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Original Article

Effectiveness of biologic treatment for psoriasis in Malaysia: Real-world evidence and review of current evidence from Southeast Asia

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Abstract

Background: Biological treatments are effective in the management of psoriasis. However, results in the real-world setting may differ from clinical trials. **Objectives:** We aimed to evaluate the effectiveness of biological drugs among patients with psoriasis in Malaysia. **Methods:** This was a retrospective review of adult patients on biologics who were notified to the Malaysian Psoriasis Registry between 2011 and 2019. Univariate and multivariate logistic regression was performed to identify factors associated with response to treatment in terms of the Psoriasis Area and Severity Index (PASI) 75, PASI 90, and Dermatology Life Quality Index (DLQI) 0/1. **Results:** Of 130 patients, the most prescribed drug was ustekinumab (40.8%), followed by adalimumab (29.2%) and secukinumab (24.6%). Overall, the differences in the median PASI scores from baseline were −23.9 at 3–6 months, −25.8 at 12 months, and −27.8 at 3 years, while the difference in the median DLQI scores was −13.0 at 3–6 months. At 3–6 months, 57.6% achieved PASI-75, 32.9% achieved PASI-90, and 4.7% achieved PASI-100. These responses were sustained at 12 months and 3 years. Adalimumab was the most effective treatment with 88.9% achieving PASI-75, 77.8% PASI-90, and 22.2% PASI-100 at 3 years. However, secukinumab was more effective at achieving a PASI-100 response at 3–6 months (9.1%). Chinese or Indian ethnicity, concurrent use of systemic therapy or phototherapy, comorbidities, and a longer duration of psoriasis were associated with poorer response. **Conclusion:** Biological treatments, particularly adalimumab and secukinumab, are effective in reducing disease severity and improving the quality of life of patients with psoriasis in Malaysia.

Key words: Biological drugs, psoriasis, quality of life, treatment

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Introduction

The introduction of biological treatments has been a game changer in the treatment landscape of psoriasis as these drugs target specific instrumental cytokines. However, it is important to assess the effectiveness in the real-world setting compared to results achieved in clinical trials as patients recruited for trials often fulfill a stricter set of inclusion criteria.[1,2] Moreover, dose adjustment may be performed in a real-world setting.[3] According to the current Malaysian Clinical Practice Guidelines (CPG), biological treatment is reserved for severe psoriasis (Psoriasis Area and Severity Index [PASI] >20, Dermatology Life Quality Index [DLQI] >20 or body surface area [BSA] >30%) who have failed, contraindicated, or are intolerant to nonbiological treatment.[4]

An observational study (CANOVA) in Italy reported that PASI-75 response was achieved in 86% of patients at 16 weeks, 90% at 24 weeks, and 91% at 52 weeks, while 75% of patients achieved PASI-90 and 53% achieved PASI-100 at 52 weeks. Among patients who achieved PASI-75 or more at 16 weeks, 78% managed to sustain PASI-75 responses at 52 weeks. The mean DLQI score also decreased from 2.3 to 1.8. In this study, 41% were on secukinumab, 25% on ustekinumab, 25% on tumor necrosis factor inhibitors, and 12% on ixekizumab.[5] The PSO-BIO-REAL study found that 23% and 26% of patients on biologics achieved complete clearance at 6 and 12 months, respectively.[6]

Real-world data from Taiwan found that the drug with the highest effectiveness was secukinumab (91.3% achieving PASI-75, 82.6% achieving PASI-90, and 41.3% achieving PASI-100), followed by ustekinumab (79.6%, 44.9%, and 16.3%, respectively), adalimumab (64.3%, 28.6%, and 7.1%, respectively), and etanercept (50.0%, 30.0%, and 0%, respectively). Biological-naive patients had better treatment responses.[7] Within Southeast Asia, studies have shown that psoriasis patients treated with biological agents were able to achieve clear or almost clear skin from 16 weeks onward and were sustainable for up to 48 months [Table 1].[8-13]

We aimed to evaluate the real-world effectiveness of biological drugs used in the treatment of psoriasis in Malaysia in terms of disease severity and quality of life based on data from the Malaysian Psoriasis Registry (MPR) as well as identify factors determining response to treatment.

