

# Impact of previous biologic use and body weight on the effectiveness of guselkumab in moderate-to-severe plaque psoriasis: a real-world practice

Yi-Teng Hung , Yu-Jr Lin, Hsien-Yi Chiu  and Yu-Huei Huang 

## Abstract

**Background:** Real-life data on patients with psoriasis treated with guselkumab are few and are needed to compare with trial-based data. We investigated the effect of clinical factors on real-world effectiveness of guselkumab.

**Methods:** This multicentre study retrospectively included 135 patients with psoriasis treated with guselkumab from June 2018 until November 2020. Effectiveness was assessed using the degree of improvement in the Psoriasis Area and Severity Index (PASI) scores at baseline and after 4, 12, 20, 28, and 36 weeks. Predictors of effectiveness were also evaluated.

**Results:** At week 36, 67% of the patients achieved PASI 75. Multivariate logistic regression analysis revealed that heavier patients were less likely to achieve PASI 75 at week 4 than patients with lower body weights. Fewer patients exposed to only one biologic achieved PASI 75 at weeks 4, 20, 28, and 36 [odds ratio (OR) = 0.08 (95% CI, 0.01–0.48), 0.21 (95% CI, 0.05–0.74), 0.04 (95% CI, 0.00–0.35), and 0.07 (95% CI, 0.00–0.68), respectively] than biologic-naïve patients. Patients previously treated with more than one biologic were less likely to achieve PASI 75 at weeks 12, 20, 28, and 36 [OR = 0.05 (95% CI, 0.01–0.22), 0.03 (95% CI, 0.01–0.16), 0.00 (95% CI, 0.00–0.03), and 0.00 (95% CI, 0.00–0.044), respectively] than biologic-naïve patients. Patients with previous anti-interleukin (IL)-17 exposure, rather than tumour necrosis factor- $\alpha$  and IL-12/23 inhibitors, had lower PASI improvements to guselkumab than biologic-naïve patients at weeks 12, 20, and 28 [OR = 0.19 (95% CI, 0.03–0.90), 0.10 (95% CI, 0.02–0.55), and 0.03 (95% CI, 0.00–0.29), respectively].

**Conclusions:** The effectiveness of guselkumab was compromised in a real-world setting. Delayed onset of therapeutic response was noted in heavier patients. Biologic exposure, the number of previously used biologics, and previous exposure to IL-17 inhibitors were clinical predictors of a reduced response to guselkumab. Physicians may share this information with patients to make treatment decisions.

**Keywords:** biologic exposure, body weight, effectiveness, guselkumab, interleukin-12/23 inhibitor, interleukin-17 inhibitor, interleukin-23 inhibitor, real-world, tumour necrosis factor- $\alpha$  inhibitor

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## Introduction

Psoriasis is a chronic inflammatory cutaneous disease, and its treatment has evolved over the past

decades. The comprehension of its pathogenesis had oriented the target therapies that chose cytokines targeting tumour necrosis factor

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Correspondence to:

**Hsien-Yi Chiu**  
Department of  
Dermatology, National  
Taiwan University Hsin-  
Chu Hospital, No. 25, Lane  
442, Section 1, Jingguo  
Road, Hsinchu City 300.  
Department of  
Dermatology, National  
Taiwan University Hospital,  
Taipei  
Department of  
Dermatology, College of  
Medicine, National Taiwan  
University, Taipei  
[extra.owl0430@yahoo.com.tw](mailto:extra.owl0430@yahoo.com.tw)

**Yu-Huei Huang**  
Department of  
Dermatology, Chang Gung  
Memorial Hospital, Linkou  
Branch, No. 5, Fuxing  
Street, Guishan District,  
Taoyuan City 333.  
School of Medicine,  
College of Medicine,  
Chang Gung University,  
Taoyuan City  
[huang3764@mail2000.com.tw](mailto:huang3764@mail2000.com.tw)

