Original Article

Comparison Of The Efficacy And Safety Of Secukinumab, Ustekinumab And Guselkumab For The Treatment Of Moderate To Severe Plaque Psoriasis: A Systematic Review

Gusti Ayu Dea Dwi Apriza Dharmayani[1], Ketut Kwartantaya Winaya[2]

[1]Medical Faculty, Udayana University, Bali, Indonesia. E-mail: deaapriza@gmail.com
[2]Dermatology and Venereology Department, Sanglah General Hospital, Bali, Indonesia. E-mail: kkwartantaya@yahoo.com
DOI: 10.47750/pnr.2023.14.02.62

Abstract

Psoriasis is a chronic inflammatory skin condition characterized by scaly erythematous patches or plaques affecting the extensor surfaces that are prominent but spreading to all areas of the body, including the flexor surfaces. Psoriasis occurs when the body's immune system attacks the skin; the interleukin (IL)-12 and IL-17/23 axes play a major role in its pathogenesis. Biologic therapies targeting IL-17 or IL-23 have emerged as an important treatment option for psoriasis and have led to substantial improvements in patients' quality of life. This systematic review aimed to evaluate the comparative efficacy and safety of secukinumab, ustekinumab and guselkumab for the treatment of moderate to severe plaque psoriasis. Based on the final analysis, there were 10 articles, namely 5 RCTs and 5 observational. We found that patients who were given secukinumab showed a rapid response, whereas guselkumab was superior in terms of long-term response (approximately 1 year) and complete remission compared to other biologics. Among all the biologics assessed, ustekinumab showed relatively low efficacy.

Keywords: Secukinumab, Ustekinumab, Guselkumab, Plaque Psoriasis.

INTRODUCTION

Psoriasis is a chronic inflammatory skin condition characterized by scaly erythematous patches or plaques affecting the extensor surfaces that are prominent but spreading to all areas of the body, including the flexor surfaces. Psoriasis occurs when the body's immune system attacks the skin; the interleukin (IL)-12 and IL-17/23 axes play a major role in its pathogenesis. Biologic therapies targeting IL-17 or IL-23 have emerged as an important treatment option for psoriasis and have led to substantial improvements in patients' quality of life due to their superior effect in reducing subjective disease burden compared to conventional therapy. Various biologic drugs are used for the treatment of psoriasis in clinical practice; including secukinumab (fully humanized anti-IL-17A IgG1κ monoclonal antibody), ixekizumab (humanized anti-IL-17A IgG4 monoclonal antibody), ustekinumab (humanized anti-IL-12/23 p40 subunit IgG1κ monoclonal antibody), guselkumab (fully humanized anti-IL-23 p19 subunit IgG1 monoclonal antibody) and risankizumab (fully humanized anti-IL-23 p19 subunit IgG1λ monoclonal antibody). Previous psoriasis studies evaluating the relative efficacy of biologics have concluded that biologics that target IL-17A, such as secukinumab and ixekizumab, show superior efficacy compared to IL-12/23 inhibitors, such as ustekinumab; however, the safety profiles of the two groups were found to be similar. The improved efficacy profile of IL-23 p19 inhibitors with IL-12/23 p40 inhibitors has also been confirmed with comparable safety results. Because psoriasis is a chronic and incurable disease, long-term response (approximately 1 year) and complete remission are more relevant (compared to short-term response) in real clinical practice. Therefore, we aimed to compare the efficacy and safety of three biologic drugs commonly used in the treatment of psoriasis (secukinumab, ustekinumab and guselkumab). [1]

METHOD

Literature Identification

A literature search was conducted on online databases, namely Pubmed, Science Direct, Google Scholar and Research Gate. The keywords used in the literature search were developed based on population, intervention, comparison and outcome (PICO)

criteria as shown in **Table 1.** The identified literature was then sorted to eliminate duplicates and filtered based on inclusion and exclusion criteria.

The last keyword used is:

"Secukinumab" and "ustekinumab" and "guselkumab" and "plaque psoriasis" and "efficacy", "secukinumab" and "ustekinumab" and "guselkumab" and "plaque psoriasis" and "safety", "secukinumab" and "ustekinumab" and "guselkumab" and "plaque psoriasis" and "moderate to severe", "secukinumab" and "ustekinumab" and "plaque psoriasis" and "efficacy", "secukinumab" and "ustekinumab" and "plaque psoriasis" and "safety", "secukinumab" and "ustekinumab" and "plaque psoriasis" and "moderate to severe", "ustekinumab" and "guselkumab" and "plaque psoriasis" and "efficacy", "ustekinumab" and "guselkumab" and "plaque psoriasis" and "safety", "ustekinumab" and "guselkumab" and "plaque psoriasis" and "moderate to severe", "guselkumab" and "secukinumab" and "plaque psoriasis" and "efficacy", "guselkumab" and "secukinumab" and "plaque psoriasis" and "safety", "guselkumab" and "secukinumab" and "plaque psoriasis" and "moderate to severe", "secukinumab" and "plaque psoriasis" and "efficacy", "secukinumab" and "plaque psoriasis" and "safety", "secukinumab" and "plaque psoriasis" and "moderate to severe", "ustekinumab" and "plaque psoriasis" and "efficacy", "ustekinumab" and "plaque psoriasis" and "safety", "ustekinumab" and "plaque psoriasis" and "moderate to severe", "guselkumab" and "plaque psoriasis" and "efficacy", "guselkumab" and "plaque psoriasis" and "safety", "guselkumab" and "plaque psoriasis" and "moderate to severe."