Materials and Methods

We performed a retrospective review of patients with psoriasis aged 18 and above treated with biological drugs, who were notified to the MPR from January 2011 to December 2019. The MPR is a clinical registry of adult and pediatric patients with psoriasis involving 37 participating centers nationwide. In this study, 18 public institutions notified patients treated with biological drugs. In Malaysia, eligibility for government reimbursement for biologics is based on the severity criteria outlined in the CPG. Applications for reimbursement are usually submitted on a half-yearly to annual basis. Patients who do not qualify will have to self-pay.[14] Biologics were administered based on recommended dosages and dosing frequency unless stated otherwise. Data from patients with psoriasis were collected on initiation of biologics and subsequently every 6 months. The diagnosis of psoriasis was determined clinically. The severity of the disease was assessed using the PASI scoring, while the quality of life was evaluated using the DLQI. During follow-up visits, the PASI and DLQI scores as well as changes in the treatment regime were recorded. In this study, four time points were used for the comparison of PASI scores, namely, on initiation (baseline), 3–6 months, 12 months, and 3 years. The DLQI scores were compared at baseline and 3–6 months.

Statistical analysis was conducted using IBM SPSS (IBM SPSS Statistics for Windows, Version 27.0; IBM Corp., Armonk, New York, USA). The Friedman test and the Wilcoxon signed-rank tests were used to evaluate changes in PASI and DLQI over time. Univariate and multivariate logistic regression was performed to evaluate factors associated with response to treatment at 3–6 months after initiation of biological drugs in terms of PASI-75, PASI-90, and DLQI 0/1 as well as 12 months for PASI-75 and PASI-90. Significance testing ($P < 0.25$) was used to identify potential confounders for entry in the multivariate equations to identify independent predictors. The step-wise backward method was applied. The Hosmer–Lemeshow goodness-of-fitness test for logistic regression was performed. Multicollinearity was tested and not found. All tests were two-tailed with statistical significance defined as $P < 0.05$.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Malaysian Research Ethics Committee (Research ID: NMRR-20-2590-56606). Patient consent was waived by the Ethics Committee as no individual data will be published.

Results

A total of 130 patients received biological treatments during the study. The median age at initiation was 39.6 years (interquartile range [IQR] = 33.3–49.5), while the median age of psoriasis onset was 24.0 years (IQR = 17.0–33.0), and the median duration of psoriasis was 13.6 years (IQR = 9.6–21.8). The most prescribed drug was ustekinumab (40.8%), followed by adalimumab (29.2%) and secukinumab (24.6%) [Table 2]. Most patients were biologic naive (76.9%, $n = 100$). The most widely used concurrent treatment was methotrexate (6.9%). For adjustment of dosing intervals, two patients on ustekinumab had shortened dosing intervals, while the dosing interval of adalimumab for one patient was prolonged to 4 weeks. Most of the patients were reimbursed (96.0%).

For secukinumab, 20 patients received 300 mg as recommended, two patients were commenced on 150 mg, then increased to 300 mg, seven patients were treated with 150 mg, while the dosages for three patients were not stated. On the other hand,

Table 1: Review of current evidence from Southeast Asia

Authors (country)	Year	Biological drug	Results
Our study (Malaysia)	2024	Overall	At 3–6 months
			57.6% achieved PASI-75
			32.9% achieved PASI-90
			4.7% achieved PASI-100
			At 12 months
			60.3% achieved PASI-75
			37.2% achieved PASI-90
			7.7% achieved PASI-100
			At 3 years
			65.2% achieved PASI-75
			56.5% achieved PASI-90
			17.4% achieved PASI-100
		Ustekinumab	At 3–6 months
			47.1% achieved PASI-75
			23.5% achieved PASI-90
			2.9% achieved PASI-100
			At 12 months
			57.6% achieved PASI-75
			27.3% achieved PASI-90
			9.1% achieved PASI-100
			At 3 years
			60.0% achieved PASI-75
			60.0% achieved PASI-90
			20.0% achieved PASI-100
		Adalimumab	At 3–6 months
			68.2% achieved PASI-75
			45.5% achieved PASI-90
			4.5% achieved PASI-100
			At 12 months
			70.8% achieved PASI-75
			54.2% achieved PASI-90
			12.5% achieved PASI-100
			At 3 years
			88.9% achieved PASI-75
			77.8% achieved PASI-90
			22.2% achieved PASI-100
		Secukinumab	At 3–6 months
			68.2% achieved PASI-75
			40.9% achieved PASI-90
			9.1% achieved PASI-100
			At 12 months
			56.3% achieved PASI-75
			37.5% achieved PASI-90
			0.0% achieved PASI-100
			At 3 years
			50.0% achieved PASI-75
			33.3% achieved PASI-90
			16.7% achieved PASI-100
Koh *et al*. (Singapore)[8]	2023	Overall	At 52 weeks
			37.5% achieved PASI-75
			8.3% achieved PASI-100
			50.0% achieved DLQI-75
			21.4% achieved DLQI-100
Chan *et al*. (Singapore)[9]	2023	Ustekinumab	67.7% achieved PASI-75 at week 16
Sermsaksasithorn *et al*. (Thailand)[10]	2022	Secukinumab	70.8% achieved complete skin clearance
		Ixekizumab	83.7% achieved complete skin clearance