**Yi-Teng Hung**  
Department of  
Dermatology, Chang Gung  
Memorial Hospital, Linkou  
Branch, Taoyuan City

**Yu-Jr Lin**  
Research Services Center  
for Health Information,  
Chang Gung University,  
Taoyuan City

(TNF)- $\alpha$ , interleukin (IL)-12/23, IL-23, and IL-17. Due to the different pathways, trials had affirmed the drug capability. However, real-life data continue to offer fruitful insights on biologics to clinicians.<sup>1</sup> Guselkumab is an IL-23 inhibitor that targets the p19 subunit of IL-23 and thereby inhibits the downstream signalling of IL-23 along with differentiation and survival of T-helper 17 cells.<sup>2-4</sup> Two phase III randomised controlled trials (RCTs), VOYAGE 1<sup>2</sup> and VOYAGE 2,<sup>4</sup> concluded that guselkumab has greater efficacy in moderate-to-severe plaque psoriasis compared with a placebo and adalimumab administered with acceptable safety precautions during a period of 1 year. This efficacy is consistent among patients who showed no response to adalimumab. In another phase III trial (NAVIGATE), patients with inadequate response to ustekinumab achieved better psoriasis control after switching to guselkumab compared with those who continued taking ustekinumab.<sup>5</sup> Nevertheless, daily clinical practice is quite different from the setting of RCTs, wherein the study populations are selected with strict inclusion and exclusion criteria to attain internal validity. Patients with significant comorbidities, those administered a combination of different therapies, or those who have been previously administered biologics are often ineligible for RCTs. A washout period is also commonly requested in an RCT before switching from a failed biologic to a new agent. However, this is not applicable in a clinical scenario involving patients with an active disease. Hence, external validity from RCTs tends to differ in daily practice. In previous studies, the Psoriasis Area Severity Index (PASI) improvements after receiving biologics were lower in real-life setting than in RCTs.<sup>6-9</sup> The efficacy could be determined by various factors including age, weight, baseline PASI, prior biologic failures, and prior exposure to biologics.<sup>6,7,10-14</sup> There is limited information available on the efficacy of guselkumab in psoriasis in real-world studies, particularly in the Asian population. Therefore, its effectiveness in daily practice remains unclear. Moreover, it can either be lower or comparable to that in RCTs (VOYAGE 1 and VOYAGE 2) as seen in limited post-marketing studies.<sup>8,15-18</sup> However, the impact of various factors on the effectiveness of guselkumab remains elusive.<sup>8,15-19</sup> Thus, we conducted this multicentre study to assess the effectiveness and identify the predictors affecting clinical response to guselkumab in

patients with moderate-to-severe plaque psoriasis in real-world practice.

## Materials and methods

### Study population

This retrospective cohort study was conducted from June 2018 until November 2020 at four dermatology centres in Taiwan. The study population comprised reimbursed and non-reimbursed patients older than 18 years of age with a diagnosis of chronic plaque-type psoriasis. According to the Bureau of National Health Insurance's reimbursement criteria of biologic use for psoriasis in Taiwan, guselkumab (Tremfya®; Janssen Biotech, Inc., Horsham, PA, USA) was reimbursed since April 2018 for patients with psoriasis who had a PASI 10 for at least 6 months and inadequate response, contraindication, or intolerance to a 3-month combination of at least two of three traditional systemic medications, which include cyclosporine (2.5–5 mg/kg/day), methotrexate (15 mg/week), and acitretin (0.3–1 mg/kg/day), along with phototherapy (psoralen ultraviolet A or narrow-band ultraviolet B) at least twice weekly.<sup>6</sup> Guselkumab was administered at a standard dose of 100 mg subcutaneously at weeks 0 and 4 and every 8 weeks thereafter. This study was approved by the Institutional Review Board of the Ethical Standards Committee of Chang Gung Memorial Hospital, Linkou and Taipei branches (202100142B0), National Taiwan University Hospital (201904124RINC), and National Taiwan University Hospital Hsin-Chu branch (103-082-E). Informed consent was not required by the Ethical Standards Committee due to the retrospective nature of the study.

### Effectiveness assessment and outcome measures

The effectiveness of guselkumab was measured using PASI assessment at weeks 0, 4, 12, 20, 28, and 36. The principal outcome measure was PASI 75 (75% or greater reduction in PASI scores from baseline) during guselkumab treatment at weeks 4, 12, 20, 28, and 36. The demographic data of patients, including age, sex, body weight (BW), body mass index (BMI), comorbidities, psoriatic arthritis, alcohol and smoking habits, disease duration, family history of psoriasis, previous exposure of biologics, and traditional systemic

agents (methotrexate, acitretin, and cyclosporine), were obtained from clinical records. Previously used biologics in this study included TNF- $\alpha$  inhibitor (etanercept and adalimumab), IL-12/23 inhibitor (ustekinumab), IL-17 inhibitor (secukinumab, ixekizumab, and brodalumab), and IL-23 inhibitor (risankizumab).

### Statistical analysis

Results were presented as mean  $\pm$  standard deviation (SD) for continuous variables and numbers with percentages for categorical variables. Univariate logistic regression analyses were conducted to study the factors associated with PASI 75 response. Stepwise multivariate logistic regression analyses were used to evaluate the association between dependent variables resulting in a PASI 75 response at weeks 4, 12, 20, 28, and 36. In addition, univariate logistic regression analysis was performed to identify the impact of previously used biologics (TNF- $\alpha$ , IL-12/23, and IL-17 inhibitors) on PASI 75 response. Odds ratio (OR) and 95% confidence intervals (CIs) were presented. In all cases, a value of  $p < 0.05$  (two-tailed) was considered statistically significant. Statistical analysis of the data was performed using R3.3.2.