Table 1. PICO Criteria for Literature Identification

Population	Patients with Moderate to Severe Plaque Psoriasis
Intervention	Secukinumab and Ustekinumab and Guselkumab
Comparison	Secukinumab or Ustekinumab or Guselkumab
Result	Efficacy and Safety for the Treatment of Moderate to Severe Plaque Psoriasis

The search results were selected based on the eligibility for inclusion analysis which was based on the methodology used, the year of publication and the variables studied. Methodological criteria for inclusion were clinical trials or observational studies with interesting results in the treatment of moderate to severe plaque psoriasis, namely the efficacy and safety of the drug. Literature limitations with the treatment of specific psoriasis plaques with biologic therapy used as outcomes were identified in the initial search. The time frame used for inclusion criteria was set from 2012 to 2022. We excluded review articles from the analyses, but references from these articles were mined for further literature that might have been missed in the initial literature search. We also excluded case reports, case series and in vitro and in vivo studies that did not involve human subjects.

Quality Assessment

Prior to data extraction and analysis, articles that pass the screening will undergo a quality assessment. Quality assessment was carried out based on the CASP (Critical Appraisal Skills Programme) checklist for appropriate study designs used in each specific article. The quality assessment aims to review the validity of the methodology as well as the significance of the reported results prior to further extraction and analysis.

Data Extraction and Analysis

Articles that passed the quality assessment were then extracted for the variables of interest. The main variables of interest in this review are the efficacy found in each study as well as the reported safety of the drug. To characterize each study, we also extract information about the methodology and sample size. After that we analyzed the results by thematic analysis to synthesize the general theme of the results reported from this study to answer the research questions.

RESULT

Research Inclusion Characteristics

Based on the final analysis, it was found that 10 articles passed the screening and quality assessment. The articles used were 5 RCTs and 5 observational. The article with the largest sample size was 1102 patients and the newest article was in 2022, while the oldest article was in 2015. In the observational study, it was found that 4 articles had no comparisons used to see efficacy or safety comparisons, only judging from one drug, namely secukinumab or ustekinumab or guselkumab alone. One observational study comparing the efficacy and safety of three biologics (secukinumab, ustekinumab and guselkumab) showed a rapid response to secukinumab, whereas guselkumab was superior in terms of long-term response (approximately 1 year) and complete remission compared to other biologics. Among all the biologics assessed, ustekinumab showed relatively low efficacy [1]. One RCT study demonstrated higher efficacy rates for guselkumab compared to secukinumab [2]. One RCT study showed that guselkumab was effective in patients who did not achieve optimal clinical efficacy with ustekinumab [3]. Three RCT studies

showed that secukinumab was superior to ustekinumab which was proven statistically significant [4], [5], [6].