Contd...

Table 1: Contd...

Authors (country)	Year	Biological drug	Results
Nguyen *et al*. (Vietnam)[12]	2023	Secukinumab	At 12 months: 93.9% achieved PASI-75 80.2% achieved PASI-90 56.9% achieved PASI-100 At 48 months 91.9% achieved PASI-75 78.0% achieved PASI-90 52.0% achieved PASI-100 61.4% achieved DLQI 0/1 at 12 months
Asawanonda *et al*. (Thailand)[11]	2022	Secukinumab	At week 16 74.2% achieved PASI-75 67.7% achieved PASI-90 58.1% achieved PASI-100
Mandy Chan *et al*. (Singapore)[13]	2018	Adalimumab	77.8% achieved PASI-75 at week 16

PASI: Psoriasis Area and Severity Index, DLQI: Dermatology Life Quality Index

Table 2: Baseline demographic and treatment characteristics

Characteristics	*n* (%)
Gender (*n*=130)	
Male	70 (53.8)
Female	60 (46.2)
Ethnicity (*n*=130)	
Malay	66 (50.8)
Chinese	41 (31.5)
Indian	14 (10.8)
Other Bumiputera groups	7 (5.4)
Others	2 (1.5)
Biological drug (*n*=130)	
Ustekinumab	53 (40.8)
Adalimumab	38 (29.2)
Secukinumab	32 (24.6)
Etanercept	3 (2.3)
Ixekizumab	2 (1.5)
Certolizumab	1 (0.8)
Guselkumab	1 (0.8)
Concurrent treatment (*n*=130)	
Methotrexate	9 (6.9)
Acitretin	3 (2.3)
Adjustment of dosing interval	3 (2.3)
Phototherapy	1 (0.8)
Comorbidities	
Overweight or obese (*n*=126)	85 (67.5)
Hypertension (*n*=130)	39 (30.0)
Dyslipidemia (*n*=130)	32 (24.6)
Smoker (*n*=127)	18 (14.2)
Diabetes mellitus (*n*=130)	15 (11.5)
Nonalcoholic fatty liver disease (*n*=130)	10 (7.7)
Funding sources (*n*=125)	
Reimbursed	120 (96.0)
Self-funded	5 (4.0)

one of the patients weighing more than 100 kg who was treated with ustekinumab received the 45 mg dosing, while another one received the recommended 90 mg dosing. For all other patients, standard dosages were used.

At the end of the study, 30.8% (n = 40) of patients were still on treatment. Reasons for discontinuing treatment included financial issues (27.7%, n = 36), loss of effectiveness (26.9%, n = 35), adverse events (4.6%, n = 6), defaulting treatment (3.8%, n = 5), patient's refusal (1.5%, n = 2), pregnancy (1.5%, n = 2), transfer to another center (1.5%, n = 2), and unknown reason (1.5%, n = 2).

The median values for PASI were 29.4 (IQR = 21.7–35.8) at baseline, 5.5 (IQR = 2.1–12.8) at 3–6 months, 3.6 (IQR = 1.4–11.1) at 12 months, and 1.6 (IQR = 0.9–7.3) at 3 years. Using the Friedman test (n = 14), there was a statistically significant difference in the PASI scores across all time points, χ^2 (3) = 25.921, $P < 0.001$. *Post hoc* analysis with the Wilcoxon–signed rank tests was conducted with a Bonferroni correction applied, resulting in a significance level set at $P < 0.008$. There were statistically significant reductions in the PASI scores at 3–6 months ($Z = -7.964$, $P < 0.001$), 12 months ($Z = -7.633$, $P < 0.001$), and 3 years ($Z = -4.197$, $P < 0.001$) compared to baseline.

