Biologic drug survival in psoriasis: insights from a multi-center retrospective study in West Malaysia

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ABSTRACT

Introduction: Psoriasis is a chronic immune-mediated skin disorder with significant impact on patients' quality of life. Biologic therapies have revolutionized the treatment of moderate-to-severe psoriasis, but data on their long-term effectiveness, measured through drug survival rates, remains limited in Malaysia. This study aimed to analyze the drug survival of biologic therapies and identify factors influencing treatment discontinuation among psoriasis patients in Malaysia.

Materials and Methods: This retrospective cohort study analyzed 285 psoriasis patients receiving 437 biologic treatment courses in 10 tertiary hospitals in West Malaysia. Data on demographic characteristics, clinical profiles, and biologic treatments were collected and analyzed. Drug survival was evaluated using Kaplan-Meier analysis, and predictors of treatment discontinuation were identified using Cox proportional hazards modeling.

Results: The study cohort had a mean psoriasis onset age of 28 (± 13) years, with biologic initiation at 39 (± 16) years. Secukinumab (53.7%) was the most commonly prescribed first-line biologic, followed by Ustekinumab (28.1%). Loss of efficacy was the leading cause of discontinuation, increasing from 49.6% in the first line to 100% by the fifth. Kaplan-Meier analysis showed Secukinumab had the longest mean survival (45.5 months), followed by Ustekinumab (41.4 months) and Rizankizumab (41.3 months). Cox regression revealed prior biologic use significantly increased discontinuation risk (HR = 1.415, p = 0.049), while diabetes mellitus approached significance increase discontinuation risk (HR = 1.575, p = 0.054).

Conclusion: Biologic drug survival in Malaysian psoriasis patients reflects global trends, with Secukinumab demonstrating superior durability. Loss of efficacy and funding issues were key barriers to persistence. The findings emphasize the need for optimized treatment strategies with wider access to biological treatment.

KEYWORDS:
Psoriasis, biologic therapy, drug survival, Malaysia, treatment discontinuation

INTRODUCTION

Psoriasis is a chronic, immune-mediated skin disorder characterized by hyperproliferation of keratinocytes and inflammation, significantly impacting patients' quality of life. Immunopathogenesis of the psoriasis involves the abnormal activation of the immune system, particularly T cells, leading to inflammation and hyperproliferation of keratinocytes. Dendritic cells in the skin act as antigen-presenting cells, activating naive T cells and initiating the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), and interleukin-23 (IL-23). These cytokines play pivotal roles in the pathogenesis of psoriasis, driving inflammation and promoting rapid keratinocyte proliferation. IL-17 induces the release of other pro-inflammatory cytokines that recruit neutrophils to the site of inflammation, further exacerbating the disease. IL-23, on the other hand, is crucial for the differentiation and persistence of Th17 cells, which are central to the inflammatory cascade in psoriasis.[1]

Biologic therapies have been designed to target specific cytokines involved in this immunopathogenesis. TNF-α inhibitors, such as adalimumab, etanercept, and infliximab, block the action of TNF-α, which is a key mediator in the inflammatory process of psoriasis.[2] Similarly, IL-17 inhibitors like secukinumab, ixekizumab, and brodalumab block IL-17A or its receptor, thereby preventing the inflammatory effects triggered by IL-17. By targeting IL-17, these biologics reduce the production of other inflammatory mediators and neutrophil infiltration, leading to symptom improvement.[1] IL-23 inhibitors, such as guselkumab, risankizumab, and tildrakizumab, target the p19 subunit of IL-23, which plays a critical role in activating Th17 cells. By inhibiting IL-23, these biologics help reduce the inflammatory response by lowering IL-17 levels and other inflammatory cytokines.[3] Additionally,

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ustekinumab, which targets both IL-12 and IL-23, further helps control inflammation by interfering with the activation of both Th1 and Th17 cells.[4] These biologics represent a significant advancement in psoriasis treatment, offering more specific, targeted therapeutic options that address the underlying immune dysfunction in psoriasis and have shown substantial efficacy in both clinical trials and real-world settings.[5-7]

When selecting a biologic therapy for psoriasis, patient profiling is a critical step to ensure that treatment is tailored to the unique needs of each individual. Factors such as presence of comorbidities, previous treatment history, and the patient's ability to adhere to dosing schedules all play an important role in the decision-making process. The presence of psoriatic arthritis or axial involvement can significantly influence the choice of biologic. For patients with psoriatic arthritis, especially those with spinal inflammation, biologics which target IL-17, are often preferred due to their ability to address both skin and joint symptoms. Comorbidities, such as inflammatory bowel disease (IBD), may lead to the use of biologic, which targets IL-23, providing dual benefits for psoriasis and IBD. The frequency of dosing is also an important consideration, as some biologics require more frequent injections while others offer longer dosing intervals.[8] Additionally, cost considerations and patient access to biologic treatments play a significant role in therapy selection. Ultimately, the selection of biologic therapy should be personalized based on a comprehensive patient profile, ensuring that each treatment choice is optimal for the patient's specific condition, preferences, and lifestyle.

