EFFICACY AND SAFETY OF GUSELKUMAB IN THE TREATMENT OF PLAQUE PSORIASIS

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ABSTRACT

Objectives: To evaluate the efficacy and safety of guselkumab in the treatment of patients with moderate to severe plaque psoriasis.

Materials and methods: A clinical trial was conducted on 32 patients with moderate to severe psoriasis. Patients received subcutaneous injections of guselkumab 100 mg at weeks 0, 4, 12, and 20. Treatment response was evaluated using PASI (Psoriasis Area and Severity Index) and DLQI (Dermatology Life Quality Index). Adverse events were recorded throughout the 20 weeks treatment period.

Results: After 20 weeks of treatment, both PASI and DLQI scores showed a statistically significant reduction. PASI75 and PASI90 response rates were significantly increased from week 4, immediately following the first dose, reaching 93.8% and 71.9%, respectively, at week 20. PASI100 responses were first observed at week 12 and reached 15.6% by week 20. No adverse events were reported in the study population.

Conclusions: Guselkumab demonstrates high efficacy with marginal side effects in the treatment of moderate to severe plaque psoriasis.

Keywords: *Psoriasis, biologics, guselkumab, IL-23 inhibitor.*

INTRODUCTION

Psoriasis is a common dermatological disorder and among the most extensively investigated diseases in dermatology. It exerts a substantial impact on patients' outlook, daily functioning, and overall quality of life. According to data from the United States in 2020, approximately 7.55 million adults (aged ≥ 20 years) were affected by psoriasis, accounting for approximately 3% of the population. In Vietnam, the prevalence is estimated at about 2 million individuals, corresponding to 2 - 3% of the population. The pathogenesis of psoriasis is driven by the interplay of genetic predisposition, immune dysregulation, and environmental triggers. Among these, immune dysfunction involving cutaneous T lymphocytes such as Th17 cells stimulated by IL-23 is fundamental. These cells secrete key pro-inflammatory cytokines, including IL-17, TNF-α, IL-6, and IL-22, which are central mediators in the disease pathogenesis.[3,4]

The treatment of psoriasis depends on the severity of the disease. Conventional systemic

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agents, such as methotrexate, acitretin, and cyclosporine A, have been utilized for decades. Their efficacy is influenced by multiple factors, and numerous adverse effects have been documented.[4,5] Biologic therapies, which are monoclonal antibodies, have been investigated in recent years and have demonstrated both efficacy and safety in the treatment of psoriasis. The biologic agents currently approved for psoriasis include tumor necrosis factor-alpha (TNF-α) inhibitors, interleukin-17 (IL-17) inhibitors, interleukin-12/23 (IL-12/IL-23) inhibitors, interleukin-23 (IL-23) inhibitors, and, more recently, small-molecule Janus kinase (JAK) inhibitors. Among these, guselkumab - an IL-23 inhibitor was approved by the U.S. Food and Drug Administration (FDA) for the treatment of moderate to severe plaque psoriasis in 2017. Published studies have demonstrated its superior efficacy and safety compared to conventional systemic therapies and other biologic agents. In 2022, guselkumab was officially approved for the treatment of psoriasis in Vietnam. In the present study, we evaluated the efficacy and safety of guselkumab in patients with moderate-to-severe plaque psoriasis in a real-world setting at National Hospital of Dermatology and Venereology.

MATERIALS AND METHODS

Study population

The study enrolled 32 adult patients diagnosed with moderate to severe plaque psoriasis at the National Hospital of Dermatology and Venereology between January 2023 and June 2024. Eligibility required a definitive diagnosis of plaque psoriasis with disease severity categorized as moderate to severe. Patients were excluded if they had contraindications to guselkumab, including known hypersensitivity to the drug, ongoing active infections (such as bacterial infections or tuberculosis), pregnancy, or lactation.