Table 2. Research Characteristics

No	Researcher	Year	Title	Design	Sampel Size
1	Thaci, D et al	2015	Secukinumab is Superior to Ustekinumab in Clearing Skin of Subjects with Moderate to Severe Plaque Psoriasis: CLEAR, A Randomized Controlled Trial	Randomized, Double Blind, Active Comparator, Parallel Group, Superiority Phase IIIb	Secukinumab n=337 Ustekinumab n=339
2	Bagel, J et al	2018	Secukinumab is Superior to Ustekinumab in Clearing Skin in Patients with Moderate to Severe Plaque Psoriasis (16-Week CLARITY Results)	Multicenter, Randomized, Double Blinded, Active Controlled, Parallel Group, Phase 3b Trial	Secukinumab n=550 Ustekinumab n=552
3	Bagel, J et al	2020	Secukinumab Maintains Superiority Over Ustekinumab in Clearing Skin and Improving Quality of Life in Patients with Moderate to Severe Plaque Psoriasis: 52-Week Results from A Double-Blind Phase 3b Trial (CLARITY)	Multicenter, Randomized, Double Blind, Parallel Group, Phase 3b Study	Secukinumab n=550 Ustekinumab n=552
4	Jung, W et al	2022	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	Observational, Retrospective, Single Center, Cohort Study	Secukinumab n=27 Ustekinumab n=61 Guselkumab n=23
5	Blauvelt, A et al	2021	Efficacy of Guselkumab Versus Secukinumab in Subpopulations of Patients with Moderate-to-Severe Plaque Psoriasis: Results from the ECLIPSE Study	Multicenter, Randomized, Double Blinded	Guselkumab n=534 Secukinumab n=514
6	Langley, R et al	2018	Efficacy and Safety of Guselkumab in Patients with Psoriasis Who Have An Inadequate Response to Ustekinumab: Results of the Randomized, Double-Blind, Phase III NAVIGATE Trial	Phase III, Randomized, Double Blind Trial	871 patients received open label ustekinumab (45 mg or 90 mg) at weeks 0 and 4. Week 16, 268 patients with an inadequate response to ustekinumab were randomized to guselkumab 100 mg or to continue ustekinumab; 585 of 871 patients with IGA 0/1 at week 16 continued open label ustekinumab.
7	Maria, J et al	2019	A Prospective Multicenter Study Assessing Effectiveness and Safety of Secukinumab in A Real-Life Setting in 158 Patients	Multicenter, Prospective, Observational Study	Secukinumab n=158
8	Yang, J et al	2022	Effectiveness and Safety of Guselkumab for the Treatment of Psoriasis in Real-World Settings at 52 Weeks: A Retrospective, Observational, Multicenter Study from China	Retrospective, Observational, Multicenter Study	Guselkumab n=27
9	Alcazar, E et al	2021	Effectiveness and Safety of Guselkumab for the Treatment of Psoriasis in Real-World Settings at 24 Weeks: A Retrospective, Observational, Multicentre Study by the Spanish Psoriasis Group	Retrospective, Observational, Multicenter Study	Guselkumab n=343
10	Raposo, I et al	2019	Ustekinumab in Real-Life Practice: Experience in 116 Patients with Moderate to Severe Psoriasis	Retrospective, Observational, Cohort	Ustekinumab n=116

Efficacy of Secukinumab, Ustekinumab and Guselkumab for the Treatment of Moderate to Severe Plaque Psoriasis

One observational study demonstrated a rapid response to secukinumab, whereas guselkumab was superior in terms of long-term response, potentially inducing complete disease remission. Among all the biologics assessed, ustekinumab showed relatively low efficacy [1]. In the observational study of 4 studies there were no comparisons so it could not be proven statistically [7], [8], [9], [10]. However one observational study showed guselkumab to be effective in patients with other biologic failures, particularly in terms of long-term efficacy. It was said that six patients continued to take medication and had stable lesion control (PASI 0) for a follow-up period of 2 years [10]. One RCT study demonstrated numerically higher efficacy rates with guselkumab compared with secukinumab [2]. One RCT study showed that guselkumab was effective in patients who did not achieve optimal clinical efficacy with ustekinumab [3]. Three RCT studies showed that secukinumab was superior to ustekinumab which was proven statistically significant [4], [5], [6].

Table 3. Efficacy of Secukinumab, Ustekinumab and Guselkumab for the Treatment of Moderate to Severe Plaque Psoriasis

No	Researcher	Treatment	Comparison	Result
1	Thaci, D et al	Use of secukinumab 300 mg at baseline and weeks 1, 2 and 3, then every 4 weeks from week 4 to week 48	Use of ustekinumab 45 mg for subjects ≤100 kg and 90 mg for subjects >100 kg at baseline and week 4, then every 12 weeks from week 16 to week 40	Secukinumab was superior to ustekinumab with 79.0% of subjects in the secukinumab group and 57.6% of subjects in the ustekinumab group achieving a PASI response of 90 at week 16 (P<0.0001). The proportion of subjects achieving a PASI response of 100 at week 16 was significantly greater with secukinumab (44.3%) than with ustekinumab (28.4%) (P<0.0001). Secukinumab was superior to ustekinumab with respect to a PASI 75 response at week 4 in 50.0% in the secukinumab and 20.6% in the ustekinumab group (P<0001).
2	Bagel, J et al	Use of subcutaneous secukinumab 300 mg at baseline, weeks 1, 2, 3 and then every 4 weeks from week 4 to 48	Use of ustekinumab 45 mg for patients weighing ≤100 kg or 90 mg for patients weighing >100 kg at baseline, week 4 and then every 12 weeks	Secukinumab was superior to ustekinumab for the proportion of patients achieving a PASI response of 90 at week 12 (66.5% vs 47.9%; P<0.0001) and for the proportion of patients achieving an IGA mod 2011 0/1 response at week 12 (72.3% vs 55.4%; P<0.0001). PASI response was 90 greater with secukinumab than with ustekinumab from week 4 (16.7% vs 4.0%; P<0.0001) to week 16 (76.6% vs 54.2%; P<0.0001). Similarly, IGA mod 2011 0/1 was greater with secukinumab at week 4 (26.9% vs 7.8%; P<0.0001) and week 16 (78.6% vs 59.1%; P<0,0001). PASI 100 was also greater among patients treated with secukinumab than with ustekinumab from week 4 to week 16. The proportion of patients with a DLQI response of 0/1 was greater with secukinumab than with ustekinumab at week 4 (33.9% vs 18.0%; P<0.0001), week 12 (64.0% vs