Drug survival, defined as the duration of time a patient remains on a specific treatment before discontinuation, serves as a vital indicator of treatment success and patient adherence.[6] Factors influencing drug survival include the patient's previous treatment history, comorbidities, adverse events (AEs), and the specific characteristics of the biologic agent.[7] For instance, studies have shown that biologics targeting IL-23, such as guselkumab and risankizumab, exhibit superior drug survival rates compared to traditional TNF-α inhibitors.[9-10] Furthermore, the persistence of treatment is often linked to the initial response to therapy, with patients experiencing significant improvements in their psoriasis symptoms more likely to continue their treatment regimen.[9]

In Malaysia, the landscape of psoriasis treatment is evolving, yet there is limited data on the drug survival of biologics within this population. Recent studies have highlighted the need for comprehensive evaluations of treatment outcomes in Malaysian patients, particularly as access to biologic therapies remains restricted compared to Western countries.[11-12] Understanding the drug survival rates of biologics in this demographic is essential for optimizing treatment strategies and improving patient outcomes. This retrospective study aims to analyse the drug survival of biologic therapies among psoriasis patients in a Malaysian hospital setting, contributing valuable insights to the existing body of literature and informing clinical practice.

MATERIALS AND METHODS

This retrospective cohort study was conducted by reviewing electronic records of psoriasis patients treated with biologic agents at the dermatology clinic of 10 tertiary government hospitals in West Malaysia. The inclusion criteria comprised of all patients diagnosed with psoriasis who received at least one biologic treatment from 1st Jan 2006 to 30th Jun 2024(18.5 years).

Data were extracted from patient records and included demographic information such as age, gender, ethnicity, body weight, and body mass index (BMI). The BMI classification followed the World Health Organization guidelines for the Asian population, where BMI values between 23 and 27.49 were classified as overweight, and values of 27.5 or higher indicated obesity. Clinical data included the age of psoriasis onset, the age at biologic initiation, the type of psoriasis (categorized as chronic plaque, pustular, or erythrodermic), the presence of psoriatic arthritis, and any comorbidities, which included hypertension, diabetes mellitus, and dyslipidaemia. Additionally, details on the concurrent use of methotrexate. Information regarding biologic treatment initiation, including PASI score and reasons for discontinuation, were also noted.

Statistical Analysis

Demographic data were analysed using descriptive statistics, with results expressed as counts (n) and percentages (%) for categorical variables. For continuous variables, the mean and standard deviation (SD) were used to summarize normally distributed data, while the median with interquartile range (IQR) was reported for data that were not normally distributed. Comparisons of categorical variables were conducted using chi-square analysis. All statistical analyses were performed with SPSS software, version 29.0 (IBM Corp, Armonk, NY, USA). Drug survival was evaluated through the Kaplan–Meier method, and a Cox proportional hazards model was used for multivariate analysis to identify predictors of drug survival, including factors such as patient age of onset, gender, prior biologic therapy , comorbidities , and concomitant methotrexate use.

Ethics approval

This study received ethical approval from the Ministry of Health Institutional Review Board and the Medical Research Ethics Committee (NMRR ID-24-01376-RE7).

RESULTS

A total of 285 patients who have received 437 treatment courses were analysed.

Baseline Characteristics

This study analysed the demographic and clinical characteristics of 285 patients initiating their first biologic therapy for psoriasis (Table I). The mean age of psoriasis onset was 28 ±13 years, with patients beginning biologic treatment at an average age of 39 ±16 years. Gender distribution was nearly balanced, with 47.4% female and 52.6% male. Ethnically, the cohort was primarily Malay (64.9%), followed by Chinese (21.1%) and Indian (12.6%)

Table I: Demographic and clinical characteristics of study population with all biologic