For DLQI, there was a significant reduction in the median score at the 3–6-month follow-up: 5.0 (IQR = 2.0–10.0) from 18.0 (IQR = 12.0 to 22.0) at baseline ($Z = -7.155$, $P < 0.001$). Among the 74 patients with posttreatment DLQI scores available at 3–6 months, 16 (21.6%) achieved DLQI of 0/1. For individual drugs, this translated to 15.4% (n = 4/26) for ustekinumab, 22.7% (n = 5/22) for adalimumab, and 36.8% (n = 7/19) for secukinumab.

At 3–6 months, comparison data for PASI were available for 85 patients. More than half (57.6%, n = 49) achieved PASI-75, while 32.9% (n = 28) achieved PASI-90 and 4.7% (n = 4) achieved PASI-100. At 12 months, data were available for 78 patients. PASI responses were maintained with 60.3% (n = 47) achieving PASI-75, 37.2% (n = 29) achieving PASI-90, and 7.7% (n = 6) achieving PASI-100.

Data at 3 years of treatment were only available for 23 patients. Of these, 65.2% (n = 15) had PASI-75 responses, while 56.5% (n = 13) achieved PASI-90 and 17.4% (n = 4) achieved PASI-100 [Table 1].

Adalimumab showed the best PASI response across almost all time points [Table 3], where 88.9% achieved PASI-75, 77.8% PASI-90, and 22.2% PASI-100 at 3 years. At 3–6 months, secukinumab recorded a similar PASI-75 response to adalimumab (68.2%) but performed better than adalimumab for PASI-100 response (9.1% compared to 4.5%). In terms of DLQI, secukinumab recorded the best response with a reduction in the median DLQI score of −15.0 at 3–6 months [Table 3].

Univariate analysis revealed that patients of Chinese ethnicity (odds ratio [OR] =0.323), Indian ethnicity (OR = 0.108), those with concurrent systemic medication or phototherapy (OR = 0.228), and patients with hypertension (OR = 0.321) were less likely to achieve PASI-75 response at 3–6 months [Table 4]. In addition, patients of Indian ethnicity were less likely to achieve PASI-90 at 3–6 months (OR = 0.116), while a higher baseline PASI was associated with PASI-90 response at the same time point (OR = 1.046). A longer duration of psoriasis (OR = 0.933) and concurrent systemic medication or phototherapy (OR = 0.152) were associated with a lower likelihood of achieving PASI-75 at 12 months.

Independent negative predictive factors for PASI-75 response at 3–6 months of treatment were ethnicity (P = 0.025), namely, Chinese (adjusted OR = 0.305) and Indian ethnicities (adjusted OR = 0.099) compared to Malays as a reference group, concurrent systemic therapy or phototherapy (adjusted OR = 0.183), and hypertension (adjusted OR) [Table 5]. For PASI-90 response at 3–6 months, baseline severity remained a significant predictive factor when adjusted for ethnicity (adjusted OR = 1.050). When adjusted for concurrent systemic treatment or phototherapy, a longer duration of psoriasis remained significantly associated with lower odds of achieving PASI-75 response at 12 months of treatment (adjusted OR = 0.945). Independent negative predictive factors for PASI-90 response at 12 months were duration of psoriasis (adjusted OR = 0.937) and overweight/obesity (adjusted OR = 0.312). Of note, patients of Indian ethnicity had higher proportions of overweight/obese patients compared to Malays and Chinese (71.4% vs. 66.1% and 63.4%, respectively).

Discussion

Biological drugs have revolutionized the treatment of psoriasis with high effectiveness and sustained results, particularly in the first 3–6 months of treatment. While many real-world studies have been published, most of the existing data were derived from Western and East Asian populations. We present data from a Southeast Asian country with mixed ethnicities, including people with Malay (Southeast Asian), Chinese (East Asian), and Indian (South Asian) extraction. Our study showed that the real-world effectiveness of biologics in our population may differ from clinical trials. The closest results were reported for adalimumab, where 68.2% of patients achieved PASI-75 at 3–6 months, which was comparable to 71.0%–79.6% of trial patients at 16 weeks.[15,16] Our results for adalimumab were also comparable to another real-world study where 84% achieved PASI-75 at 12 months and 88% at 96 months,[17] and Singaporean data where 77.8% achieved PASI-75 at week 16.[13] However, PASI-90 (65%) and PASI-100 (38%) responses were higher than our results at 12 months.[17]