## Results

### Patient demographics, clinical characteristics, and therapeutic efficacy

A total of 135 patients with moderate-to-severe psoriasis were enrolled in this retrospective study with a mean PASI score of  $16.23 \pm 7.87$  (Table 1). Among these patients, 121 (90%) were reimbursed. Most of the patients were men (78%), and the average age was  $46.46 \pm 13.32$  years. Most patients had been treated with traditional systemic medications ( $n = 121$ , 90%), phototherapy ( $n = 126$ , 93%), and biologics ( $n = 95$ , 70%). The mean PASI improvement at weeks 4, 12, 20, 28, and 36 was 43.87%, 69.08%, 74.67%, 81.41%, and 80.56%, respectively. At week 36, the proportion of patients achieving PASI 75 and PASI 90 was 67% and 37%, respectively (Figure 1 and Supplementary Table S1).

### Clinical factors affecting the PASI 75 response

We further analysed the predictors of PASI 75 response, and univariate logistic analysis showed

that patients who received previous biologic treatment were less likely to achieve PASI 75 response at weeks 12, 20, 28, and 36 than those who were biologically naïve (Table 2). The number of previous biologic use was associated with reduced PASI 75 improvement at weeks 12, 20, 28, and 36 (Table 2). At week 4, fewer patients who had higher BW achieved PASI 75 than those with lower BW ( $p < 0.006$ ) (Table 2). However, this difference was not observed after 4 weeks of guselkumab treatment.

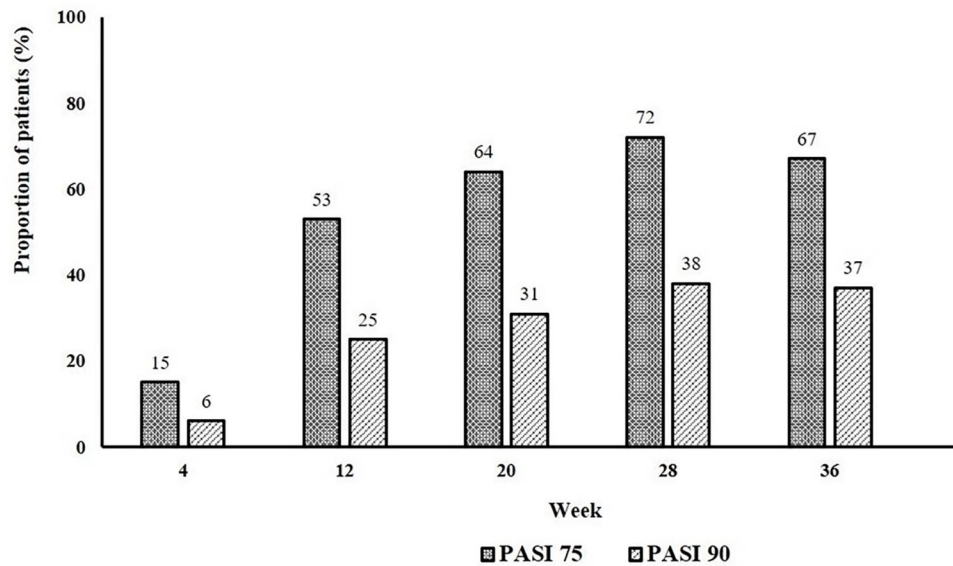
Multivariate logistic regression analysis showed that a lower proportion of patients previously treated with one biologic achieved PASI 75 than that of biologic-naïve patients at weeks 4 (OR = 0.08; 95% CI, 0.01–0.48), 12 (OR = 0.39; 95% CI, 0.13–1.11), 20 (OR = 0.21; 95% CI, 0.05–0.74), 28 (OR = 0.04; 95% CI, 0.00–0.35), and 36 (OR = 0.07; 95% CI, 0.00–0.68) (Figure 2). Patients previously exposed to more than one biologic ( $\geq 2$ ) were less likely to achieve PASI 75 at weeks 12, 20, 28, and 36 [OR = 0.05 (95% CI, 0.01–0.22), 0.03 (95% CI, 0.01–0.16), 0.00 (95% CI, 0.00–0.03), and 0.00 (95% CI, 0.00–0.044), respectively] than biologic-naïve patients, suggesting that the number of previous biologic use was associated with a worse response to guselkumab (Figure 2). Higher BW was associated with a reduced PASI 75 response at week 4 (OR = 0.94; 95% CI, 0.88–0.99) (Figure 2). However, there was no significant difference in the effectiveness of guselkumab due to different BW from week 12 until the end of our study.

### Association of different classes of previously used biologics with the effectiveness of guselkumab

To examine whether the treatment response to guselkumab was different among patients receiving prior biologic treatment with a different mode of action (MOA), we further analysed the patients using their prior use of biologics that belonged to different classes, including TNF- $\alpha$ , IL-12/23, and IL-17 inhibitors (Table 3). Only previous exposure to IL-17 inhibitors was significantly associated with reduced PASI 75 response at weeks 12, 20, and 28 (OR = 0.19, 0.10, and 0.03, respectively). On the contrary, no association was observed in patients previously receiving TNF- $\alpha$  or IL-12/23 inhibitors (Table 3).