Characteristics	N (%)	All biologic (N=285)
Age (years, mean ± SD)	Onset	28 ± 13
	Starting biologic	39 ± 16
Gender n(%)		
	Female	135 (47.4)
	Male	150 (52.6)
Ethnicity n(%)		
	Malay	185 (64.9)
	Chinese	60 (21.1)
	Indian	36 (12.6)
	Others	4 (1.4)
Baseline weight (kg, mean ± SD)		76.6 ± 22.1
BMI (mean ± SD)		28.8 ± 7.5
Baseline BSA (mean ±SD)		48.5 ± 27.6
Baseline PASI (mean ± SD)		24.1 ± 13.2
Comorbidities (n, %)		
	Obesity	97 (34.0)
	DM	72 (25.3)
	HPT	101 (35.4)
	Dyslipidemia	90 (31.6)
Type of psoriasis n(%)		
	Chronic plaque psoriasis	253 (88.8)
	Pustular psoriasis	8 (2.8)
	erythrodermic	19 (6.7)
	others	5 (1.8)
Psoriasis arthritis n(%)		53 (18.6)
Nail Psoriatic n(%)		253 (88.8)
Concomitant use of methotrexate n(%)		8 (2.8)

Table II: Type of biologic in this study

Biologic	1st biologic (n, %)	2nd biologic (n, %)	3rd biologic (n, %)	4th biologic (n, %)	5th biologic (n, %)
Etanercept (ETN)	6 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infliximab (IFX)	1 (0.4)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Adalimumab (ADA)	28 (9.8)	5 (4.8)	1 (2.5)	0 (0.0)	0 (0.0)
Ustekinumab (UST)	80 (28.1)	22 (21.0)	5 (12.5)	3 (30.0)	1 (25.0)
Secukinumab (SEC)	153 (53.7)	40 (38.1)	10 (25.0)	0 (0.0)	1 (25.0)
Ixekizumab (IXE)	4 (1.4)	14 (13.3)	5 (12.5)	0 (0.0)	1 (25.0)
Brodalumab (BRO)	1 (0.4)	0 (0.0)	1 (2.5)	1 (10.0)	0 (0.0)
Guselkumab (GUS)	5 (1.8)	16 (15.2)	9 (22.5)	3 (30.0)	1 (25.0)
Rizankizumab (RIZ)	6 (2.1)	7 (6.7)	9 (22.5)	3 (30.0)	0 (0.0)
Certolizumab (CZP)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	285 (100)	105 (100)	40 (100)	10 (100)	4 (100)

Table III: Reason for discontinuation of existing biologic treatment

Reason for discontinuation	1st biologic (n, %)	2nd biologic (n, %)	3rd biologic (n, %)	4th biologic (n, %)	Category total (n, %)
Treatment failure/loss of efficacy	70 (49.6)	31 (65.0)	9 (69.2)	3 (60.0)	2 (100.0)
Adverse event	4 (2.8)	2 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)
Loss to follow up	9 (6.4)	1 (2.1)	0 (0.0)	1 (20.0)	0 (0.0)
Inadequate funding	36 (25.5)	10 (20.4)	3 (23.1)	1 (20.0)	0 (0.0)
Completion of clinical trial	1 (0.7)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
Patient request	0 (0.0)	0 (0.0)	1 (7.7)	0 (0.0)	0 (0.0)
Achieve remission	7 (5.0)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
Pregnancy	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	5 (3.6)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
Undisclosed reason/others	8(5.7)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
Total	141 (100)	48 (100)	13 (100)	5 (100)	2 (100)

Table IV: Cox regression analyses: Hazard ratio for risk treatment discontinuation of biologic (n=437)

Variable	Value	Confidence Interval	p-value
Gender(1)	2.123	0.753 - 0.788	0.340
Gender(2)	0.971	-0.030 - 0.221	0.894
Age at Biologic Initiation (years)	0.990	-0.010 - 0.007	0.128
Bodyweight (kg)	1.014	0.014 - 0.013	0.268
BMI	0.981	-0.019 - 0.033	0.572
Obesity	0.833	-0.183 - 0.241	0.449
DM (Diabetes Mellitus)	1.575	0.454 - 0.236	0.054
HPT (Hypertension)	0.934	-0.069 - 0.201	0.732
Dyslipidemia	1.056	0.055 - 0.248	0.825
Psoriatic Arthritis	0.935	-0.067 - 0.175	0.700
Nail Psoriasis	1.099	0.095 - 0.235	0.688
BSA (%)	1.000	0.000 - 0.005	0.968
PASI	1.016	0.016 - 0.009	0.087
Previous Biologic Use	1.415	0.347 - 0.176	0.049
Concomitant Systemic Therapy	1.367	0.312 - 0.206	0.129

Table V: Kaplan Meier drug survival for all the biologic treatment (n=437)

Biologic used	Mean Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Etanercept	31.556	9.233	13.458	49.653
Infliximab	18.500	14.500	.000	46.920
Adalimumab	17.597	3.261	11.204	23.989
Ustekinumab	41.406	4.499	32.589	50.224
Secukinumab	45.470	4.045	37.543	53.398
Ixekizumab	12.526	1.953	8.699	16.354
Brodalumab	7.667	1.785	4.169	11.165
Guselkumab	33.985	5.609	22.991	44.978
Rizankizumab	41.273	4.899	31.671	50.875
Others	9.200	3.184	2.959	15.441
Overall	40.256	2.867	34.636	45.875

patients. This ethnic breakdown is consistent with the percentage of patients seeking treatment at public dermatology centres in Malaysia.

