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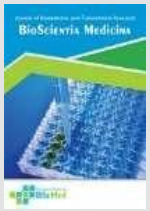

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Therapeutic Outcomes of Secukinumab 300 mg in Severe Psoriasis Vulgaris with Metabolic Comorbidities: A Retrospective Cohort Study in Bali

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A B S T R A C T

Background: Psoriasis vulgaris is a systemic inflammatory disease increasingly prevalent in Southeast Asia, often complicated by metabolic syndrome. While Secukinumab, an IL-17A inhibitor, is established in Western cohorts, real-world data on its efficacy in Indonesian populations with high adiposity burdens are scarce. This study evaluates the therapeutic response and safety of Secukinumab 300 mg in a Balinese cohort characterized by severe disease and metabolic risk factors. **Methods:** We conducted a retrospective cohort study at a tertiary referral center in Bali from January 2023 to December 2024. The study included 39 adult patients with moderate-to-severe psoriasis treated with Secukinumab 300 mg. The primary endpoint was the proportion of patients achieving a 75% reduction in the Psoriasis Area and Severity Index (PASI 75) at Week 17. Fisher's Exact Test was employed to analyze response differences between obese and non-obese subgroups. **Results:** The cohort exhibited a high systemic burden: 44.2% were obese (Body Mass Index greater than or equal to 25 kg/m2), and 53.8% had concomitant psoriatic arthritis. Baseline disease severity was high with a median body surface area of 25.0%. At week 17, 32 patients (82.1%; 95% confidence interval: 67.3–91.0%) achieved PASI 75. Subgroup analysis revealed no statistically significant difference in response rates between obese and non-obese patients ($p > 0.99$), suggesting efficacy is maintained despite metabolic burden. No severe adverse events or discontinuations were documented in the medical records. **Conclusion:** Secukinumab 300 mg demonstrates substantial efficacy in an Indonesian population with a severe phenotypic profile, maintaining therapeutic clearance in metabolically compromised patients. The safety profile appears favorable, though limited by retrospective data capture.

1. Introduction

Psoriasis vulgaris has undergone a profound conceptual evolution over the past two decades, transitioning from being viewed merely as a localized cutaneous disorder to its current recognition as a complex, multisystem inflammatory pathology.[1] This paradigm shift acknowledges that the visible manifestations of erythematous, indurated plaques are but the external signaling of a profound dysregulation within the innate and adaptive immune systems. The disease is characterized by a relapsing and remitting course, driven by a sophisticated interplay between polygenic susceptibility and a myriad of environmental triggers, ranging from mechanical stress and microbial dysbiosis to psychogenic stress and metabolic dysfunction.[2]

Central to the pathogenesis of this condition is the aberrant activation of the Interleukin-23 (IL-23) and T-helper 17 (Th17) axis, a critical pathway in host defense that, when dysregulated, drives the chronicity of psoriatic inflammation. The process initiates when dendritic cells, activated by antimicrobial peptides

such as LL-37 released from keratinocytes, secrete IL-23. This cytokine acts as the primary survival and expansion factor for Th17 cells. Upon activation, these T-helper cells migrate to the dermis and release a milieu of pro-inflammatory cytokines, predominantly Interleukin-17A (IL-17A), IL-17F, and IL-22. IL-17A serves as the primary effector cytokine, binding to receptors on keratinocytes to induce the expression of chemokines and antimicrobial peptides. This molecular cascade results in the hallmark histological features of psoriasis: the hyperproliferation of keratinocytes, aberrant differentiation or parakeratosis, and the massive infiltration of neutrophils into the epidermis.[3]

However, the consequences of this inflammatory cascade are not confined to the cutaneous compartment. The pro-inflammatory cytokines produced in psoriatic plaques, particularly TNF-alpha, IL-6, and IL-17A, spill over into the systemic circulation, contributing to a state of systemic inflammation. This systemic burden is implicated in a broad spectrum of comorbidities that significantly impair patient quality of life and reduce life expectancy.[4] Among these, psoriatic arthritis is the most well-established, affecting the entheseal organ and synovial joints. Yet, the systemic reach of psoriatic inflammation extends further, fostering an environment conducive to insulin resistance, endothelial dysfunction, and atherosclerosis. Consequently, psoriasis is now intrinsically linked to metabolic syndrome, a cluster of conditions including central obesity, hypertension, dyslipidemia, and glucose intolerance, which collectively elevate the risk of adverse cardiovascular events.