				51.7%; P<0.0001) and week 16 (68.4% vs 55.9%; P<0.0001).
3	Bagel, J et al	Use of secukinumab 300 mg at baseline, weeks 1, 2, 3 and 4 and then every 4 weeks thereafter until week 48	Subcutaneous use of ustekinumab 45 mg for patients weighing ≤100 kg or 90 mg for patients weighing >100 kg at baseline, week 4 and then every 12 weeks thereafter until week 40	At week 52, a greater proportion of patients receiving secukinumab than those receiving ustekinumab achieved PASI 75 (89.0% vs 82.1% P=0.0013), PASI 90 (73.2% vs 59.8% P<0.0001), PASI 100 (48.9% vs 33.5% P<0.0001), IGA mod 2011 0/1 (76.0% vs 60.2% P<0.0001), IGA mod 2011 0 (50.3% vs 33.8% P<0.0001) and DLQI 0/1 (69.9% vs 61.2% P=0.0028).
4	Jung, W et al	Use of secukinumab 300 mg injected as two subcutaneous injections of 150 mg at weeks 0, 1, 2, 3 and 4 and every 4 weeks thereafter	Use of ustekinumab at a dose of 45 mg initially and after a period of 4 weeks followed by a dose of 45 mg given every 12 weeks and guselkumab 100 mg at week 0, 4 and 12 and every 8 weeks thereafter	With respect to response to PASI 75, secukinumab was significantly superior to guselkumab (88.9% for secukinumab vs 55.2% for guselkumab, P<0.01) and (88.9% for secukinumab vs 33.4% for ustekinumab, P<0.001) in the early phase of week 16. PASI 90 was similar to that observed with a response to PASI 75. In the final phase of week 56, guselkumab showed greater efficacy than secukinumab; but the difference was not significant (91.3% guselkumab vs 81.5% secukinumab, P=0.318). At week 56, a significantly lower proportion of patients in the ustekinumab group achieved a PASI of 100 compared to the guselkumab group (82.6% guselkumab vs 36.1% ustekinumab, P<0.001) and the secukinumab group (63.0% secukinumab vs 36.1% ustekinumab, P=0.019). A higher proportion of patients in the guselkumab group achieved a PASI response of 100 compared to those in the secukinumab group; however, the difference was not significant (82.6% for guselkumab vs 63.0% for secukinumab, P=0.123).
5	Blauvelt, A et al	Use of guselkumab 100 mg subcutaneously at week 0, 4, 12 and every 8 weeks thereafter until week 44	Use of secukinumab 300 mg given subcutaneously as two injections of 150 mg at week 0, 1, 2, 3, 4 and every 4 weeks thereafter until week 44	PASI 90 and PASI 100 response rates were numerically higher at week 48 in the guselkumab group than in the sekukinumab group across all 3 age categories (PASI 90 <45 years 85.4% vs 75.2%, 45 to <65 years 84.3 % vs 68.6% ≥65 years 81.5% vs 46.7% and PASI 100 <45 years 58.8% vs 55.3%, 45 to <65 years 58.7% vs 44.9% ≥65 years 53.7% vs 45%. IGA 0/1 (<45 years 85.8% vs 81.3%, 45 to <65 years 85.4 vs 73.4%, ≥65 years 79.6 vs 44.4 % and IGA 0 (<45 years 64.6 vs 58.0%, 45 to <65 years: 61.4 vs 46.4%, >65 years 55.6 vs 24.4%. Proportion of patients achieving a PASI 90 or PASI 100 response at 48 weeks based on baseline