Baseline characteristics indicated a high prevalence of comorbidities, with obesity present in 34% of patients with mean BMI of 28.8 ± 7.5. This is followed by hypertension (35.4%), dyslipidemia (31.6%), and diabetes mellitus (25.3%). In terms of severity, the mean Body Surface Area (BSA) affected was 48.5% ±27.6 with the baseline Psoriasis Area and Severity Index (PASI) score of 24.1 ±13.2.

Majority (88.8%) were diagnosed with chronic plaque psoriasis, with smaller incidences of pustular (2.8%) and erythrodermic psoriasis (6.7%). Additionally, 18.6% of patients presented with psoriatic arthritis, and 88.8% exhibited nail involvement.

Biologic Usage

Table II shows the distribution of biologics used across multiple lines of therapy. In the first line of biologic therapy (n=285), Secukinumab was the most commonly prescribed biologic (53.7%), followed by Ustekinumab (28.1%) and Adalimumab (9.8%). As patients transitioned to the second line of biologic therapy (n=105), Secukinumab remained widely used (38.1%), while the use of Guselkumab (15.2%) and Ixekizumab (13.3%) increased. In the third line of therapy (n=40), Guselkumab and Rizankizumab each accounted for 22.5% of treatments. In the fourth line of therapy (n=10), Ustekinumab, Guselkumab, and Rizankizumab were each prescribed in 30% of cases. By the fifth line of therapy (n=4), there was an equal distribution of Ustekinumab, Secukinumab, Ixekizumab, and Guselkumab, with each constituting 25% of the treatments.

Reasons for Drug Discontinuation

Table III highlights that treatment failure or loss of efficacy was consistently the leading cause of biologic therapy discontinuation across all therapy lines, increasing from 49.6% in the first line to 100% by the fourth line. Inadequate funding was the second most common reason, contributing 25.5% in the first line, 20.4% in the second line, 23.1% in the third line, and 20.0% in the fourth line treatment. Other less frequent causes included loss to follow-up (6.4% in the first line, 20.0% in the fourth line), adverse events (2.8% in the first line), and achieving remission (4.9% in the first line).

Drug Survival

The Cox regression analysis (Table IV) highlighted that diabetes mellitus (HR=1.575, p=0.054) approached significance, suggesting a potential association with biologic treatment discontinuation. Additionally, prior biologic use

was significantly associated with an increased risk of discontinuation, with a hazard ratio of 1.415 (p=0.049). Other factors, including gender, age at biologic initiation, comorbidities (e.g., obesity, hypertension, dyslipidemia, psoriatic arthritis, nail psoriasis), and disease severity measures (body surface area and PASI score), were not significantly associated with treatment discontinuation.

The Kaplan-Meier drug survival analysis (Table IV) shows that Secukinumab had the longest mean survival time at 45.5 months, followed by Ustekinumab at 41.4 months and Rizankizumab at 41.3 months and. Guselkumab also demonstrated a relatively high mean survival time at 34.0 months, while Etanercept had a mean survival of 31.6 months. Adalimumab and Infliximab had shorter mean survival times of 17.6 and 18.5 months, respectively. Ixekizumab and Brodalumab showed the shortest mean survival times, at 12.5 and 7.7 months, respectively. Across all biologics, the overall mean survival time was 40.3 months

DISCUSSION

Baseline characteristic

The baseline characteristics of our study cohort reveal notable demographic and clinical trends compared to those documented in the local data registry.[13] Our study cohort of 285 patients, who were initiating biologic therapy for psoriasis, had a mean age of psoriasis onset at 28 years and began biologic treatment at an average age of 39 years. This is younger than the age reported in the registry, which documented a mean onset age of 34.1 years among adult patients. This is due to the fact that our study cohort only capture patients who received biologic treatment, where it is noted that early onset of psoriasis is related with more severe psoriasis, hence the requirement of biologic therapy.[14]

The gender distribution was nearly equal. Ethnically, Malay patients predominated, followed by Chinese and Indian patients. This finding indeed similar with our local data registry[13] and corresponded to Malaysian racial distribution. Our cohort exhibits a higher rate of comorbidities compared to the registry data, in all diseases including obesity, hypertension, dyslipidemia, and diabetes mellitus (34% vs 31.4%, 35.4% vs 28.5%, 31.6% vs 22.7%, and 25.3% vs 19.2%, respectively). This is likely because the study cohort exclusively included patients initiating biologic therapy, and the severity of the psoriasis is related with higher metabolic syndrome.[15]