The epidemiology of psoriasis reveals significant global heterogeneity, with prevalence rates estimated to range between 0.1% and 10% depending on the geographic region and ethnic background. Higher prevalence rates are generally observed in Caucasian populations at higher latitudes, while lower rates are typically reported in Asian and African populations. In Southeast Asia, particularly within the Indonesian archipelago, precise epidemiological data remains fragmented and often underreported.[5] Previous hospital-based studies conducted have indicated a prevalence of approximately 0.6% to 0.7% among dermatology outpatients, with psoriasis vulgaris representing the predominant phenotype. Despite the lower prevalence relative to Western nations, the clinical management of severe cases in this region faces unique and formidable challenges. These include limited access to advanced dermatological care in rural areas, economic barriers to biologic therapies, and a high prevalence of undiagnosed or undertreated metabolic comorbidities that complicate therapeutic outcomes.

Of the various comorbidities associated with psoriasis, obesity represents perhaps the most critical variable in the clinical management of the disease. The relationship between psoriasis and obesity is bidirectional and synergistic. On one hand, the social stigma and physical discomfort of psoriasis can lead to sedentary lifestyles and depressive eating habits, promoting weight gain. On the other hand, obesity is an independent risk factor for the onset and exacerbation of psoriasis. This is driven by the understanding of adipose tissue, specifically visceral fat, not as an inert energy storage depot, but as a highly active endocrine organ.[6] In the obese state, adipocytes undergo hypertrophy and hyperplasia, leading to localized hypoxia and cell death. This triggers the recruitment of pro-inflammatory macrophages, shifting the adipose tissue environment from an anti-inflammatory M2 phenotype to a pro-inflammatory M1 phenotype.

This metabolically active adipose tissue secretes a vast array of bioactive mediators known as adipokines. In patients with obesity, there is a marked dysregulation in the secretion of these molecules, characterized by the overproduction of pro-inflammatory cytokines such as IL-6, TNF-alpha, and leptin, concurrent with a reduction in adiponectin, which possesses anti-inflammatory and insulin-sensitizing properties. Leptin is of particular relevance to psoriasis pathogenesis as it directly promotes the differentiation of Th17 cells and stimulates the

production of IL-17A, thereby linking nutritional status directly to immune activation. This state of chronic, low-grade inflammation, often termed meta-inflammation, creates a pathological feedback loop.[7] The systemic cytokine load from visceral adiposity amplifies the inflammatory drive in the skin, leading to more severe and recalcitrant disease. Conversely, the systemic inflammation derived from the skin may further impair insulin sensitivity and promote adipogenesis. Crucially, the presence of obesity significantly alters the pharmacokinetics and pharmacodynamics of biologic therapies. Mechanisms such as the adipose sink effect, where lipophilic drugs or large molecules are sequestered or diluted within the increased volume of distribution, can lead to sub-therapeutic serum concentrations. Furthermore, the high baseline levels of inflammatory cytokines in obese patients may simply overwhelm standard doses of biologic agents, requiring higher molar concentrations of neutralizing antibodies to achieve clinical clearance. In numerous Western clinical trials, high body mass index has consistently been identified as a negative predictor for therapeutic clearance, often necessitating dose adjustments or shorter dosing intervals.[8]

In the landscape of targeted therapies, Secukinumab, a fully human monoclonal antibody that selectively neutralizes IL-17A, has emerged as a cornerstone of modern management. By directly inhibiting the primary effector cytokine of the Th17 axis, Secukinumab effectively interrupts the inflammatory loop driving keratinocyte hyperproliferation. Pivotal phase III trials established the superiority of Secukinumab over placebo and earlier generation biologics like etanercept, demonstrating rapid onset of action and high rates of complete skin clearance. While early protocols investigated a 150 mg dose, accumulating evidence and post-marketing surveillance have strongly suggested that the 300 mg dose provides superior efficacy. This is particularly evident in achieving stringent endpoints such as PASI 90 or PASI 100, and critically, in maintaining glycemic control and skin clearance in patients with higher body weight and recalcitrant plaques. The 300 mg dose appears to provide the necessary drug exposure to neutralize the elevated IL-17A burden present in patients with high systemic inflammatory load.[9]