**Table 1.** Baseline clinical characteristics of patients with psoriasis.

Clinical characteristic	Number/mean value	Percentage (%)/ SD
General		
Reimbursed, <i>n</i> (%)	121	90
Age (years)	46.46	13.32
Male sex, <i>n</i> (%)	105	78
BW (kg)	79.37	16.81
BMI	27.95	5.18
Smoking, <i>n</i> (%)	58	44
Alcohol drinking, <i>n</i> (%)	48	36
Disease characteristics		
PASI at baseline	16.23	7.87
Disease duration (years)	17.41	9.52
Family history of psoriasis, <i>n</i> (%)	38	28
Presence of psoriatic arthritis, <i>n</i> (%)	50	37
Comorbidities, <i>n</i> (%)		
HTN	47	35
DM	24	18
CVD	8	6
Previous treatment of psoriasis		
Traditional systemic medications, <sup>a</sup> <i>n</i> (%)	121	90
Phototherapy, <i>n</i> (%)	126	93
Number of previous biologic <sup>b</sup> use	1.17	1.18
Biologic <sup>b</sup> naïve, <i>n</i> (%)	40	30
1 biologic used, <i>n</i> (%)	62	46
TNF- $\alpha$ inhibitor <sup>b</sup> exposure only	3	5
IL-12/23 inhibitor <sup>b</sup> exposure only	49	82
IL-17 inhibitor <sup>b</sup> exposure only	8	13
$\geq 2$ biologics used, <i>n</i> (%)	33	24
TNF- $\alpha$ inhibitor <sup>b</sup> used, <i>n</i> (%)	28	21
IL-12/23 inhibitor <sup>b</sup> used, <i>n</i> (%)	78	58
IL-17 inhibitor <sup>b</sup> used, <i>n</i> (%)	33	24
IL-23 inhibitor <sup>b</sup> used, <i>n</i> (%)	1	1
BMI, body mass index; BW, body weight; CVD, cardiovascular disease; DM, diabetes mellitus; HTN, hypertension; IL, interleukin; <i>n</i> , number; PASI, Psoriasis Area Severity Index; SD, standard deviation; TNF- $\alpha$ , tumour necrosis factor- $\alpha$ . <sup>a</sup> Traditional systemic medications in the study include methotrexate, cyclosporine, and acitretin. <sup>b</sup> Biologics included in the study: TNF- $\alpha$ inhibitor (etanercept and adalimumab), IL-12/23 inhibitor (ustekinumab), IL-17 inhibitor (secukinumab and ixekizumab), and IL-23 inhibitor (risankizumab).		



**Figure 1.** Effectiveness of guselkumab in psoriatic patients on achievement of PASI 75 and 90 responses over 36 weeks. The proportion (%) of patients treated with guselkumab in achieving PASI 75 and 90 responses is presented for each time point. PASI, Psoriasis Area and Severity Index.

## Discussion

This is a real-world retrospective cohort study that analysed clinical predictors of the efficacy of guselkumab in the Asian population. We identified prior exposure to biologics and the number of previously used biologics as predictors for poor PASI 75 response. Patients with lower weight achieved PASI 75 more quickly at week 4, but the impact of weight on the effectiveness of guselkumab remained unchanged during the following treatment course.

Guselkumab has been more effective than adalimumab, ustekinumab, and secukinumab in various clinical trials.<sup>3,5,20,21</sup> Post hoc analyses of these clinical trials showed that the advantage of guselkumab over placebo, adalimumab, and secukinumab was maintained regardless of the baseline disease characteristics, demographic characteristics, and previous psoriasis treatments.<sup>3,19,22</sup> In VOYAGE 1 trial, 73.3%, 80.2%, and 76.3% of patients treated with guselkumab achieved PASI 90 at weeks 16, 24, and 48, respectively.<sup>2</sup> Compared with VOYAGE 1 trial, patients in this study seemed to have a less effective response, which might be explained by their race and by the higher percentage of patients previously treated with multiple regimens. Real-life studies on the use of guselkumab in the treatment

of psoriasis are relatively few compared with those of other biologics. These studies are mostly short-term, have small population sizes, and comprise non-Asian populations.<sup>8,15–19,21</sup> PASI 75 and PASI 90 responses to guselkumab in two short-term (16 weeks) multicentre real-life studies showed that 82.1% and 72.2% of patients achieved PASI 75, whereas 55.4% and 50.6% achieved PASI 90 at week 16.<sup>8,15</sup> Our patients responded to guselkumab even worse compared with those in other real-life studies. The reimbursed patients in this study, who experienced treatment failure with at least 3 months of phototherapy and two types of traditional systemic medications, were recalcitrant towards treatment.<sup>6</sup> Most of them had also experienced biological failures. Furthermore, the effectiveness of guselkumab remained consistent among patients with a higher BW or patients who were treated with or had experienced failure with other biologics in some real-life experiences.<sup>15,16,19,21</sup> Predictors of a PASI response to guselkumab available from real-life studies are relatively lacking and inconsistent.<sup>15–18</sup>

The efficacy of biologics was lower in patients with higher BW, which might be due to the increased volume of drug distribution and low level of drug concentration.<sup>23</sup> The efficacy was