Study design

A single-arm clinical trial was conducted. Patients who met the eligibility criteria and presented to the National Hospital of Dermatology and Venereology between January 2023 and June 2024 were enrolled in the study. All participants provided written informed consent. Patients received guselkumab 100 mg administered subcutaneously at weeks 0, 4, and every 8 weeks thereafter. The study drug, Tremfya® (guselkumab 100 mg solution in a prefilled pen), had been approved by the Ministry of Health of Vietnam. Clinical assessments were performed at weeks 0, 4, 12, and 20. Efficacy was evaluated using the Psoriasis Area and Severity Index (PASI) and the Dermatology Life Quality Index (DLQI). Safety was assessed by recording any adverse events observed during the 20-week study period.

Data analysis

Data were encoded and analyzed using SPSS software, version 20.0. Descriptive statistics and frequency distributions were calculated. For comparisons of quantitative variables, Student's t-test was applied to normally distributed data, while the Mann-Whitney U test was used for non-normally distributed data. Categorical variables were compared using the Chi-square test, or Fisher's exact test when ≥ 20% of the expected frequencies were less than 5.

Ethical approval

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of the National Hospital of Dermatology and Venereology.

RESULTS

Baseline characteristics of study participants

Table 1. Baseline characteristics of study participants (N = 32)

Characteristics		
Age	45 ± 14 (18 - 69)	
Sex	Male	20 (68.7%)
	Female	12 (31.3%)
		*p = 0.034**
Duration of disease (years)	12.5 ± 7.8 (1 - 29)	
Family history of psoriasis (present)	4 (12.5%)	
Previously treated with topical therapy	32 (100%)	
Previously treated with MTX	13 (40.6%)	
Previously treated with acitretin	5 (15.6%)	
Previously treated with cyclosporin A	0 (0%)	
Previously treated with phototherapy	7 (21.8%)	
Previously treated with biologics	15 (46.8%)	
	TNF inhibitor	2 (6.3%)
	IL17 inhibitor	10 (31.3%)
	IL12/23 inhibitor	5 (15.6%)
HBsAg	Positive	2 (6.3%)
	Negative	30 (100%)
Quantiferon or IGRA (latent tuberculosis)	Positive	3 (9.4%)
	Unknown	1 (3.1%)
	Negative	28 (87.5%)
Anti-HCV	Positive	0
	Negative	32 (100%)
PASI score	14.8 ± 7.5 (4.6 - 32.2)	
	Mild	11 (35.4%)
	Moderate	10 (31.2%)
	Severe	11 (34.4%)
DLQI score	14.5 ± 6.6 (4 - 28)	
	Greatly affected	25 (78.1%)
	Extremly affected	7 (21.9%)

** Chi-square test.*

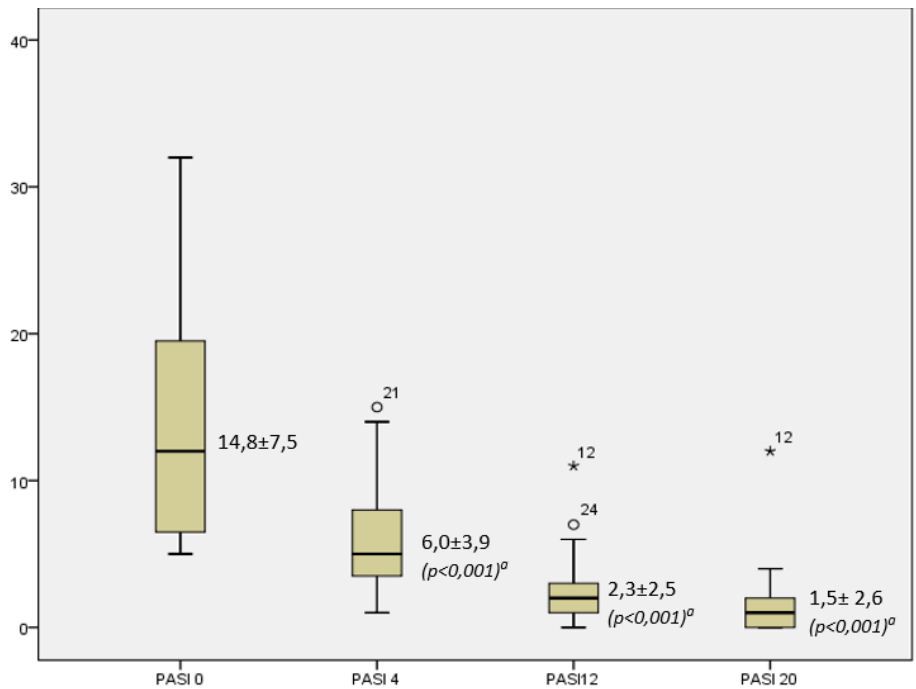
The study was conducted on 32 adult patients with a mean age of 45 ± 14 years, with males outnumbering females. The disease duration ranged from 1 to 29 years. Three patients were diagnosed