				body weight (from <60 to >110 kilograms (kg)), patients who achieved a PASI 90 based on baseline BMI, patients who achieved a PASI 90 or PASI 100 response as defined by initial disease severity including: initial BSA, duration of disease, PASI baseline, baseline IGA score, PASI component scores for the following body parts: head, trunk, upper extremity and lower extremity and previous psoriasis treatment history were numerically higher for guselkumab-treated patients.
6	Langley, R et al	Open-label ustekinumab (45 mg for patients weighing ≤100 kg; 90 mg for patients weighing >100 kg) at week 0 and 4	At week 16, patients with IGA ≥2 (ie inadequate response to ustekinumab) were randomized to guselkumab 100 mg at week 16, 20 and every 8 weeks thereafter, or to continue ustekinumab at week 16 and every 12 weeks thereafter. Patients with IGA 0 or 1 continue to receive open-label ustekinumab at week 16 and every 12 weeks	During open label 68.5% of patients (589 of 860) achieved an IGA score of 0 or 1, 73.7% achieved a PASI of 75 and 49% achieved a PASI of 90 at week 16. Among randomized patients, the guselkumab group had a significantly higher mean number of visits where patients had an IGA score of 0 or 1 and at least a two-level increase relative to week 16 from week 28 to 40 compared to the ustekinumab group (1.5 vs. 0.7; P<0.001). The mean number of visits where patients had a PASI of 90 relative to baseline between week 28 and 40 was significantly higher in the guselkumab group than in the ustekinumab group (2.2 vs 1.1 P<0.001). The mean number of visits in which patients had an IGA score of 0 between week 28 and week 40, the proportion of patients with an IGA score of 0 or 1 of at least a two-grade increase relative to week 16 at week 28 was significantly greater in the guselkumab group than in the ustekinumab group random. At week 52, most of the patients treated with guselkumab achieved a PASI of 90 (51.1% vs 24.1%; P<0.001) and a PASI of 100 (20.0% vs 7.5%; P=0.003) compared with randomized ustekinumab group. Nearly all patients (95.7%) in the nonrandomized ustekinumab group had a PASI of 75 at 16 weeks, 69.7% had a PASI of 90 and 27.2% had a PASI of 100. This response rate was maintained through week 52. The proportion of patients who had a DLQI score of 0 or 1, a PSSD score of 0 or a symptom score of 0 at week 52 was also significantly greater in the guselkumab group than in the ustekinumab group.
7	Maria, J et al	Secukinumab 300 mg subcutaneously weekly for 4 weeks and then every 4	None	The proportion of patients who reached PASI 75 at week 4, 12, 24, and 52 were 57%, 83.5%, 89% and 78.5%, respectively, while the proportion who

		weeks (followed at 12 week intervals until 52 weeks)		reached PASI 90 was 27.8 %, 62%, 64.6% and 63.2%. By week 12, 109 patients (70%) had achieved target response of <1% affected body surface area.
8	Yang, J et al	Guselkumab 100 mg subcutaneously at week 0 and week 4, followed by a maintenance dose every 8 weeks	None	Guselkumab lowered the mean PASI score from 12.46 ± 6.34 at baseline to 4.03 ± 3.25 at week 12 (P<0.001) and 0.77 ± 1.25 at week 52 (P<0.001). At week 12, PASI responses of 75, 90 and 100 were achieved in 44.4%, 18.5% and 11.1% of patients, respectively, whereas at week 28, PASI responses of 75, 90 and 100 were achieved in 80%, 68% and 52% of patients, respectively. At week 52, PASI responses of 75, 90 and 100 were achieved in 88%, 72% and 48% of patients, respectively. 80% of patients achieved a PASI score of ≤3 at week 28 and 96% of patients achieved a PASI score of ≤3 at week 52. 80% of patients achieved a PASI score <1. The mean DLQI score decreased from 11.54 ± 5.97 at baseline to 0.72 ± 1.02 at week 52 (P<0.001) and 80% of patients achieved the DLQI (0/1).
9	Alcazar, E et al	Guselkumab 100 mg at week 0 and 4 followed by a maintenance dose every 8 weeks	None	The mean PASI, which was 11.1 (7.3) at baseline, decreased to 2.4 (3.2) at week 16 and to 1.7 (2.8) at week 24, with a significant difference statistically. This showed a mean decrease in PASI of 78.4% at week 16 and 84.7% at week 24. After 6 months of treatment, 85.9% (214/249) achieved PASI ≤4 and 77.9% (194/ 249) PASI ≤2. In terms of relative response, 59.4% (148/249) achieved PASI 90 and 49.0% (122/249) achieved PASI 100. Baseline BSA mean of 13.7 (13.8) decreased to 3.8 (7.0) at week 16 and to 2.3 (4.7) at week 24. Baseline PGA 3.2 (0, 8) decreased to 1.1 (0.9) at the end of the fourth month and to 0.9 (0.9) at the end of the study. The baseline DLQI mean of 11.9 (7.3) decreased to 2.7 (4.1) at week 16 and 2.4 (4.3) at the end of the study.
10	Raposo, I et al	Ustekinumab at week 4, 12, 24, 52	None	PASI 75 response was achieved by 67.2% (78/116), 85.3% (99/116), 89.6% (104/116) and 88.7% (103/116) in week 4, 12, 24 and 52, respectively. Maximum total group follow-up was at 60 weeks, at which time the response rate was maintained at 87.9% (102/116).