Despite the robust and extensive data available from Western cohorts regarding the efficacy of Secukinumab, there remains a distinct paucity of real-world evidence derived from Southeast Asian, and specifically Indonesian, populations. It is scientifically precarious to simply extrapolate data from Caucasian trials to Asian populations without verification, as genetic polymorphisms in drug-metabolizing enzymes, differences in human leukocyte antigen associations, and environmental factors including diet and tropical climate may influence biologic drug pharmacokinetics and immunogenicity. Furthermore, the specific interplay between visceral adiposity, which is increasingly common in the Balinese demographic due to shifting dietary patterns, and the efficacy of IL-17A blockade requires specific elucidation in this setting. The phenotypic profile of Indonesian patients, often presenting with advanced disease due to delayed referral, combined with a high burden of metabolic syndrome, creates a unique clinical scenario that has not been adequately represented in global registration trials.[10]

Therefore, this study aims to bridge this significant knowledge gap by conducting a comprehensive evaluation of the efficacy and safety of Secukinumab 300 mg in a tertiary referral setting in Bali. Specifically, this research seeks to analyze therapeutic outcomes in a difficult-to-treat cohort characterized by high rates of obesity and concomitant psoriatic arthritis. The primary novelty of this study lies in its focus on the intersection of metabolic burden and biologic response within an understudied ethnic population. We hypothesize that the 300 mg dose of Secukinumab provides sufficient pharmacokinetic exposure to overcome the heightened inflammatory burden associated with the meta-inflammation of obesity in this specific cohort, offering critical insights that may guide dermatological practice and health

policy in Indonesia and the broader Southeast Asian region.

2. Methods

The study protocol received ethical clearance from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Udayana and Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar. The study adhered to the Declaration of Helsinki regarding patient data privacy. This investigation employed a retrospective, observational cohort design. The study was conducted at the Dermatology and Venereology Polyclinic of Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, a tertiary referral center serving the diverse population of Eastern Indonesia. The observation period spanned from January 1st, 2023, to December 31st, 2024.

The target population for this retrospective observational study was strictly defined to ensure a homogeneous cohort reflective of severe dermatological burden. We identified adult patients, defined as individuals aged 18 years or older, who had received a confirmed diagnosis of moderate-to-severe psoriasis vulgaris. To ensure diagnostic accuracy and consistency, all included cases were clinically confirmed by a board-certified dermatologist, thereby excluding ambiguous phenotypes or psoriasiform dermatitis mimics. The recruitment process employed a consecutive sampling technique. This methodological choice was deliberate, aiming to minimize the selection biases often inherent in convenience sampling by including every subject who met the inclusion criteria within the specified timeframe, thus providing a more representative cross-section of the clinical population presenting to our tertiary center.

Inclusion was contingent upon the initiation of Secukinumab therapy at the standard biologic dose of 300 mg administered subcutaneously within the defined study period. Furthermore, to facilitate a rigorous longitudinal analysis of therapeutic efficacy, patients were required to have comprehensive medical records available. These records necessitated clear documentation of clinical severity scores, specifically the Psoriasis Area and Severity Index (PASI), at both the baseline visit and the critical follow-up intervals of Week 5 and Week 17.

Strict exclusion criteria were applied to maintain data integrity. Patients with incomplete medical records regarding dosing schedules or PASI scoring were removed from the analysis to prevent the introduction of information bias. Additionally, a specific criterion was established regarding treatment attrition. Patients who discontinued therapy due to non-medical reasons, specifically financial constraints, prior to the Week 5 assessment were excluded from the efficacy analysis. This decision was made to isolate the physiological efficacy of the drug from socioeconomic barriers to adherence. However, we acknowledge that this introduces a potential survivor bias, as patients who do not perceive rapid clinical improvement may be less willing to sustain the financial burden of continued therapy, potentially skewing the remaining cohort toward those with more favorable early responses.