**Table 2.** Univariate analysis of the predictors for PASI 75 response.

General	Week 4			Week 12			Week 20			Week 28			Week 36		
	PASI75 n (%)	Non-PASI75 n (%)	OR (95% CI)	PASI75 n (%)	Non-PASI75 n (%)	OR (95% CI)	PASI75 n (%)	Non-PASI75 n (%)	OR (95% CI)	PASI75 n (%)	Non-PASI75 n (%)	OR (95% CI)	PASI75 n (%)	Non-PASI75 n (%)	OR (95% CI)
Age (years)	49.42 ± 13.77	45.3 ± 13.07	1.02 (0.99–1.07)	46.64 ± 13.15	46.37 ± 13.36	1.00 (0.98–1.03)	46.63 ± 13.57	46.98 ± 13.20	1.00 (0.97–1.03)	45.48 ± 13.76	45.08 ± 10.88	1.00 (0.97–1.04)	45.40 ± 13.72	42.86 ± 12.49	1.01 (0.98–1.06)
Sex (M), n (%)	13 (68.42)	86 (79.63)	0.55 (0.19–1.73)	53 (76.81)	46 (76.67)	1.01 (0.44–2.29)	57 (76.00)	34 (80.95)	0.75 (0.28–1.85)	45 (72.58)	17 (70.83)	1.09 (0.37–3.03)	31 (68.89)	16 (72.73)	0.83 (0.25–2.51)
BW (kg)	69.42 ± 12.65	81.31 ± 17.06	0.95 (0.91–0.98)	76.99 ± 15.45	82.92 ± 17.92	0.98 (0.96–1.00)	78.67 ± 15.31	80.67 ± 19.46	0.99 (0.97–1.02)	78.53 ± 15.30	83.92 ± 18.87	0.98 (0.95–1.01)	80.14 ± 14.75	85.91 ± 19.39	0.98 (0.95–1.01)
Smoking, n (%)	8 (42.11)	46 (42.59)	0.95 (0.34–2.53)	31 (44.93)	23 (39.66)	1.24 (0.61–2.54)	32 (42.67)	16 (38.10)	1.27 (0.59–2.79)	25 (40.98)	9 (37.50)	1.16 (0.44–3.14)	20 (31.82)	7 (45.45)	1.79 (0.62–5.47)
Alcohol drinking, n (%)	4 (21.05)	43 (39.81)	0.39 (0.11–0.14)	25 (36.23)	20 (34.48)	1.08 (0.52–2.26)	20 (27.40)	17 (40.48)	0.55 (0.25–1.24)	18 (29.51)	9 (37.50)	0.70 (0.26–1.93)	12 (27.27)	9 (40.91)	0.54 (0.18–1.61)
Disease characteristics															
Duration of PsO (years)	18.39 ± 12.26	17.15 ± 9.06	1.01 (0.96–1.07)	17.18 ± 9.50	18.02 ± 9.32	0.99 (0.95–1.03)	17.48 ± 9.48	18.26 ± 10.16	0.99 (0.95–1.03)	18.48 ± 10.42	17.67 ± 7.87	1.01 (0.96–1.06)	18.42 ± 10.42	18.91 ± 8.94	0.99 (0.94–1.05)
Family history of PsO, n (%)	12 (63.16)	25 (23.15)	5.62 (2.04–16.60)	22 (32.35)	16 (26.67)	1.32 (0.61–2.86)	20 (27.03)	10 (23.81)	1.19 (0.50–2.93)	19 (31.15)	7 (29.17)	1.10 (0.40–3.24)	15 (34.09)	6 (27.27)	1.38 (0.46–4.50)
PsA, n (%)	8 (42.11)	37 (34.26)	1.40 (0.50–3.75)	24 (41.67)	25 (34.78)	0.75 (0.36–1.52)	30 (40.00)	16 (38.10)	1.08 (0.50–2.38)	24 (38.71)	14 (58.33)	0.45 (0.17–1.17)	21 (46.67)	11 (50.00)	0.88 (0.31–2.44)
Baseline PASI	16.36 ± 8.71	16.44 ± 7.90	1.00 (0.93–1.06)	16.92 ± 8.49	15.42 ± 7.26	1.02 (0.98–1.07)	16.91 ± 8.90	14.66 ± 6.14	1.04 (0.99–1.10)	17.26 ± 9.11	16.19 ± 7.05	1.02 (0.96–1.08)	18.02 ± 9.22	16.45 ± 7.38	1.02 (0.96–1.09)
Comorbidities, n (%)															
HTN	6 (31.58)	36 (33.33)	0.92 (0.30–2.55)	22 (31.88)	22 (36.67)	0.81 (0.39–1.68)	27 (36.00)	14 (33.33)	1.12 (0.51–2.53)	24 (38.71)	8 (33.33)	1.26 (0.48–3.53)	20 (44.44)	5 (22.73)	2.72 (0.90–9.44)
DM	5 (26.32)	13 (12.04)	2.61 (0.75–8.17)	10 (14.49)	12 (20.00)	0.68 (0.26–1.70)	11 (14.67)	10 (23.81)	0.55 (0.21–1.45)	13 (20.97)	5 (20.83)	1.01 (0.33–3.49)	8 (17.78)	2 (9.10)	2.14 (0.48–15.25)
CVD	2 (10.53)	4 (3.70)	3.06 (0.40–16.99)	2 (2.90)	5 (8.33)	0.33 (0.05–1.59)	4 (5.33)	4 (9.52)	0.54 (0.12–2.38)	5 (6.06)	2 (8.33)	0.96 (0.19–7.08)	3 (6.67)	2 (9.10)	0.71 (0.11–5.75)