Psoriasis

Safety is discussed in the 10 studies included in this article. One observational study showed all three of the commonly used biologics (secukinumab, ustekinumab and guselkumab) to have a similar favorable safety profile; however, severe allergic reactions, resulting in discontinuation or biologic changes, were significantly more common in the secukinumab group [1]. One observational study with long-term use of ustekinumab showed an excellent safety profile and no major side effects [9]. One observational study showed secukinumab is a safe treatment [8]. Two observational studies have shown guselkumab to be a safe treatment [7], [10]. One RCT study did not assess safety comparisons in any subpopulation between the two treatments (guselkumab and secukinumab) because the safety of each treatment was relatively similar [2]. One RCT study showing transition to guselkumab in patients who failed to achieve a response to ustekinumab was not associated with additional safety concerns [3]. Two RCT studies have shown that secukinumab exhibits a similar safety profile to ustekinumab [5], [6]. One RCT study that assessed the superiority of secukinumab over ustekinumab also demonstrated a favorable safety profile of secukinumab without any new safety signals [4].

Table 4. Safety of Secukinumab, Ustekinumab and Guselkumab for the Treatment of Moderate to Severe Plaque Psoriasis

No	Researcher	Treatment	Comparison	Result
1	Thaci, D et al	Use of secukinumab 300 mg at baseline and week 1, 2 and 3, then every 4 weeks from week 4 to week 48	Use of ustekinumab 45 mg for subjects ≤100 kg and 90 mg for subjects >100 kg at baseline and week 4, then every 12 weeks from week 16 to week 40	The proportion of subjects experiencing at least 1 AE was 64.2% in the secukinumab group and 58.3% in the ustekinumab group. AEs in the organ system class "infection and infestation" were most frequently reported (29.3% for secukinumab and 25.3% for ustekinumab); however, most of the infectious AEs were not serious, of mild to moderate severity, easy to manage and did not lead to discontinuation of the study drug. The most common AEs are mild to moderate headaches and nasopharyngitis. Serious AE (SAE) is low 3.0% in each group.
2	Bagel, J et al	Use of subcutaneous secukinumab 300 mg at baseline, week 1, 2, 3 and then every 4 weeks from week 4 to 48	Use of ustekinumab 45 mg for patients weighing ≤100 kg or 90 mg for patients weighing >100 kg at baseline, week 4 and then every 12 weeks	The total number of reported AEs was comparable between the secukinumab group (47.5%) and the ustekinumab group (46.4%). There were two deaths, one due to acute cocaine poisoning and one due to sudden cardiac death (the patient had a history of hypertension and atherosclerosis). The incidence of serious non-fatal AEs (SAE) was low for both groups (2.5% secukinumab and 1.6% ustekinumab). The most frequently reported AEs of the "infection and infestation" organ system class (22.2% secukinumab and 21.2% ustekinumab); however, the majority of events were non-serious, manageable and did not lead to discontinuation of the study drug.
3	Bagel, J et al	Use of secukinumab 300 mg at baseline, week 1, 2, 3 and 4 and then every 4 weeks thereafter until week 48	Subcutaneous use of ustekinumab 45 mg for patients weighing ≤100 kg or 90 mg for patients weighing >100 kg at baseline, week 4 and then every 12 weeks thereafter until week 40	The proportion of patients with any AE was comparable between secukinumab and ustekinumab (68.5% vs 70.7%); the incidence of possibly drug-related AEs was studied between treatment groups (secukinumab 20.0%; ustekinumab 20.8%). The incidence of candida infection was slightly higher with