Psoriasis severity in our study cohort was reflected by a higher baseline PASI score of 24.1 and a mean BSA involvement of 48.5%, which is in line with current Malaysian Clinical Practice Guidelines (CPG), biological treatment is reserved for severe psoriasis (PASI >20, DLQI >20 BSA >30%) who have failed, contraindicated, or are intolerant to nonbiological treatment.[16] Interestingly, nail involvement was significantly higher in our cohort at 88.8% compared to the local registry data at 57.7% [13], indicating a potentially more severe presentation of psoriasis in patients with nail involvement.[17] Lastly, psoriatic arthritis is present in 18.6% of patients, consistent with the recognized association between psoriasis and joint involvement and almost similar to local registry at 18.8%.[13]

Biologic usage

Secukinumab was the most commonly prescribed biologic in our cohort study, this is similar with our local registry[13], as well as other country where there is increasing of the usage of Secukinumab as initial biologic.[18] This preference is driven by Secukinumab's robust efficacy and favourable safety profile, which have been demonstrated in clinical trials and real-world settings.[19-20] Additionally, compassionate use programs for Secukinumab have contributed to its accessibility and widespread adoption as a first-line biologic option. Upon selection of 2nd biologic onwards, there is a trend of increase usage of IL23, namely Guselkumab and Rizankuzumab. It is largely based on the favourable safety profile, high efficacy, and superior drug survival associated with IL-23 inhibitors.[10,21]

Reason of discontinuation

Treatment failure or loss of efficacy was identified as the leading cause of discontinuation across all lines of therapy, starting at 49.6% in the first line and increasing trend toward the fourth line. Factors contributing to loss of efficacy include drug-related factors, such as the presence of anti-drug antibodies22; patient-related factors, such as genetic susceptibility23; and treatment-related factors, such as dosage interval, frequency, or duration.[22] However, this study did not examine the specific factors associated with treatment failure or loss of efficacy in detail. The second most common reason for discontinuation was inadequate funding. This is particular similar to previous local studies 24, as well as studies in Korea and Asian pacific where cost is a major factor for noncompliance, especially in settings where the treatment is not reimbursed.[25-26]

Drug Survival

The Cox regression analysis indicates that certain factors may influence the discontinuation of biologic treatments. Notably, prior biologic use was significantly associated with an increased risk of discontinuation (HR = 1.415, p = 0.049). This suggests that patients with a history of biologic therapy use or exposure are more likely to discontinue subsequent treatments. This finding aligns with previous research, which has shown that biologic-experienced patients often have higher discontinuation rates compared to biologic-naïve patients.[27] One possible explanation is that biologic-experienced patients tend to have higher rates of treatment resistance or adverse reactions to subsequent biologics, which may contribute to a higher discontinuation rate. This has been noted in real-world evidence studies across multiple countries, where patients previously exposed to biologics are more likely to experience secondary loss of efficacy due to the development of anti-drug antibodies or tolerance to the medication.[22-28] Studies have shown that patients who have failed prior biologic treatments, particularly due to ineffectiveness, tend to have lower drug survival when switching to subsequent biologic therapies. This is likely because these patients may have more complex forms of psoriasis that do not respond well to treatments targeting different mechanisms. For instance, when patients fail to respond to first-line biologics like ustekinumab, their disease may not be driven by the same immune pathways targeted

by second-line treatments such as secukinumab or ixekizumab, leading to poorer outcomes. Additionally, dosing regimens can play a crucial role in treatment failure. Inadequate dosing, especially with IL-17A inhibitors like secukinumab and ixekizumab, can result in higher attrition rates, particularly for patients on second- or third-line treatments. These medications may fail to maintain an effective response in certain patients, leading to early discontinuation.[10] However, in our study, prior biologic use as an indicator for discontinuation only achieved marginal significance. There remains potential that it might not be a definitive factor, as shown in findings from the Danish region.[29]

Additionally, diabetes mellitus approached statistical significance as a factor associated with treatment discontinuation (HR = 1.575, p = 0.054). This suggests a potential link between diabetes and the likelihood of stopping biologic therapy. While the association was not statistically significant in this analysis, it is consistent with other studies that have identified comorbid conditions, including diabetes, as factors that may influence treatment adherence and persistence.[30] There is no clear study explaining the factors that relate comorbidities to drug survival. A possible explanation could be that patients with diabetes, especially those on subcutaneous(SC) insulin, may experience reduced efficacy of drug delivery. SC insulin can alter the local tissue microenvironment in which biologics are administered. The injection site of insulin can experience localized inflammation, which may influence the absorption of subsequent biologics introduced at the same site. This phenomenon raises concerns that insulin administration might hinder the absorption and efficacy of biologics, potentially leading to suboptimal treatment outcomes for psoriasis. Local cutaneous reactions or modifications to the tissue architecture induced by frequent insulin injections may interfere with the pharmacokinetics of biologics, leading to decreased drug survival and efficacy over time. Additionally, the complexity of the disease, such as the need for multiple medications and more systemic inflammation compared to the general population, may contribute to this relationship.