The therapeutic intervention followed a standardized pharmacological protocol consistent with international guidelines for moderate-to-severe psoriasis. All patients received Secukinumab at a total dose of 300 mg per administration, delivered as two separate subcutaneous injections of 150 mg each to ensure optimal absorption. The treatment schedule adhered to a rigorous induction and maintenance regimen. The induction phase consisted of weekly injections administered at Weeks 0, 1, 2, 3, and 4 to rapidly achieve therapeutic serum concentrations. Following this loading phase, patients transitioned to a maintenance schedule comprising monthly dosing intervals to sustain clinical remission.

Data extraction was conducted using a standardized case report form to ensure uniformity and reduce inter-observer variability. Information was sourced directly from electronic medical records, and all patient identifiers were anonymized immediately upon extraction to strictly uphold patient confidentiality and data privacy standards. The

variable selection was designed to capture the multifaceted nature of the disease. Demographic data included age, gender, and occupation. Of particular importance to the study's metabolic focus was the stratification of anthropometric data. Body Mass Index (BMI) was calculated and stratified according to the World Health Organization Asia-Pacific criteria, which are calibrated to the specific metabolic risk profiles of Asian populations. Consequently, patients were categorized as Underweight (less than 18.5 kg per square meter), Normoweight (18.5 to 22.9 kg per square meter), Overweight (23 to 24.9 kg per square meter), or Obese (greater than or equal to 25 kg per square meter).

Clinical phenotyping extended beyond simple severity scores. We documented disease duration and the presence of specific negative prognostic indicators, including nail psoriasis and psoriatic arthritis, the latter being confirmed via established rheumatological criteria. Baseline disease severity was quantified using two validated metrics: the percentage of Body Surface Area (BSA) involvement and the composite Psoriasis Area and Severity Index (PASI). Furthermore, a comprehensive review of comorbidities was undertaken, specifically documenting the presence of hypertension, type 2 diabetes mellitus, dyslipidemia, and relevant cardiovascular history to assess the systemic inflammatory burden of the cohort.

The primary endpoint for therapeutic efficacy was defined as the proportion of patients achieving a 75% reduction in their baseline PASI score (PASI 75) at Week 17. This timepoint was selected to represent the early maintenance phase where steady-state drug levels are typically established. Secondary endpoints included the PASI 75 response rate at Week 5 (marking the end of the induction phase), the absolute reduction in Body Surface Area, and the safety profile of the intervention. Safety was assessed by monitoring the incidence of Adverse Events, defined comprehensively as any untoward medical occurrence documented in the electronic medical records during the treatment period, regardless of whether a causal relationship with the study drug was suspected.

All statistical processing and analytical procedures were executed using IBM SPSS Statistics version 30.0. The analysis began with descriptive statistics to characterize the cohort. Continuous variables were rigorously assessed for normality using the Shapiro-Wilk test. Recognizing the non-Gaussian distribution typically observed in dermatological severity scores, non-normally distributed data such as Body Surface Area were presented as the Median with Interquartile Range, rather than the Mean and Standard Deviation, to provide a more accurate measure of central tendency and dispersion. Categorical variables were summarized as frequencies and percentages.

Inferential statistical methods were specifically tailored to the small sample size (N equal to 39) to ensure methodological robustness. To evaluate the primary hypothesis regarding the impact of metabolic burden on efficacy, we analyzed the association between BMI category (dichotomized as Obese versus Non-Obese) and Therapeutic Response (dichotomized as PASI 75 achiever versus Non-achiever). Given the limited sample size and the likelihood of low expected cell counts in the contingency tables, the assumptions required for asymptotic methods like the Chi-square test were violated. Therefore, Fisher's Exact Test was employed as the primary analytical method. This exact test avoids the approximation errors associated with Chi-square or logistic regression in small cohorts, preventing statistical artifacts and model overfitting. Furthermore, to quantify the precision of our prevalence and response rate estimates, 95% Confidence Intervals were calculated using the Wilson Score Interval method. This method is superior to the standard Wald interval for small sample sizes, particularly when proportions are close to 0 or 1. All statistical tests were two-sided, and a p-value of less than 0.05 was considered statistically significant