(Continued)

**Table 2.** (Continued)

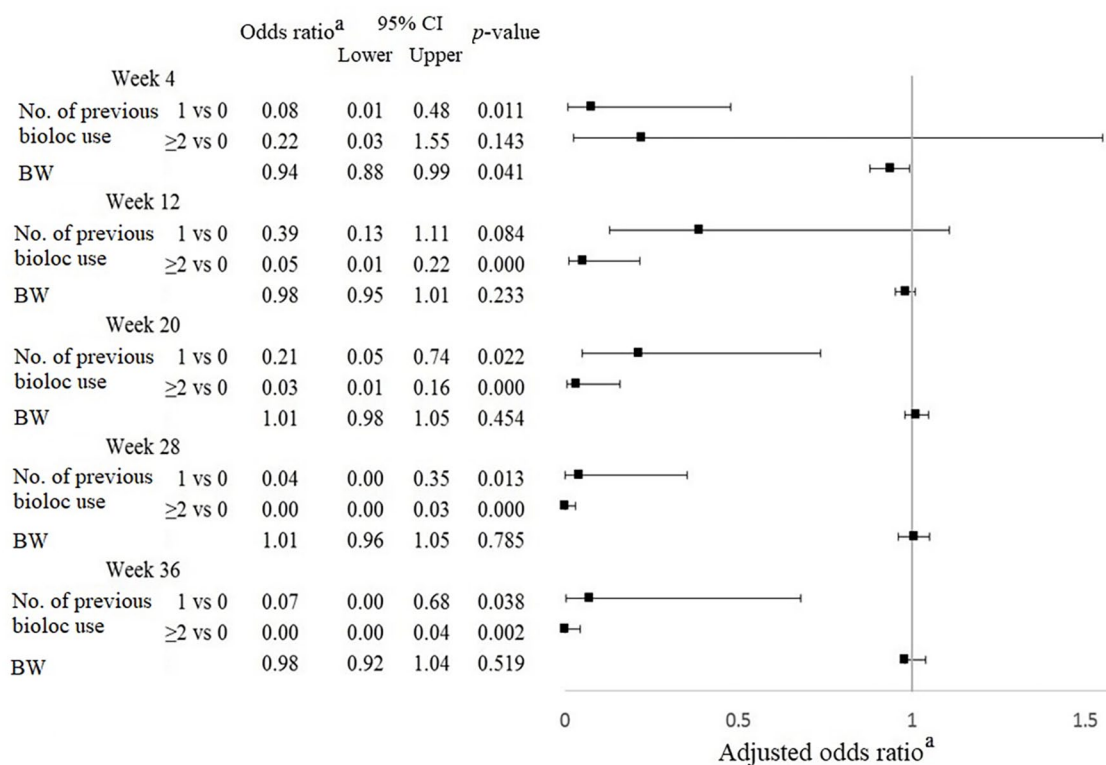
General	Week 4			Week 12			Week 20			Week 28			Week 36		
	PASI75 n (%) / mean ± SD	Non-PASI75 n (%) / mean ± SD	OR <sup>a</sup> (95% CI)	PASI75 n (%) / mean ± SD	Non-PASI75 n (%) / mean ± SD	OR <sup>a</sup> (95% CI)	PASI75 n (%) / mean ± SD	Non-PASI75 n (%) / mean ± SD	OR <sup>a</sup> (95% CI)	PASI75 n (%) / mean ± SD	Non-PASI75 n (%) / mean ± SD	OR <sup>a</sup> (95% CI)	PASI75 n (%) / mean ± SD	Non-PASI75 n (%) / mean ± SD	OR <sup>a</sup> (95% CI)
Previous PsO treatment, n (%)															
Traditional systemic medications <sup>b</sup>	15 (78.95)	99 (91.67)	0.34 (0.10–1.38)	60 (86.9%)	55 (91.67)	0.22 (0.05–0.77)	65 (88.00)	39 (92.86)	0.56 (0.12–1.99)	52 (83.87)	23 (95.83)	0.26 (0.05–1.27)	39 (86.67)	21 (95.45)	0.31 (0.02–1.98)
Previous biologic <sup>c</sup> use	10 (52.63)	81 (75.00)	0.37 (0.14–1.02)	41 (59.42)	51 (85.00)	0.26 (0.10–0.59)	47 (62.67)	37 (88.10)	0.23 (0.07–0.60)	36 (58.06)	23 (95.83)	0.06 (0.00–0.31)	24 (53.33)	20 (90.91)	0.11 (0.02–0.45)
1 previously used biologic <sup>c</sup>	6 (31.58)	54 (50.00)	0.33 (0.10–1.02)	34 (49.28)	26 (43.33)	0.42 (0.16–1.02)	37 (49.33)	20 (47.62)	0.33 (0.10–0.93)	26 (41.94)	11 (45.83)	0.09 (0.00–0.52)	16 (35.56)	8 (36.36)	0.19 (0.03–0.89)
≥ 2 previously used biologics <sup>c</sup>	4 (21.05)	27 (25.00)	0.44 (0.11–1.54)	7 (10.14)	25 (41.67)	0.09 (0.03–0.26)	10 (10.14)	17 (40.48)	0.11 (0.03–0.34)	10 (16.13)	12 (50.00)	0.03 (0.00–0.19)	8 (17.78)	12 (54.55)	0.06 (0.01–0.30)