with latent tuberculosis (positive Quantiferon test), and two patients tested positive for HBsAg. None of the patients were positive for HIV or hepatitis C. A family history of psoriasis was recorded in 4 patients (12.5%).

All patients had previously received topical therapy (100%), while the most commonly used systemic agent was methotrexate (40.6%). Only five patients had been treated with acitretin, and none had received cyclosporine A. Notably, 46.8% of patients had been treated with at least one class of biologic agents, with IL-17 inhibitors being the most frequent (31.3%).

Regarding disease severity at baseline, the mean PASI score was 14.8 ± 7.5. Severe psoriasis accounted for 34.4%, moderate disease for 31.2%, while patients with PASI < 10 represented 34.4%, comparable to the severe group. The baseline DLQI score was 14.5 ± 6.6, indicating a substantial or very substantial impact on patients' quality of life.

Changes in PASI score over 20 weeks



aT-Test.

Figure 1. Changes in PASI score over 20 weeks (N = 32)

PASI scores demonstrated a progressive decline over the 20 weeks treatment period, with statistical significance observed from the first administration ($p < 0.001$; 99% confidence). A marked reduction was evident by week 4 (6.0 ± 3.9), and the improvement remained statistically significant through week 20 (1.5 ± 2.6).

Response over time according to PASI 50, PASI 75, PASI 90, and PASI 100 responses

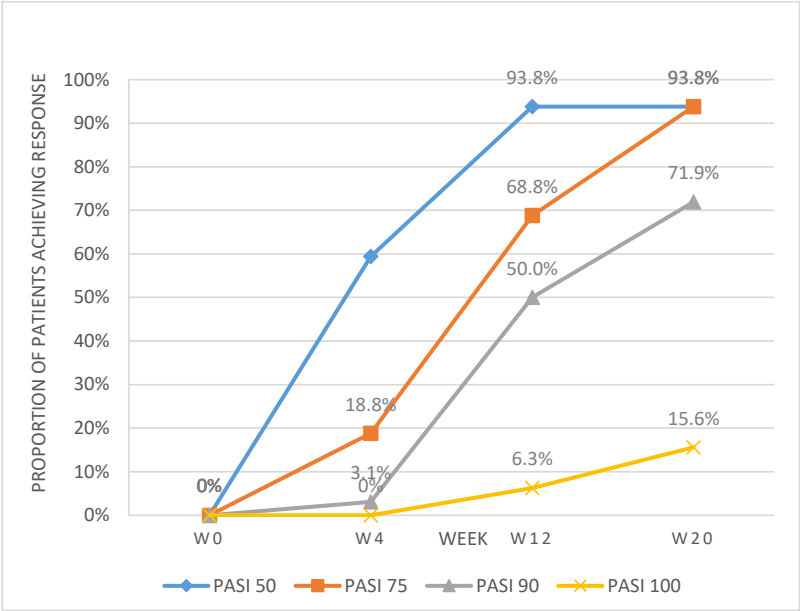


Figure 2. Response over time in achieving PASI 50, PASI 75, PASI 90, and PASI 100 (N = 32)

Treatment responses began to emerge at week 4, immediately after the first injection, with 59.4% of patients achieving PASI50, 18.8% achieving PASI75, and 3.1% achieving PASI90. The proportion of patients achieving PASI50 increased rapidly, reaching 93.8% by week 12 and remaining stable through week 20. PASI75 and PASI90 responses continued to rise, reaching 93.8% and 68.8%, respectively, at week 20. For PASI100, the first responses were observed at week 12, with 15.6% of patients achieving complete clearance.