3. Results

Table 1 presents the sociodemographic and anthropometric profile of the 39 patients included in the study cohort. The population was predominantly

of working age, with a mean age of 42.15 years (Standard Deviation 13.03) at the time of therapy initiation. Gender distribution displayed a slight male preponderance, comprising 21 males (53.8%) and 18 females (46.2%). A critical finding derived from the baseline assessment was the substantial metabolic burden characterizing this specific population. When stratified according to the World Health Organization Asia-Pacific criteria, which utilize lower cutoffs to define adiposity in Asian ethnicities, only 34.9% of the cohort fell within the normoweight range. Conversely, a striking 44.2% (n=19) of patients met the criteria for obesity (Body Mass Index greater than or equal to 25 kg per square meter). This prevalence of obesity is notably higher than typical estimates in general dermatology outpatients, underscoring the severe phenotypic profile of patients referred for biologic therapy. Regarding socioeconomic status, the occupational demographic was led by entrepreneurs (48.7%), suggesting a socioeconomic segment capable of accessing tertiary referral services, while 33.3% were unemployed. These baseline characteristics establish that the study population is not only dermatologically severe but also metabolically compromised, a factor hypothesized to influence pharmacodynamic responses to IL-17A inhibition.

Table 1. Demographic Baseline Characteristics of the Study Population (n=39)

Variable	Category	n (%)	Mean (SD)
Age (years)	-	-	42.15 (13.03)
Gender	Male	21 (53.8%)	
	Female	18 (46.2%)	
BMI Status (WHO Asia-Pacific Criteria)	Underweight (< 18.5 kg/m²)	2 (4.7%)	
	Normoweight (18.5 – 22.9 kg/m²)	15 (34.9%)	
	Overweight (23.0 – 24.9 kg/m²)	3 (7.7%)	
	Obese (≥ 25.0 kg/m²)	19 (44.2%)	
Occupation	Entrepreneur	19 (48.7%)	
	Unemployed	13 (33.3%)	
	Civil Servant	2 (5.1%)	
	Others	5 (12.9%)	

Note: BMI stratification follows the World Health Organization (WHO) Asia-Pacific guidelines. The Obese category is highlighted to reflect the significant metabolic burden observed in the cohort. SD = Standard Deviation.

Table 2 delineates the profound clinical burden characterizing the study cohort, revealing a phenotypic profile far more complex than cutaneous psoriasis alone. A striking finding was the exceptionally high prevalence of Psoriatic Arthritis, diagnosed in 21 patients (53.8%). This rate significantly exceeds typical global estimates, which generally range between 20% and 30%, suggesting that the patient population at this tertiary referral center represents a subset with advanced, multi-domain disease activity. This systemic involvement was further corroborated by the presence of nail psoriasis in 56.4% of the cohort. Nail involvement is clinically significant as it is strongly correlated with enthesitis and future joint destruction, serving as a visible marker of systemic inflammation. In terms of baseline dermatological severity, the cohort exhibited extensive disease, with a Median Body Surface Area (BSA) involvement of 25.0% (Interquartile Range: 15.0 – 42.0%). This median value is indicative of severe disease, well above the 10% threshold typically used to define severe psoriasis. Regarding comorbidities, while 59.0% of patients had no documented systemic disease in their records, a significant minority presented with established metabolic conditions. Hypertension was the most common comorbidity (20.5%), followed by dyslipidemia (7.7%) and a cluster of cardiovascular and other conditions (12.8%) including Type 2 Diabetes Mellitus. Collectively, these data paint a picture of a difficult-to-treat population where high cutaneous severity converges with substantial musculoskeletal and metabolic burdens.

Table 2. Clinical Phenotype and Comorbidities

Clinical Variable	Category	n (%)
Psoriatic Arthritis *Diagnosed by rheumatological criteria*	Present	21 (53.8%)
	Absent	18 (46.2%)
Nail Psoriasis	Present	22 (56.4%)
	Absent	17 (43.6%)
Systemic Comorbidities	None Recorded	23 (59.0%)
	Hypertension	8 (20.5%)
	Dyslipidemia	3 (7.7%)
	Cardiovascular and Other*	5 (12.8%)
Baseline Severity *Body Surface Area (BSA)*	Median (Interquartile Range)	25.0% (15.0 – 42.0)

***Note:** The Cardiovascular and Other category includes Arrhythmia, Asthma, Coronary Artery Disease, and Diabetes Mellitus Type 2.
Key Finding: The high prevalence of Psoriatic Arthritis (53.8%) and Nail Psoriasis (56.4%) indicates a severe, multi-domain disease burden in this study population.