BW, body weight; CI, confidence interval; CVD, cardiovascular disease; DM, diabetes mellitus; F, female; HTN, hypertension; IL, interleukin; M, male; n, number; OR, odds ratio; PsA, psoriatic arthritis; PsO, psoriasis; PASI, Psoriasis Area Severity Index; SD, standard deviation; TNF- $\alpha$ , tumour necrosis factor- $\alpha$ .

<sup>a</sup>OR for achieving PASI 75.

<sup>b</sup>Traditional systemic medications in the study included methotrexate, cyclosporine, and acitretin.

<sup>c</sup>Biologics in the study included TNF- $\alpha$  inhibitor (etanercept and adalimumab), IL-12/23 inhibitor (ustekinumab), IL-17 inhibitor (secukinumab and ixekizumab), and IL-23 inhibitor (risankizumab).



**Figure 2.** PASI-75 responder rates in patients with different number of prior biologic use compared with biologic-naïve patients and patients with different body weight after multivariate analysis over 36 weeks. BW, body weight; CI, confidence interval; No., number; PASI, Psoriasis Area and Severity Index.

<sup>a</sup>Odds ratio of achieving PASI 75 after multivariate analysis adjusted for confounding variables including age, sex, smoking, alcohol drinking, duration of psoriasis, traditional systemic medications, family history of psoriasis, hypertension, diabetes mellitus, cardiovascular disease, psoriatic arthritis, baseline PASI, BW, and previous biologic use.

maintained in weight-based dosage of biologics such as infliximab, even with increasing weight.<sup>24–26</sup> However, fixed-dosed biologics may have compromised efficacy in individuals with higher BW.<sup>24–26</sup> Therefore, it is necessary to evaluate the impact of weight on the efficacy of biologics. Guselkumab was not administered according to a weight-based dosage, and pooling data from VOYAGE 1 and VOYAGE 2 demonstrated consistent efficacy of guselkumab compared with placebo at weeks 16 and 24 across all weight quartiles, especially those weighing  $\geq 100$  kg.<sup>19</sup> However, real-life data on the effectiveness of anti-IL-23 biologics (guselkumab, risankizumab, or tildrakizumab) for patients with higher BW are very scarce. In a retrospective study enrolling 52 patients with psoriasis treated with guselkumab for up to 1 year, the presence of comorbidities, including hypertension, obesity, diabetes mellitus, dyslipidaemia, and psychiatric disorders, emerged as a predictor of reduced response in both univariate and multivariate

analyses.<sup>16</sup> Nevertheless, obesity *per se* was not associated with lower response.<sup>16</sup> Lower PASI 75 response in our patients with higher BW was only shown at week 4, and this effect was not observed during the following period. BW is a robust predictor of biologic response in a real-life setting of etanercept, adalimumab, infliximab, golimumab, secukinumab, and ustekinumab administration.<sup>13,24,27–33</sup> In one systematic review and meta-analysis, pooled analysis showed that obesity is a contributing predictor of biologic discontinuation due to the overall causes, including side effects and ineffectiveness.<sup>30</sup> Although dose adjustment of guselkumab based on BW was not recommended according to pharmacokinetic modelling,<sup>34</sup> a delayed onset of therapeutic response to guselkumab was noted in patients with higher BW.

Biologic switch due to efficacy failure, side effects, convenience, or insurance is frequent in the treatment of psoriasis in clinical practice.<sup>35</sup> In the



**Table 3.** Association of different classes of previously used biologics with PASI 75 response.

Week	Previous biologic use	OR <sup>a</sup> (95% CI)	p value
Week 12	Biologic <sup>b</sup> naïve	1.00	
	TNF- $\alpha$ inhibitor	0.62 (0.05–14.27)	0.710
	IL-17 inhibitor	0.19 (0.03–0.90)	0.041
	IL-12/23 inhibitor	0.42 (0.16–1.06)	0.071
Week 20	Biologic <sup>b</sup> naïve	1.00	
	TNF- $\alpha$ inhibitor	0.17 (0.01–4.83)	0.240
	IL-17 inhibitor	0.10 (0.02–0.55)	0.010
	IL-12/23 inhibitor	0.39 (0.12–1.17)	0.109
Week 28	Biologic <sup>b</sup> naïve	1.00	
	TNF- $\alpha$ inhibitor	0.08 (0.00–2.42)	0.107
	IL-17 inhibitor	0.03 (0.00–0.29)	0.007
	IL-12/23 inhibitor	0.12 (0.01–0.75)	0.056

CI, confidence interval; IL, interleukin; OR, odds ratio; PASI, Psoriasis Area and Severity Index; TNF- $\alpha$ , tumour necrosis factor- $\alpha$ .