Response in the subgroup of patients with a history of prior biologic therapy

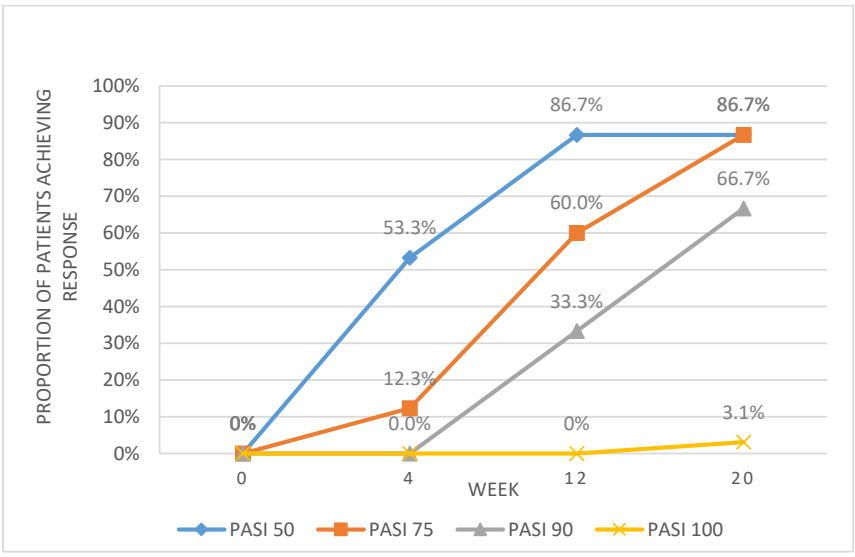


Figure 3. Response in the subgroup of patients with a history of prior biologic therapy (N = 32)

In the subgroup of patients who had previously received at least one biologic agent before switching to guselkumab, the proportions achieving PASI75 and PASI90 increased steadily from the first injection through week 20, reaching 86.7% and 66.7%, respectively. The proportion of patients achieving PASI100 remained low, at 3.1% after 20 weeks.

Changes in DLQI scores over 20 weeks of treatment

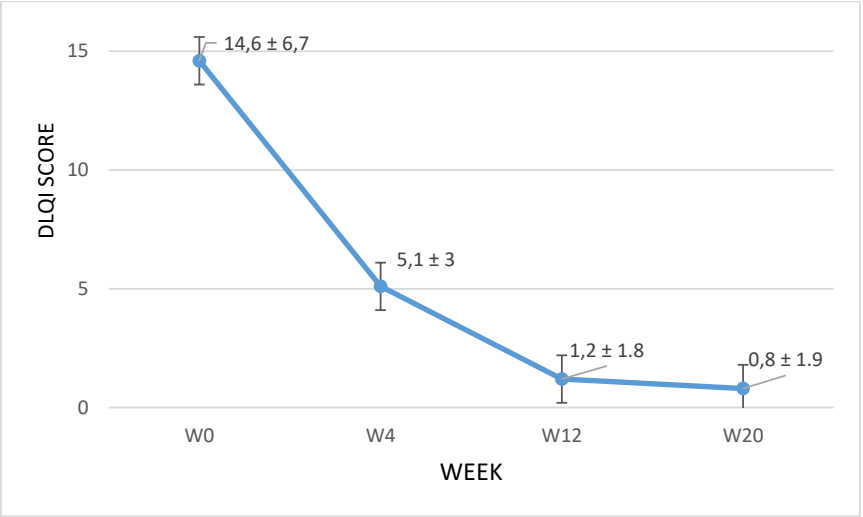


Figure 4. Changes in DLQI scores over 20 weeks of treatment (N = 32)

The change in DLQI scores demonstrated a marked improvement in patients' quality of life throughout the 20-week treatment period. A statistically significant reduction in DLQI was observed from week 4 onward ($p < 0.001$, 99% confidence level). By weeks 12 and 20, mean DLQI scores had decreased to 1.2 and 0.8, respectively. After 20 weeks, the majority of patients reported no impact of the disease on their quality of life.