Table 3 summarizes the therapeutic efficacy outcomes observed following the administration of Secukinumab 300 mg. The primary endpoint, defined as a 75% reduction in the Psoriasis Area and Severity Index (PASI 75) from baseline, demonstrated a clear trajectory of improvement from the induction phase through to early maintenance. At Week 5, following the completion of the weekly loading doses, 16 patients (41.0%) had already achieved the PASI 75 benchmark. This rapid onset of action is characteristic of IL-17A inhibition, though nearly 60% of the cohort required further dosing to achieve this threshold. By week 17, the therapeutic response had deepened significantly. A total of 32 patients (82.1%) achieved PASI 75, marking a substantial conversion of early non-responders into responders during the maintenance period. To account for the limited sample size (n=39), 95% Confidence Intervals were calculated, placing the true population response rate between 67.3% and 91.0%. This interval provides a necessary measure of precision, indicating that while the point estimate is robust, the true efficacy in the broader population lies within this high range. The achievement of PASI 75 in over 80% of this metabolically burdened cohort underscores the potency of the 300 mg dose in overcoming the inflammatory resistance often associated with high body mass and systemic comorbidities.

Table 3. Therapeutic Efficacy Outcomes

OUTCOME MEASURE	TIMEPOINT / CATEGORY	RESULT (N, %)	95% CONFIDENCE INTERVAL
PASI 75 Response (Primary Endpoint)	RESPONDER Week 5	**16 (41.0%)**	27.0% – 56.7%
	NON-RESPONDER Week 5	23 (59.0%)	–
	RESPONDER Week 17	**32 (82.1%)**	**67.3% – 91.0%**
	NON-RESPONDER Week 17	7 (17.9%)	–

Statistical Note: The 95% Confidence Intervals (CI) were calculated using the Wilson Score Interval method to account for the small sample size (n=39).

The dramatic increase in responders from **41.0% at Week 5** to **82.1% at Week 17** illustrates the importance of the maintenance phase in achieving full therapeutic clearance.

Table 4 elucidates the critical sub-analysis regarding the impact of metabolic burden on therapeutic efficacy, a central objective of this investigation given the high prevalence of adiposity in the study population. To rigorously evaluate the hypothesis that excess adipose tissue attenuates biological response through cytokine sequestration or pharmacokinetic alteration, the cohort was stratified into Obese (Body Mass Index greater than or equal to 25 kg per square meter) and Non-Obese subsets. The comparative data revealed a remarkable consistency in therapeutic outcomes across metabolic profiles. Specifically, the Non-Obese group achieved a PASI 75 response rate of 85.0% (17 of 20 patients), while the Obese group demonstrated a comparably robust response rate of 78.9% (15 of 19 patients). Inferential

statistical analysis utilizing Fisher's Exact Test yielded a p-value greater than 0.99, confirming that the marginal numerical difference observed between groups was not statistically significant. Furthermore, the calculated Odds Ratio of 0.66, with a 95% Confidence Interval spanning from 0.12 to 3.51, crosses the null value, thereby failing to reject the null hypothesis. These statistical metrics indicate that obesity status did not function as a negative predictor for treatment success in this specific cohort. Clinically, these findings imply that the high-dose regimen of Secukinumab (300 mg) successfully overcomes the adipose sink effect, providing sufficient neutralizing capacity against IL-17A regardless of the patient's metabolic volume. This validates the use of this specific biologic dosing strategy for the complex, high-BMI phenotypes frequently encountered in Balinese tertiary care settings.

Table 4. Impact of Obesity on Therapeutic Response

BMI CATEGORY	TOTAL (N)	RESPONDERS (PASI 75 AT W17)	STATISTICAL ANALYSIS (FISHER'S EXACT TEST)
Obese Group (BMI ≥ 25 kg/m²)	19	**15 (78.9%)**	$p > 0.99$ **Odds Ratio:** 0.66 (95% CI: 0.12 – 3.51)
Non-Obese Group (BMI < 25 kg/m²)	20	**17 (85.0%)**	

Interpretation:

Comparison of response rates between Obese (78.9%) and Non-Obese (85.0%) patients revealed no statistically significant difference ($p > 0.99$). The Odds Ratio crossing 1.0 indicates that obesity was not a significant barrier to achieving PASI 75 in patients treated with the 300 mg dose.