The Kaplan-Meier analysis shows Secukinumab with the longest mean survival time at 45.5 months. This result can be attributed to several factors specific to its use and real-world treatment dynamics. Secukinumab's earlier market introduction compared to newer biologics, such as guselkumab and other IL-23 inhibitors, likely contributed to its observed longevity in the dataset. Approved in 2016 in Malaysia , Secukinumab had a head start in accumulating real-world evidence and was widely adopted as a standard biologic for treating moderate-to-severe psoriasis. Additionally, previous local data from Malaysia showed that ustekinumab had the longest drug survival among biologics compared to others. This is likely because ustekinumab was introduced earlier than secukinumab.[24] This earlier availability allowed for larger sample sizes, longer follow-up periods, and more comprehensive data in real-world studies compared to newer biologics, providing an advantage in Kaplan-Meier survival analysis.[31]

Besides that, patient characteristics, such as treatment-naïve populations and the sequencing of biologics, may contribute to the findings. Secukinumab, being an earlier option for treatment, was more commonly used as a first-line biologic, which is associated with higher persistence rates in treatment. In contrast, newer biologics such as guselkumab might have been prescribed for patients who had previously failed or discontinued other biologics, potentially reducing their drug survival due to prior treatment resistance or adverse experiences.[10,27] In the recent studies, there is also support that IL-23 is having more longer drug survival.[10] When comparing Ustekinumab with Secukinumab, although Ustekinumab has been approved for a longer time, Secukinumab demonstrates the longest drug survival. This aligns with real-world data, where Secukinumab is superior in both efficacy and drug survival compared to Ustekinumab.[32]

Lastly, Rizankizumab had the 3rd-longest mean drug survival then followed by guselkinumab. Several factors may explain this result. Firstly, the small number of patients treated with Rizankizumab compared to other biologics may have contributed to bias in the mean survival estimate in the Kaplan-Meier survival analysis.[31] Secondly, this could be attributed to improved compliance, as the reduced frequency of hospital visits required for Rizankizumab compared to other biologics may enhance adherence to the medication.[33]

An interesting finding from Taiwan, as observed in a 2022 study, is that ustekinumab has the best drug survival, followed by secukinumab. These results are particularly relevant to Taiwan, where the reimbursement system for biologics and the limited use of secukinumab during the data collection period played a role.[34] This finding is similar to a previous study conducted in Malaysia in 2022.[24] However, there is a limited number of studies from other ASEAN countries. This contrasts with meta-analyses suggesting guselkumab is the superior biologic in terms of drug survival.[10]

LIMITATIONS

Our study has several notable limitations. First, as a retrospective analysis, the study lacked random assignment of participants to treatment groups. Additionally, the data on biologic therapies varied due to differences in their timelines of availability. Additionally, the study did not capture the frequency and duration gaps between subsequent biologic injections.

Second, there is potential for selection bias in prescribing patterns commonly observed in routine clinical settings. For instance, our analysis revealed a significantly higher number of patients receiving Secukinumab. This reflects real-world practices, where treatment decisions are influenced by factors such as cost, clinical efficacy, safety profiles, ease of administration, and the preferences of both healthcare providers and patients.

Third, the study did not account for cases where patients returned to a previously used biologic after trying another (e.g., switching from Drug A to Drug B and then back to Drug

A). These switching patterns could have affected the evaluation of treatment durability and overall effectiveness, introducing potential biases.

Fourth, The Kaplan-Meier analysis assessed overall drug survival without distinguishing between biologic-naïve and biologic-experienced patients, limiting the depth of the analysis.

Finally, the study lacked detailed data on the long-term drug survival of newer biologic therapies. Future research should aim to evaluate the sustained duration and performance of recently introduced treatments to provide a more comprehensive understanding of their long-term clinical outcomes.