				secukinumab than with ustekinumab (2.4% vs 0.7%); no candida infection was considered serious or resulted in discontinuation of treatment. Two patients in the secukinumab group died (44 year old man with a medical history of arteriosclerosis, obesity (initial weight 188 kg), hypertension and peripheral edema died of sudden cardiac death and 50 year old man with a history of hypertension, hyperlipidemia, hypothyroidism and obesity (initial weight 150 kg) died of acute cocaine poisoning. There was no causal link between these deaths and the study drug that the investigators suspected.
4	Jung, W et al	Use of secukinumab 300 mg injected as two subcutaneous injections of 150 mg at week 0, 1, 2, 3 and 4 and every 4 weeks thereafter	Use of ustekinumab at a dose of 45 mg initially and after a period of 4 weeks followed by a dose of 45 mg given every 12 weeks and guselkumab 100 mg at week 0, 4 and 12 and every 8 weeks thereafter	A similar proportion of AEs among biologics was found, with 18.5% (5/27), 18.0% (11/61) and 17.4% (4/23) of patients experiencing at least one AE with secukinumab, ustekinumab and guselkumab, respectively. Only 4 patients with SAE (3.6%) were reported: 3 in the secukinumab group (2 due to an injection site reaction resulting in biologic discontinuation and 1 due to a systemic allergic reaction resulting in a biologic change in guselkumab) and 1 in the ustekinumab group (due to worsening of psoriasis, resulting in biologic conversion to risankizumab). In the secukinumab group, SAE was more common than the other two biologics and all were associated with local or systemic allergic reactions.
5	Blauvelt, A et al	Use of guselkumab 100 mg subcutaneously at week 0, 4, 12 and every 8 weeks thereafter until week 44	Use of secukinumab 300 mg given subcutaneously as two injections of 150 mg at week 0, 1, 2, 3, 4 and every 4 weeks thereafter until week 44	Comparison of safety in each subpopulation was not assessed between the two treatments, because the safety of each treatment is relatively the same.
6	Langley R, et al	Open-label ustekinumab (45 mg for patients weighing ≤100 kg; 90 mg for patients weighing >100 kg) at week 0 and 4	At week 16, patients with IGA ≥2 (ie inadequate response to ustekinumab) were randomized to guselkumab 100 mg at week 16, 20 and every 8 weeks thereafter, or to continue ustekinumab at week 16 and every 12 weeks thereafter. Patients with IGA 0 or 1 continue to receive open-label ustekinumab at week 16 and every 12 weeks	Among 871 patients who received ustekinumab during the initial open-label period, 254 patients (29.2%) had at least one AE by week 16. The most common AEs were nasopharyngitis (5.4%) and upper respiratory tract infections (3 8%). Eleven patients (13%) had at least one serious AE (SAE). In the two randomized groups, 64.4% of patients in the guselkumab group and 55.6% of patients in the ustekinumab group had at least one AE from week 16 to week 60. Infection was the most common AE (guselkumab

				41.5%; ustekinumab 35.3%). The higher overall AE rate in the guselkumab group appears to be related to the higher reported incidence of AEs in musculoskeletal and connective tissue disorders (guselkumab 12.6%; ustekinumab 6.8%). SAE was reported in nine patients treated with guselkumab (6.7%) and six patients treated with ustekinumab (4.5%). The most common AEs in the nonrandomized ustekinumab group were nasopharyngitis and upper respiratory tract infections. Twenty patients (3.4%) had at least one SAE from week 16 to week 60. Five patients developed serious infections after week 16.
7	Maria, J et al	Secukinumab 300 mg subcutaneously weekly for 4 weeks and then every 4 weeks (followed at 12 week intervals until 52 weeks)	None	During the study, side effects were experienced by 28 patients (17.7%). The most frequent side effects were headaches (9 patients, 5.7%), nasopharyngitis (9 patients, 5.7%), hypertension (6 patients, 3.8%), oral candidiasis (5 patients, 3.2%) and diarrhea (2 patients, 1.3%).
8	Yang, J et al	Guselkumab 100 mg subcutaneously at week 0 and week 4, followed by a maintenance dose every 8 weeks	None	No patients withdrew from the study because of AE. Between week 12 and 20, two mild adverse events occurred in two patients, respectively (tinea capitis in one patient and diarrhea in another).
9	Alcazar, E et al	Guselkumab 100 mg at week 0 and 4 followed by a maintenance dose every 8 weeks	None	Adverse effects were reported by 9.9% (34/343) of patients, with infection being the most common. Only nine patients (2.6%) stopped treatment because of side effects: two headaches, two joint pains, two COVID-19 pneumonia, one flu like symptoms, one respiratory infection and one acute myocardial infarction. Other reasons for discontinuing treatment were: patient judgment (2), poor adherence (2), failure of primary treatment (3) and lack of efficacy in joint disease (2).
10	Raposo, I et al	Ustekinumab at weeks 4, 12, 24, 52	None	Ustekinumab was discontinued in seven patients (3 due to primary failure, 3 due to secondary treatment failure and one due to side effect (facial paralysis)).

DISCUSSION

Psoriasis is a complex disease associated with a well-known patient burden and comorbidities [4]. Several biologic classes with different mechanisms of action and different efficacy and safety profiles are available for the treatment of psoriasis and differentiation between these therapies is an important option for good decision-making regarding treatment [5]. Studies comparing the effectiveness of therapy in moderate to severe plaque psoriasis are important to facilitate the right choice of treatment for patients [4]. We found that patients who were given secukinumab showed a rapid response, whereas guselkumab was superior in terms of long-term response (approximately 1 year) and complete remission compared to other biologics. Among