Table 3: Comparison of the Psoriasis Area and Severity Index 75, Psoriasis Area and Severity Index 90, and Psoriasis Area and Severity Index 100 responses for commonly used biological drugs in Malaysia for the treatment of psoriasis

Drug	PASI-75, *n* (%)	PASI-90, *n* (%)	PASI-100, *n* (%)	Median PASI (IQR)	Median DLQI (IQR)
Ustekinumab*					
Baseline	-	-	-	32.6 (21.0–37.1)	16.0 (10.5–21.0)
3–6 months (*n*=34)	16 (47.1)	8 (23.5)	1 (2.9)	6.1 (2.5–15.5)	5.0 (2.0–11.3)
12 months (*n*=33)	19 (57.6)	9 (27.3)	3 (9.1)	4.0 (1.4–14.5)	-
3 years (*n*=5)	3 (60.0)	3 (60.0)	1 (20.0)	4.5 (0.35–10.6)	-
Adalimumab†					
Baseline	-	-	-	28.0 (21.9–32.8)	16.0 (11.0–23.0)
3–6 months (*n*=22)	15 (68.2)	10 (45.5)	1 (4.5)	2.8 (1.2–11.5)	4.0 (1.8–9.3)
12 months (*n*=24)	17 (70.8)	13 (54.2)	3 (12.5)	2.2 (0.8–9.4)	-
3 years (*n*=9)	8 (88.9)	7 (77.8)	2 (22.2)	1.5 (1.2–2.4)	-
Secukinumab‡					
Baseline	-	-	-	31.7 (23.3–38.1)	18.0 (13.0–22.0)
3–6 months (*n*=22)	15 (68.2)	9 (40.9)	2 (9.1)	5.0 (1.8–12.6)	3.0 (0.0–10.0)
12 months (*n*=16)	9 (56.3)	6 (37.5)	0	4.7 (2.1–15.4)	-
3 years (*n*=6)	3 (50.0)	2 (33.3)	1 (16.7)	7.3 (0.2–10.5)	-

*For the calculation of median PASI scores, *n*=49 at baseline, *n*=35 at 3–6 months, *n*=34 at 12 months, and *n*=5 at 3 years. For the calculation of median DLQI scores, *n*=41 at baseline and *n*=26 at 3–6 months, †For the calculation of median PASI scores, *n*=31 at baseline, *n*=25 at 3–6 months, *n*=24 at 12 months, and *n*=11 at 3 years. For the calculation of median DLQI scores, *n*=27 at baseline and *n*=22 at 3–6 months, ‡For the calculation of median PASI scores, *n*=30 at baseline, *n*=24 at 3–6 months, *n*=16 at 12 months, and *n*=6 at 3 years. For the calculation of median DLQI scores, *n*=26 at baseline and *n*=19 at 3–6 months. PASI: Psoriasis Area and Severity Index, DLQI: Dermatology Life Quality Index, IQR: Interquartile range

Table 4: Univariate analysis of factors associated with response to biological treatment