Safety profile of guselkumab in the treatment of patients with plaque psoriasis.

Table 2. Adverse events (N = 32)

Event Name	n	%
Upper respiratory tract infection	0	0
Nasopharyngitis	0	0
Injection-site erythema	0	0

No adverse events were observed during guselkumab treatment.

DISCUSSION

Guselkumab is a biologic agent that selectively inhibits IL-23, an interleukin shown to play a central role in the pathogenesis of psoriasis. In July 2017, the U.S. Food and Drug Administration (FDA) approved Tremfya (guselkumab) for the treatment of adults with moderate-to-severe plaque psoriasis[6]. Our study, conducted on 32 patients with plaque psoriasis, showed a mean baseline PASI score of 14.8 ± 7.5.

Among them, 65.6% had moderate-to-severe disease (34.4% severe and 31.2% moderate), while 34.4% of patients had a PASI score < 10. The baseline PASI in our cohort was lower compared with several clinical trials,[7, 8] This can be explained by the relatively high proportion of patients in our cohort who had previously received biologic or other systemic therapies, resulting in less severe skin involvement. On the other hand, it highlights that psoriasis significantly impacts quality of life even with milder skin lesions, and that patients in our study cohort had higher expectations for complete skin clearance when treated with biologic therapy.

Clinical outcomes during the first 20 weeks showed a statistically significant gradual reduction in PASI scores from baseline to week 20, and a statistically significant decrease in DLQI scores from week 4, immediately after the first injection. The highest proportion of patients achieving PASI 50 was observed at week 12, and this response was maintained through week 20 at 93.8%. The proportion of patients achieving PASI 75 increased steadily from week 4, reaching 68.8% at week 12 and 93.8% at week 20. These results are comparable to findings reported in the VOYAGE 1 and 2 trials, as well as several real-world studies worldwide, which demonstrated high rates of PASI 75 and PASI 90 responses from week 12 onward.[9] Meanwhile, the proportion of patients achieving PASI 90 continued to increase through week 20, reaching 71.9%, which is comparable to the results from the study involving 880 patients conducted by K. Schäke.[10] PASI 100 was observed at week 12 in 6.3% of patients and gradually increased to 15.6% by week 20, which is lower than the 39.4% at week 20 reported in the study by K. Schäke. The difference in PASI 100 responses may be attributed to the longer disease duration in our cohort (mean 12.5 years), which is a potential factor affecting PASI 100 achievement in patients with psoriasis.[10]

Fifteen out of 32 patients in our study had previously received other biologic therapies before switching to guselkumab; this subgroup had experienced either biologic treatment failure or had not achieved the desired PASI response. Upon switching to guselkumab, the rates of achieving PASI 75 and PASI 90 were 86.7% and 66.7%, respectively. These rates are higher compared with the study by Matteo et al. on patients switching from ustekinumab to guselkumab, as well as the VOYAGE 2 study in patients switching from adalimumab to guselkumab.[11,8] These findings indicate that guselkumab can achieve relatively high PASI 75 and PASI 90 responses in patients who have previously failed other biologic therapies. Longer-term data are needed to evaluate the durability of response in this patient population.

During the 20-week follow-up period, no adverse events were observed in the 32 patients included in our study, which is lower than reported in some clinical trials of guselkumab. However, other long-term studies worldwide, with follow-up periods of 3 - 5 years, have also demonstrated the safety profile of guselkumab, with adverse events generally being mild and infrequent.[7,8,12] These findings indicate that guselkumab is commonly considered a safe therapy with minimal adverse events in Vietnamese patients. However, our study is limited by the small sample size and short follow-up duration, highlighting the need for larger-scale studies to further evaluate its safety and efficacy.

CONCLUSIONS

Guselkumab demonstrates an efficacious therapeutic option, achieving high levels of skin clearance with a favorable safety profile in patients with moderate-to-severe plaque psoriasis. Its efficacy and safety are consistent with previously published data.

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