies assessing time-to-event analyses. Rather, such studies should examine time taking the drug (eg, with incidence rates [discontinuation rates per treatment year]), and tests for significant differences should be performed by using Cox

regression controlling for potential confounders/predictors of discontinuation such as sex and number of previous treatments. However, the present study would be underpowered to assess such differences (as well as individual treatment lines). Importantly,

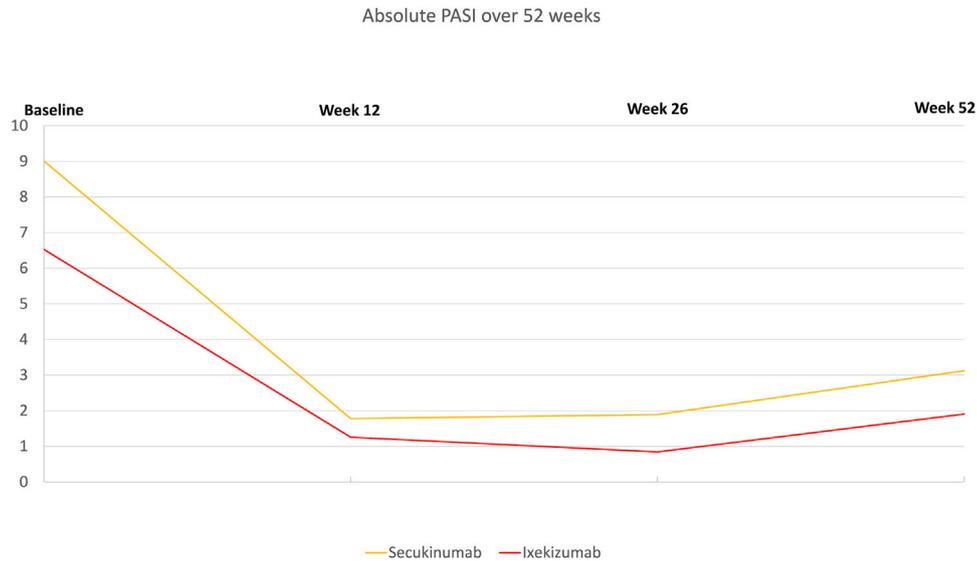


Fig 4. Mean absolute Psoriasis Area Severity Index (PASI) over 52 weeks of treatment with secukinumab and ixekizumab.

because this was not a randomized controlled trial, patient characteristics (including number of previous treatments and baseline disease severity) differed, and as a result, between-drug comparisons of drug performances should be done with caution.

CONCLUSION

In this nationwide cohort of patients with moderate-to-severe plaque psoriasis treated with secukinumab and ixekizumab, we confirmed the findings from previous studies reporting on the drug survival for secukinumab. Notably, drug survival was higher for ixekizumab than expected on the basis of the results of secukinumab drug survival, even though secukinumab-treated patients had been treated with significantly fewer biologics before starting to take this drug. Although these data represent the largest real-world study of secukinumab and ixekizumab to date, we emphasize that the number of patients remains modest.

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