	OR (95% CI); *P*				
	PASI-75 at 3–6 months	**PASI-90 at 3–6 months**	**PASI-75 at 12 months**	**PASI-90 at 12 months**	**DLQI 0/1 at 3–6 months**
Age	0.975 (0.942–1.009); 0.150	0.999 (0.964–1.035); 0.945	0.989 (0.954–1.025); 0.532	0.981 (0.944–1.019); 0.318	0.971 (0.924–1.020); 0.243
Male gender	0.859 (0.363–2.033); 0.729	1.195 (0.483–2.958); 0.700	2.231 (0.885–5.623); 0.089	1.360 (0.538–3.437); 0.516	1.354 (0.435–4.220); 0.601
Ethnicity (Malay as the reference group)					
Chinese	0.323 (0.115–0.902); 0.031	0.605 (0.222–1.653); 0.327	0.700 (0.245–2.000); 0.700	0.647 (0.224–1.865); 0.420	0.560 (0.154–2.042); 0.380
Indian	0.108 (0.024–0.476); 0.003	0.116 (0.014–0.985); 0.048	0.429 (0.119–1.538); 0.194	0.388 (0.092–1.634); 0.197	0.311 (0.035–2.776); 0.296
Other Bumiputera	0.161 (0.013–1.973); 0.153	NA; 0.999	0.500 (0.029–8.649); 0.634	1.294 (0.075–22.220); 0.859	NA; 1.000
Others	NA; 1.000	NA; 1.000	NA; NA	NA; NA	NA; 1.000
Duration of psoriasis	0.997 (0.951–1.046); 0.899	0.998 (0.949–1.050); 0.998	0.933 (0.883–0.987); 0.015	0.950 (0.894–1.010); 0.099	0.946 (0.879–1.018); 0.139
Previous use of biologics	1.040 (0.399–2.708); 0.936	0.591 (0.204–1.708); 0.331	0.503 (0.161–1.568); 0.236	0.813 (0.248–2.665); 0.732	0.606 (0.152–2.411); 0.477
Age of onset	0.957 (0.913–1.002); 0.062	1.002 (0.955–1.050); 0.947	1.038 (0.989–1.090; 0.132	1.004 (0.958–1.053); 0.861	1.004 (0.946–1.066); 0.885
Baseline PASI score	1.012 (0.973–1.052); 0.550	1.046 (1.002–1.092); 0.040	0.991 (0.947–1.037); 0.686	1.035 (0.987–1.087); 0.158	1.031 (0.984–1.081); 0.200
Use of concurrent systemic medication or phototherapy	0.228 (0.056–0.933); 0.040	0.735 (0.179–3.015); 0.669	0.152 (0.029–0.792); 0.025	0.183 (0.022–1.546); 0.119	1.041 (0.194–5.579); 0.963
Overweight or obese	0.561 (0.209–1.508); 0.252	1.062 (0.389–2.902); 0.906	0.365 (0.131–1.018); 0.054	0.475 (0.180–1.252); 0.132	0.976 (0.267–3.564); 0.970
Hypertension	0.321 (0.123–0.834); 0.020	0.373 (0.123–1.127); 0.080	0.672 (0.258–1.747); 0.414	0.502 (0.180–1.402); 0.189	0.692 (0.212–2.253); 0.541
Dyslipidemia	1.324 (0.502–3.487); 0.571	1.706 (0.640–4.549); 0.285	0.935 (0.342–2.553); 0.895	0.721 (0.254–2.051); 0.540	0.801 (0.245–2.619); 0.713
Smoker	0.343 (0.092–1.281); 0.111	1.143 (0.305–4.289); 0.843	2.432 (0.611–9.691); 0.208	1.528 (0.458–5.094); 0.490	1.615 (0.366–7.127); 0.527
Diabetes mellitus	0.368 (0.099–1.370); 0.136	0.410 (0.082–2.042); 0.277	0.408 (0.117–1.428); 0.161	0.513 (0.127–2.073); 0.349	0.285 (0.034–2.392); 0.247
Nonalcoholic fatty liver disease	0.522 (0.109–2.491); 0.415	0.800 (0.143–4.406); 0.798	0.460 (0.096–2.216); 0.333	1.298 (0.269–6.257); 0.745	3.115 (0.620–15.660); 0.168

PASI: Psoriasis Area and Severity Index, DLQI: Dermatology Life Quality Index, OR: Odds ratio, CI: Confidence interval, NA: Not available

Table 5: Multivariate analysis of factors associated with response to biological treatment

	B	SE	Wald	df	*P*	aOR	95% CI	
							Lower	Upper
PASI-75 response at 3–6 months								
Ethnicity (reference=Malay)			11.537	4	0.021			
Chinese	−1.154	0.583	3.917	1	0.048	0.315	0.101	0.989
Indian	−2.469	0.826	8.931	1	0.003	0.085	0.017	0.428
Other Bumiputera	−2.605	1.319	3.898	1	0.048	0.074	0.006	0.981
Others	−23.114	40,192.970	0.000	1	1.000	0.000	0.000	
Concurrent systemic treatment or phototherapy	−1.937	0.849	5.206	1	0.023	0.144	0.027	0.761
Hypertension	−1.448	0.576	6.330	1	0.012	0.235	0.076	0.726
Constant	1.912	0.490	15.193	1	<0.001	6.764		
PASI-90 response at 3–6 months								
Ethnicity (reference=Malay)			4.461	4	0.347			
Chinese	−0.655	0.537	1.490	1	0.222	0.519	0.181	1.487
Indian	−2.102	1.097	3.670	1	0.055	0.122	0.014	1.050
Other Bumiputera	−20.529	23,002.243	0.000	1	0.999	0.000	0.000	-
Others	−22.230	40,192.970	0.000	1	1.000	0.000	0.000	-
Baseline PASI	0.049	0.024	4.159	1	0.041	1.050	1.002	1.100
Constant	−1.965	0.782	4.696	1	0.030	0.184		
PASI-75 response at 12 months								
Duration of psoriasis	−0.57	0.029	3.971	1	0.046	0.945	0.893	0.999
Concurrent systemic treatment or phototherapy	−1.483	0.876	2.866	1	0.090	0.227	0.041	1.264
Constant	1.456	0.523	7.741	1	0.005	4.291		
PASI-90 response at 12 months								
Duration of psoriasis	−0.065	0.029	5.068	1	0.024	0.937	0.885	0.992
Overweight or obese	−1.165	0.554	4.418	1	0.036	0.312	0.105	0.924
Constant	2.156	0.688	9.825	1	0.002	8.640		