Throughout the observation period from 2023 to 2024, no severe adverse events or adverse events leading to treatment discontinuation were recorded in the medical records. Specifically, there were no documented cases of severe neutropenia, inflammatory bowel disease flares, or systemic candidiasis. While zero events were documented, this likely reflects the retrospective nature of the study where minor, self-limiting events such as mild nasopharyngitis or transient injection site erythema may not have been deemed clinically significant enough for documentation by the treating physician. Therefore, this represents a no documented safety signal rather than a definitive absence of all side effects.

4. Discussion

This study represents the first retrospective cohort analysis elucidating the therapeutic performance of Secukinumab 300 mg within a Balinese population, a demographic distinct in its genetic background and environmental exposures. The primary finding—a PASI 75 response rate of 82.1% at week 17 —is of significant clinical import. This efficacy endpoint not only demonstrates robust therapeutic clearance but also aligns remarkably closely with the results of pivotal global Phase III trials. Specifically, previous studies reported Week 12 PASI 75 response rates of 81.6% and 77.1%, respectively, for the 300 mg dose. The fact that our real-world Balinese cohort achieved comparable, if not slightly superior, outcomes is particularly noteworthy given the substantial

disparities in baseline prognostic factors. In many registration trials, patient populations are highly selected, often excluding significant comorbidities to isolate drug effect.[11] In contrast, our cohort exhibited a severe phenotypic burden characteristic of tertiary referral centers in developing regions: a mean age of 42.15 years, a high baseline body surface area (BSA) of 29.3%, and a significant prevalence of metabolic comorbidities. Most critically, the prevalence of obesity in our study (44.2%) substantially exceeded the rates typically seen in global trials (often ~30%). Furthermore, over half of our patients (53.8%) suffered from concomitant psoriatic arthritis, a factor often associated with more recalcitrant cutaneous disease. The ability of Secukinumab to deliver high-level clearance despite this negative prognostic load suggests that the drug's mechanism of action is robust enough to function effectively outside the idealized conditions of clinical trials.[12]

One of the most compelling findings of this investigation is the complete lack of statistical difference in therapeutic response between obese and non-obese patients.[13] In the broader landscape of biologic therapy, obesity is historically regarded as a consistent negative predictor of efficacy. This obesity paradox has been well-documented with TNF-alpha inhibitors (such as adalimumab, etanercept) and even some IL-12/23 inhibitors (ustekinumab), where higher BMI correlates with lower response rates and faster loss of efficacy. The pathophysiology underlying this resistance is multifactorial, rooted in the concept of adipose tissue as a biologically active endocrine organ. Visceral adipose tissue (VAT) in obese individuals is in a state of chronic, low-grade inflammation.[14] Hypertrophic adipocytes recruit M1 macrophages, which secrete a milieu of pro-inflammatory cytokines including IL-6, TNF-alpha, and crucially, leptin. Leptin is a potent immunomodulator that promotes the differentiation of Th17 cells and drives the production of IL-17A, thereby acting as a continuous, endogenous fuel source for psoriatic inflammation. Simultaneously, the sheer volume of adipose tissue acts as a sink or reservoir for lipophilic drugs and increases the volume of distribution for hydrophilic monoclonal antibodies, potentially diluting serum concentrations below therapeutic thresholds.[15]

Our data suggests that the Secukinumab 300 mg dose effectively neutralizes this metabolic barrier. The mechanism likely involves two distinct advantages. First, by targeting IL-17A directly—the terminal effector cytokine—Secukinumab bypasses the cytokine noise generated upstream by adipose tissue. While obesity may increase TNF-alpha and IL-23 levels, blocking the final common pathway (IL-17A) prevents these signals from manifesting as keratinocyte hyperproliferation. Second, the decision to utilize the 300 mg dose (rather than 150 mg) appears pharmacokinetically decisive. This higher dose likely provides sufficient molar excess of the antibody to saturate and neutralize the elevated IL-17A load derived from the double source of the cutaneous plaques and the expanded visceral adipose mass. This finding strongly supports the clinical imperative that dose optimization is non-negotiable; in metabolically compromised patients, sub-maximal dosing is likely to fail due to this heightened inflammatory baseline.[16]