CONCLUSION

This study highlights the demographic and clinical factors influencing biologic drug survival among psoriasis patients in Malaysia. Secukinumab was the most commonly prescribed biologic, with the longest survival due to its early market introduction and robust efficacy. Loss of efficacy and inadequate funding were the primary reasons for treatment discontinuation, with prior biologic use and comorbidities like diabetes affecting persistence. While IL-23 inhibitors showed promising survival rates, further research is needed to address the study's limitations, including the long-term outcomes of newer biologics and switching patterns. These findings emphasize the need for tailored treatment strategies to enhance patient outcomes.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

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REFERENCES

1. Di Cesare A, Di Meglio P, Nestle FO. The IL-23/Th17 axis in the immunopathogenesis of psoriasis. J Invest Dermatol 2009; 129(6): 1339-50.
2. Zaba LC, Cardinale I, Gilleaudeau P, Sullivan-Whalen M, Suarez-Farinas M, Fuentes-Duculan J, et al. Amelioration of epidermal hyperplasia by TNF inhibition is associated with reduced Th17 responses. J Exp Med 2007; 204(13): 3183-94.
3. Daniele SG, Eldirany SA, Damiani G, Ho M, Bunick CG. Structural basis for p19 targeting by anti-IL-23 biologics: correlations with short- and long-term efficacy in psoriasis. JID Innov 2024; 4(2): 100261.
4. Lebwohl M, Papp K, Han C, Schenkel B, Yeilding N, Wang Y, et al. Ustekinumab improves health-related quality of life in patients with moderate-to-severe psoriasis: results from the PHOENIX 1 trial. Br J Dermatol 2010;162(1): 137-46.
5. Caldarola G, Falco GM, Calabrese L, D'Amore A, Chiricozzi A, Mariani M, et al. Drug survival of biologics and non-biologics in patients affected by palmoplantar psoriasis: a "real-world", mono-center experience. Int J Dermatol 2024; 63(1): 51-8.
6. Costanzo A, Malara G, Pelucchi C, Fatiga F, Barbera G, Franchi A, et al. Effectiveness end points in real-world studies on biological therapies in psoriasis: systematic review with focus on drug survival. Dermatology 2018; 234(1-2): 1-12.
7. Augustin M, Jullien D, Martin A, Peralta C. Real-world evidence of secukinumab in psoriasis treatment - a meta-analysis of 43 studies. J Eur Acad Dermatol Venereol 2020; 34(6): 1174-85.
8. Nast A, Smith C, Spuls PI, Avila Valle G, Bata-Csorgo Z, Boonen H, et al. EuroGuiDerm guideline on the systemic treatment of Psoriasis vulgaris - part 1: treatment and monitoring recommendations. J Eur Acad Dermatol Venereol 2020; 34(11): 2461-98.
9. Ruiz-Villaverde R, Rodriguez-Fernandez-Freire L, Galan-Gutierrez M, Armario HJC, Martinez-Pilar L. Drug survival, discontinuation rates, and safety profile of secukinumab in real-world patients: a 152-week, multicenter, retrospective study. Int J Dermatol 2020; 59(5): 633-9.
10. Yiu ZZN, Becher G, Kirby B, Laws P, Reynolds NJ, Smith CH, et al. Drug survival associated with effectiveness and safety of treatment with guselkumab, ixekizumab, secukinumab, ustekinumab, and adalimumab in patients with psoriasis. JAMA Dermatol 2022; 158(10): 1131-41.
11. Robinson S, Moon TM, Eng TK, Yuen TT, Jong TJ, Selvarajah L, et al. Dermatology Life Quality Index in patients with psoriasis treated with biologic versus non-biologic treatment in Malaysia: A retrospective cross-sectional study. Drugs Real World Outcomes 2023; 10(2): 291-8.
12. Mohd Affandi A, Khan I, Ngah Saaya N. Epidemiology and clinical features of adult patients with psoriasis in Malaysia: 10-year review from the Malaysian Psoriasis Registry (2007-2016). Dermatol Res Pract 2018; 2018: 4371471.
13. Robinson ST, MM; Ramalingam R.; Voo SYM; Selvarajah L.; Jamil A.; Kwan Z.; Loo CH. The Twelfth Report of the Malaysian Psoriasis Registry 2020-2022. Kuala Lumpur, Malaysia; 2024.
14. Henseler T, Christophers E. Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. J Am Acad Dermatol 1985; 13(3): 450-6.
15. Engin B, Kutlubay Z, Yardimci G, Vehid HE, Ambarcioglu P, Serdaroglu S, et al. Evaluation of body composition parameters in patients with psoriasis. Int J Dermatol. 2014;53(12):1468-73.
16. Ministry of Health Malaysia DSoM. Management of Psoriasis Vulgaris. Putrajaya; 2013.
17. Kaeley GS, Eder L, Aydin SZ, Rich P, Bakewell CJ. Nail psoriasis: Diagnosis, assessment, treatment options, and unmet clinical needs. J Rheumatol 2021; 48(8): 1208-20.
18. Strober B, Patil D, McLean RR, Moore-Clingenpeel M, Guo N, Levi E, et al. Utilization trends and impact of secukinumab treatment on clinical outcomes in biologic-naive patients with psoriasis in a US real-world setting. Dermatol Ther (Heidelb) 2022; 12(6): 1351-65.
19. Cai L, Zhang JZ, Yao X, Gu J, Liu QZ, Zheng M, et al. Secukinumab demonstrates high efficacy and a favorable safety profile over 52 weeks in Chinese patients with moderate to severe plaque psoriasis. Chin Med J (Engl) 2020; 133(22): 2665-73.
20. Russo F, Galluzzo M, Stingeni L, Persechino S, Zichichi L, Conti A, et al. Long-term drug survival and effectiveness of secukinumab in patients with moderate to severe chronic plaque psoriasis: 42-month results from the SUPREME 2.0 study. Clin Cosmet Investig Dermatol 2023; 16: 3561-74.
21. Thomas SE, Barenbrug L, Hannink G, Seyger MMB, de Jong E, van den Reek J. Drug survival of IL-17 and IL-23 inhibitors for psoriasis: A systematic review and meta-analysis. Drugs 2024; 84(5): 565-78.