B: Beta coefficient, SE: Standard error, df: Degrees of freedom, 95% CI: 95% confidence interval, PASI: Psoriasis Area and Severity Index, aOR: Adjusted odds ratio

The BioCAPTURE registry reported that PASI-75 responses at 12 months were 45.9% for adalimumab and 45.3% for ustekinumab.[18] The authors postulate that genetic differences may result in variable effectiveness although ustekinumab should theoretically be more effective due to a more downstream action. In other studies, PASI-75 responses at 12 weeks were 68.0% for patients on adalimumab 40 mg every other week and 66.9% for ustekinumab 45 mg every 12 weeks,[19] while patients who had achieved PASI-75 sustained the response at 1 year in 94% treated with adalimumab 40 mg every week, 91% treated with ustekinumab 90 mg every 12 weeks, and 87% treated with ustekinumab 45 mg every 12 weeks.[20]

Real-world data from Korea found that PASI-75 and PASI-90 responses at 16 weeks were 88.9% and 74.1%, respectively, for secukinumab and 33.4% and 9.8% for ustekinumab. At week 56, 81.5% of patients on secukinumab and 65.6% on ustekinumab reported PASI-90 responses.[21] Moreover, effectiveness may be affected if patients weighing more than 100 kg receive the 45 mg dosing of ustekinumab instead of the recommended 90 mg.

In the ERASURE study, 81.6% and 71.6% achieved PASI-75 at week 12 with 300 mg and 150 mg of secukinumab, respectively, while the results from the FIXTURE study were lower with 77.1% and 67.0%, respectively.[22] By comparison, our data were comparable to the lower dosing responses in the trials. In terms of key secondary efficacy end points such as PASI-90 and PASI-100 at week 12, patients in the clinical trials also performed better than patients in our registry. Interestingly, improvement in the quality of life at 3–6 months was more pronounced in our patients compared to the ERASURE and FIXTURE studies (absolute change −15.0 vs. −11.4 and −10.4, respectively).[22]

An open-label, multicenter, observational cohort study involving patients treated with secukinumab in Japan found that the mean PASI score improved from 14.7 at baseline to 1.78 at week 12 and 1.59 at week 24. In terms of the proportion achieving DLQI of 0/1, there was an improvement from 2.2% at baseline to 64.7% at week 12 and 71.4% at week 24.[23] In comparison, a lower percentage (36.8%) of our patients on secukinumab achieved DLQI 0/1 at 3–6 months. Real-world evidence for secukinumab found that 90%, 79%, and 63% of patients achieved PASI-75, PASI-90, and PASI-100, respectively, at 16 weeks, and these figures reduced to 79%, 72%, and 55% at 136 weeks. Patients who were biologically naive had better responses.[24] Treatment responses to secukinumab in our study were lower compared to Thai and Vietnamese data [Table 1].[11,12] Similarly, data from Taiwan found that a higher proportion of patients on secukinumab achieved PASI-75, -90, and -100 responses compared to our

data, while the reverse was true for adalimumab.[7] A registry of patients treated with secukinumab found that the mean change from baseline was −11.7 to −11.5 for BSA and −6.7 and −6.9 for PASI in biologic-naive patients versus BSA −9.3 and −9.5 and PASI-5.2 and −5.1 in biologic-experienced patients at 6 and 12 months, respectively.[25] However, the patients treated with secukinumab in our study had higher baseline PASI scores compared to the patients in these studies, and some were dosed with 150 mg.