all the biologics assessed, ustekinumab showed relatively low efficacy. Biologics linked to the IL-23/Th17 axis, such as those that selectively target IL-23 p19 or IL-17A, are superior to biologics that target IL-12/23 p40 [1]. Interleukin (IL-23) and (IL-17A) inhibitors allow a greater proportion of patients with moderate to severe plaque psoriasis to achieve nearly clear skin [2]. The IL-23/T17 axis immune response is currently considered the main pathogenic pathway in psoriasis, which would explain why agents targeting this pathway achieve the best clinical response and are currently the most frequently used drugs to treat these patients [7]. Guselkumab, an inhibitor of the IL-23p19 subunit, has been shown to be highly efficacious and well tolerated for up to 4 years of continuous treatment for moderate to severe psoriasis [2]. The rapid onset also appears to be consistent with recent findings from the ECLIPSE trial comparing secukinumab to the IL-23 inhibitor guselkumab. In ECLIPSE, a numerically greater proportion of patients who received secukinumab achieved a PASI of 90 at week 4 to 16 than those who received guselkumab, although no formal statistical analysis was performed at this initial time point [5]. In addition, guselkumab is also said to be effective in patients who do not achieve optimal clinical efficacy with ustekinumab. While ustekinumab is highly effective, like other therapeutic agents, not all patients achieve maximal response [3]. Data on the safety and effectiveness of a drug in real-world clinical practice complements the evidence from clinical trials conducted in different settings. The profile of patients treated in clinical practice is more complex than that of patients included in trials, with real-world patients having more comorbid conditions and greater exposure to previous biologic therapies [7]. All three biologics have similar favorable safety profiles; however, severe allergic reactions, resulting in discontinuation or biologic changes, were significantly more common in the secukinumab group. Previously three patients treated with secukinumab discontinued or changed treatment regimens because of local or systemic allergic reactions. These cases are considered to have a delayed type drug sensitivity reaction, because they occur after multiple injections. Because more patients in the secukinumab group presented with severe allergic reactions than those treated with other biologics, we suggest that it is preferable to inject other biologics if there is a history of allergies or adverse drug reactions. In addition, doctors should pay more attention to patients who are given secukinumab than those who are given other biologic drugs to identify allergic reactions [1].

Conclusion

We found that patients who were given secukinumab showed a rapid response, whereas guselkumab was superior in terms of long-term response, potentially inducing complete disease remission. Among all the biologics assessed, ustekinumab showed relatively low efficacy. All three biologics have similar favorable safety profiles. Population-based studies and RCTs are needed to help establish the efficacy and safety of using this drug.

References

1. Jung, W et al. 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; 1-12.
2. Blauvelt, A et al. Efficacy of Guselkumab Versus Secukinumab in Subpopulations of Patients with Moderate-to-Severe Plaque Psoriasis: Results from the ECLIPSE Study. Journal of Dermatological Tretment., 2021; 1-8.
3. Langley, R et al. Efficacy and Safety of Guselkumab in Patients with Psoriasis Who Have an Inadequate Response to Ustekinumab: Results of The Randomized, Double-Blind, Phase III NAVIGATE Trial. British Journal of Dermatology, 2018; 114-123.
4. Bagel, J et al. Secukinumab is Superior to Ustekinumab in Clearing Skin in Patients with Moderate to Severe Plaque Psoriasis (16-Week CLARITY Results). Dermatol Ther., 2018, 1-9.
5. Bagel, J et al. Secukinumab Maintains Superiority Over Ustekinumab in Clearing Skin and Improving Quality of Life in Patients with Moderate to Severe Plaque Psoriasis: 52-Week Results from A Double-Blind Phase 3b Trial (CLARITY). Journal of the European Academy of Dermatology and Venerology, 2020; 135-142.
6. Thaci, D et al. Secukinumab is Superior to Ustekinumab in Clearing Skin of Subjects with Moderate to Severe Plaque Psoriasis: CLEAR, A Randomized Controlled Trial. J Am Acad Dermatol., 2015; 400-409.
7. Alcazar, E et al. Effectiveness and Safety of Guselkumab for the Treatment of Psoriasis in Real-World Settings at 24 Weeks: A Retrospective, Observational, Multicentre Study by the Spanish Psoriasis Group. Dermatologic Therapy, 2021; 1-10.
8. Maria, J et al. A Prospective Multicenter Study Assessing Effectiveness and Safety of Secukinumab in A Real-Life Setting in 158 Patients. J Am Acad Dermatol., 2019; 427-432.
9. Raposo, I et al. Ustekinumab in Real-Life Practice: Experience in 116 Patients with Moderate to Severe Psoriasis. Actamedicaportuguesa, 2019; 214-218.
10. Yang, J et al. Effectiveness and Safety of Guselkumab for the Treatment of Psoriasis in Real World Settings at 52 Weeks: A Retrospective, Observational, Multicenter Study from China. Dermatol Ther., 2022; 1-9.