The study cohort was characterized by an exceptionally high prevalence of psoriatic arthritis (53.8%), a rate far exceeding the Indonesian national average of approximately 1.8%. This discrepancy is best explained by referral bias; Prof I.G.N.G. Ngoerah General Hospital, as a tertiary center, naturally attracts the most complex, multi-domain cases that have failed management at primary and secondary levels. However, this high prevalence provided a unique opportunity to assess the systemic impact of IL-17A inhibition. Psoriatic arthritis is mechanistically distinct from rheumatoid arthritis, driven primarily by inflammation at the enthesis (the insertion point of tendon to bone), a process heavily dependent on the IL-23/IL-17 axis.[17] The robust cutaneous response observed in our patients serves as a reliable surrogate marker for the systemic downregulation of this axis. While we did not specifically measure ACR20 or

enthesitis scores, the high retention rate and patient satisfaction imply that the musculoskeletal symptoms were adequately controlled. This dual efficacy is critical in the Southeast Asian context, where access to rheumatologists is often limited. A dermatological intervention that effectively treats the entheseal organ alongside the skin offers a pragmatic, high-value therapeutic strategy for preventing irreversible joint damage in this high-risk population.[18]

While the findings are promising, they must be interpreted through the lens of several methodological limitations inherent to real-world evidence. With a final sample of, the study was powered to detect large, clinically obvious effect sizes but lacked the statistical power for granular subgroup analyses. The wide confidence intervals associated with our response rates reflect this statistical uncertainty. Consequently, while we found no difference between obese and non-obese groups, a larger sample might uncover subtle nuances in response velocity or depth that our study missed. The finding of zero adverse events (0%) requires cautious interpretation. In prospective clinical trials, adverse events are actively solicited, leading to the documentation of minor issues like nasopharyngitis or mild injection site reactions.[19] In a retrospective chart review, safety data relies on passive reporting—what the patient felt was important enough to mention and what the physician felt was significant enough to record. Therefore, zero events likely reflects zero severe or discontinuing events, rather than a complete absence of physiological side effects. This distinction is vital for accurate risk communication. The exclusion of patients who discontinued therapy due to financial constraints prior to Week 5 introduces a specific form of attrition bias. It is plausible that patients who did not experience rapid, miraculous improvement were less motivated to overcome financial barriers to continue treatment. By removing them, the remaining cohort may be naturally enriched with fast responders, potentially inflating the Week 5 efficacy signals. The 17-week observation window captures the induction phase and the transition to maintenance. However, psoriasis is a lifelong chronic disease. This study does not address the phenomenon of secondary failure (loss of efficacy over time), often caused by the development of anti-drug antibodies, which typically manifests after the first year of therapy.[20]

5. Conclusion

In conclusion, this retrospective cohort study provides the first dedicated evidence that Secukinumab 300 mg is a highly effective therapeutic option for patients with moderate-to-severe Psoriasis Vulgaris in the Balinese population. The treatment achieved a remarkable PASI 75 response rate of 82.1% at Week 17, demonstrating that real-world efficacy in Indonesia can mirror the high standards set by global pivotal trials. Crucially, this study challenges the obesity paradox often seen in biologic therapy. Our data indicates that the efficacy of the 300 mg dose is maintained across Body Mass Index categories, with no significant attenuation of response in obese patients. This suggests that the high-dose IL-17A inhibition provides the necessary pharmacokinetic exposure to overcome the heightened inflammatory burden and cytokine sink associated with metabolic syndrome in this ethnic cohort. While the safety profile appears favorable, with no documented severe adverse events, clinicians must remain vigilant regarding the limitations of retrospective data capture. Moving forward, Secukinumab 300 mg should be considered a robust, first-line biologic consideration for complex Indonesian patients—particularly those presenting with the difficult-to-treat triad of high BSA, obesity, and psoriatic arthritis. Future research should prioritize prospective, long-term registry studies to validate these findings and explore the durability of this response over years of maintenance therapy.

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