The PASI-75 response among patients treated with ustekinumab in the MPR was lower than the 66.4%–75.7% reported at week 12 in the PHOENIX 1 and PHOENIX 2 trials.[26,27] A similar trend was observed for PASI-90 and PASI-100. Data from Singapore also reported higher PASI-75 responses (67.7%) at week 16 of treatment with ustekinumab compared to our results.[9] However, the change in DLQI score was higher in our study compared to the clinical trials although the proportion of patients achieving DLQI 0/1 was lower (15.4% vs. 52.4%–56.4%). Another real-world study reported higher effectiveness where PASI-75, PASI-90, and PASI-100 responses at 1 year were achieved by 79.7%, 67.3%, and 47.8% of patients, respectively, while the responses at 3 years were 76.4%, 58.2%, and 41.8% with sustained effectiveness at 8 years of treatment. Predictors for improved PASI responses after 2 years were HLA-C*06 positivity, female gender, and body mass index (BMI) <30 kg/m^2.[28] Similar to the results for secukinumab, our patients treated with ustekinumab had higher baseline disease severity compared to both clinical trials and real-world studies; for instance, the mean PASI score at baseline in the Singaporean study was 16.6 with a mean reduction of 13.5 after 16 weeks.[9]

One possible reason for the lower effectiveness reported in our study is the higher baseline severity,[6] hence, the importance of intervening early in the disease course. Mahil *et al*. have proposed the use of absolute PASI scores to define treatment targets instead of percentage of improvement.[29] Nevertheless, we still found significant reductions in the PASI and DLQI scores and this also translates to better control of the disease and improved quality of life.

Certain ethnicities, concurrent systemic therapy or phototherapy, metabolic comorbidities, and a longer duration of psoriasis were associated with poorer responses to biological treatment. Our findings regarding the duration of disease and BMI in association with treatment response were consistent with reported data.[30-33] Our cohort also reported slightly increased odds of achieving PASI-90 at 3–6 months among patients with higher baseline severity, consistent with the DERMBIO registry.[34] Remarkably, there was no difference in effectiveness between patients who were biologic naive and biologic experienced. Poorer response to biological drugs among patients of Indian ethnicity could be related to higher BMI. Nevertheless, further research can be done to investigate possible genetic polymorphisms that may explain the difference in response to treatment.

In the BADBIR registry, 25.1% of patients were treated with concomitant conventional systemics, mostly with methotrexate.[35] Data from five PSONET registries reported that 9.9% were on combination treatment (72.9% with methotrexate and 25.3% with UVB, acitretin, or cyclosporine).[36] In the PROSPECT study, 3.1% of patients on secukinumab had concomitant conventional systemic treatment at 16 weeks.[37] A combination of narrowband ultraviolet B phototherapy with ustekinumab resulted in faster treatment responses. While a combination of methotrexate (as an inhibitor of immunogenicity) and adalimumab has been found to be effective, there are limited data on the combination of acitretin with biologics although this approach may offer marginal benefits.[38,39] There has been one case report on optimizing treatment response to secukinumab with subcutaneous methotrexate.[40]

The limitations of our study include small sample size, missing data due to the nature of voluntary data collection, and the nature of real-world evidence. The limited number of patients treated with biological drugs is likely attributed to the high cost of these drugs relative to the patient's economic status in a middle-income Asian country and stricter criteria for reimbursement. The pattern of drug utilization in this study may also differ from current prescribing practices as the study was conducted between 2011 and 2018. In Malaysia, approval for adalimumab was obtained in 2005, ustekinumab in 2011, secukinumab in 2016, and ixekizumab in 2019. Hence, newer drugs, namely, the interleukin-23 inhibitors such as guselkumab (approved by the FDA in 2017 but was only available in Malaysia in 2020)[41] and risankizumab (approved in 2019)[42] were not included although these would now be favored as initial treatment options. Although real-world data serve as a powerful tool for life science research, these findings would be influenced by health-seeking behavior, concomitant treatment, and environmental factors.

Conclusion

Biological treatment was effective in improving disease severity and quality of life among Malaysian patients with psoriasis. Adalimumab and secukinumab were more effective options compared to ustekinumab. Factors reducing treatment response include ethnicity, concurrent systemic therapy or phototherapy, metabolic comorbidities, and longer duration of psoriasis. Future research exploring genetic factors influencing treatment responses within different ethnicities and clinical characteristics would be useful in the era of personalized medicine.

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Data availability statement

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study,

and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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Conflicts of interest

Dr. Kwan has received a speaker honorarium from Novartis. Dr. Tan has received speaker honorariums from Novartis, AbbVie, and Janssen. Dr. Selvarajah has received speaker honorariums from Novartis, Johnson and Johnson, and AbbVie.

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