22. Jullien D, Prinz JC, Nestle FO. Immunogenicity of biotherapy used in psoriasis: The science behind the scenes. J Invest Dermatol 2015; 135(1): 31-8.
23. Bartelds GM, Krieckaert CL, Nurmohamed MT, van Schouwenburg PA, Lems WF, Twisk JW, et al. Development of antidrug antibodies against adalimumab and association with disease activity and treatment failure during long-term follow-up. JAMA 2011; 305(14): 1460-8.
24. Mashor M, Wong K, Tey K, Choon S. A retrospective study on drug survival of biologic among patients with psoriasis seen in tertiary hospital in Johor Malaysia. Med J Malaysia 2022; 77: 689-95.
25. Choi CW, Yang S, Jo G, Kim BR, Youn SW. Economic factors as major determinants of ustekinumab drug survival of patients with chronic plaque psoriasis in Korea. Ann Dermatol 2018; 30: 668-75.
26. Youn SW, Tsai TF, Theng C, Choon SE, Wiryadi BE, Pires A, et al. The MARCOPOLO study of ustekinumab utilization and efficacy in a real-world setting: Treatment of patients with plaque psoriasis in Asia-Pacific countries. Ann Dermatol 2016; 28(2): 222-31.
27. Harrold LR, Stolshek BS, Rebello S, Collier DH, Mutebi A, Wade SW, et al. Impact of prior biologic use on persistence of treatment in patients with psoriatic arthritis enrolled in the US Corrona registry. Clin Rheumatol 2017; 36(4): 895-901.
28. Hsu L, Snodgrass BT, Armstrong AW. Antidrug antibodies in psoriasis: A systematic review. Br J Dermatol 2014; 170(2): 261-73.
29. Thein D, Nielsen ML, Maul JT, Thomsen SF, Thyssen JP, Egeberg A. Impact of the pre-biologic treatment journey on biologic drug survival in psoriasis: A nationwide cohort study. J Eur Acad Dermatol Venereol. 2024.
30. Jung SW, Lim SH, Jeon JJ, Heo YW, Choi MS, Hong SP. Comparison of the efficacy and safety of biologics (secukinumab, ustekinumab, and guselkumab) for the treatment of moderate-to-severe psoriasis: Real-world data from a single Korean center. Biomedicines 2022; 10(5).
31. Bland JM, Altman DG. Survival probabilities (the Kaplan-Meier method). BMJ 1998; 317(7172): 1572.
32. Yiu ZZN, Mason KJ, Hampton PJ, Reynolds NJ, Smith CH, Lunt M, et al. Randomized trial replication using observational data for comparative effectiveness of secukinumab and ustekinumab in psoriasis: A study from the British Association of Dermatologists Biologics and Immunomodulators Register. JAMA Dermatol 2021; 157(1): 66-73.
33. Mourad AI, Gniadecki R. Biologic drug survival in psoriasis: A systematic review & comparative meta-analysis. Front Med (Lausanne) 2020; 7: 625755.
34. Huang YH, Tang CH, Goh CH, Chang CL, Qiu H, Yang YW, et al. Persistence and adherence to biologics in patients with psoriasis in Taiwan: A new biologics user cohort study. Front Pharmacol 2022; 13: 880985.