<sup>a</sup>Univariate analysis.

<sup>b</sup>Biologics included in the study: TNF- $\alpha$  inhibitor (etanercept and adalimumab), IL-12/23 inhibitor (ustekinumab), IL-17 inhibitor (secukinumab and ixekizumab), and IL-23 inhibitor (risankizumab).

NAVIGATE trial, switching to guselkumab is effective in patients who failed to achieve a high level of response with ustekinumab.<sup>5,36</sup> Although the association between the number of prior biologic use and a decreased response rate to biologics had been observed in some real-life studies,<sup>6,16</sup> real-world data on the impact of biologic switch on the effectiveness of guselkumab are relatively lacking. Moreover, the population was limited to a small-scale and the Western population.<sup>15–18</sup> The patients previously treated with biologics in this study were less likely to achieve PASI 75 than biologic-naïve patients. Furthermore, lower PASI 75 response rate to guselkumab was noted as the number of previous biologics used increased.

Large-scale studies are required to determine whether the prior use of biologics with a different MOA contributes to varying treatment responses to guselkumab. Although guselkumab was effective in patients who previously experienced failure with IL-17 inhibitors or ustekinumab<sup>17,18</sup> and since switching from TNF- $\alpha$  inhibitors to IL-23 inhibitors still remained effective in real-world studies,<sup>35</sup>

the efficacy of guselkumab switching from biologics with a different MOA was not investigated. The patients in our study who used IL-17 inhibitors prior to guselkumab were less likely to achieve PASI 75 than biologic-naïve patients; nevertheless, similar results were not found in patients who used ustekinumab or TNF inhibitors previously.

This study was one of the few real-world studies that evaluated the effectiveness and predictors for clinical response to guselkumab, particularly including a switch from anti-IL-17 to anti-IL-23 biologics. There were some limitations in this study. First, patients were not treated at the same time and were not randomised or blinded due to the retrospective design of the study. Next, the study included a small percentage of non-reimbursed patients who did not fail or were not intolerant to systemic treatment or phototherapy. As the quality-of-life modulators (i.e. pruritus)<sup>37</sup> and multiple exposures capable to modulate the inflammation (i.e. diet and circadian rhythm)<sup>38,39</sup> were not accounted in this real-world evaluation, further real-world data are needed to clarify them.

## Conclusion

In this real-life study, the effectiveness of guselkumab was lower in patients with moderate-to-severe chronic plaque psoriasis treated for over 36 weeks than that reported in other RCTs and real-world studies. Predictors for a reduced clinical response to guselkumab include BW as well as the number and classes of biologics used. BW only influences the effectiveness in the early phase of treatment, suggesting delayed onset of a therapeutic effect in patients with higher BW. Patients who had a switch from anti-IL-17 showed a worse response than those who switched from other classes of biologics.

## Author contributions

Dr Huang had full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. Y-TH, Y-JL, H-YC, and Y-HH were involved in concept and design; Y-TH, Y-JL, H-YC, and Y-HH were involved in acquisition, analysis, or interpretation of data; Y-TH and Y-HH were involved in drafting of the manuscript; Y-TH, H-YC, and Y-HH were involved in critical revision of the manuscript for important intellectual content; Y-TH, Y-JL, H-YC, and Y-HH were involved in statistical analysis; Y-HH obtained funding; H-YC and Y-HH provided administrative, technical, or material support; H-YC and Y-HH were involved in supervision. All authors read and approved the final manuscript.

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## Conflict of interest statement

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: All authors have completed the ICMJE uniform disclosure form available at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf), and they declare the following: Y-HH has conducted clinical trials or received honoraria as a consultant and speaker for Abbvie, Celgene, Janssen-Cilag, Novartis, and Pfizer Pharmaceuticals. H-YC received speaking fees from Abbvie, Novartis, Janssen-Cilag, Eli-Lilly,

Kyowa Hakko Kirin Taiwan, and Pfizer limited and conducted clinical trials for Eli-Lilly and Sanofi Pharmaceuticals. Y-TH and Y-JL declare that they have no conflict of interest.

## ORCID iDs

Yi-Teng Hung  <https://orcid.org/0000-0003-1759-7790>

Hsien-Yi Chiu  <https://orcid.org/0000-0002-0493-9707>

Yu-Huei Huang  <https://orcid.org/0000-0003-0574-1839>

## Supplemental material

Supplemental material for this article is available online.

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