THE EFFICACY AND SAFETY OF SECUKINUMAB 150MG REGIMEN IN TREATING PATIENTS WITH PSORIASIS VULGARIS

Tran Son Tung[1], Hoang Thi Phuong[2], Quach Thi Ha Giang[2], Le Thi Hai Yen[2], Dang Thi Luong[2], Trinh Thi Linh[2], Nguyen Thi Mai Huong[2], Dao Huu Ghi[2], Pham Thi Lan[1,2,*]

SUMMARY

Objectives: Evaluate the effectiveness and safety of secukinumab 150mg subcutaneous injection regimen in treating patients with moderate to severe psoriasis vulgaris.

Subjects and methods: Prospective clinical trial on 32 patients with moderate to severe psoriasis. Patients were treated with secukinumab 150mg subcutaneous injection regimen for weeks 0, 1, 2, 3, 4, 8, 12, 16. Evaluate treatment response with PASI, DLQI and IGA 2011 and record adverse effects during 16 weeks.

Results: After 16 weeks of treatment, PASI and DLQI gradually decreased during the period. The proportion of PASI 75 responses was highest at week 12 with 90.7%, while the proportion of PASI 90 and PASI 100 responses increased continuously until week 16, with 75% and 25% at week 16 respectively. There is a correlation between patients' weight and the efficacy of the regimen. 3 cases (9.4%) experienced adverse effects, including fatigue, nasopharyngitis and shingles.

Conclusions: Secukinumab 150mg regimen showed as an effective therapy with minor adverse events in the treatment of patients with moderate to severe psoriasis vulgaris.

Keywords: *Psoriasis, Secukinumab, Biologic.*

1. INTRODUCTION

Psoriasis is one of the major problems in global dermatology, with an incidence in the general population ranging from 0.91 - 8.5%[1]. According to the data of the US in 2005, the financial burden of psoriasis in this country was up to 35.2 billion USD[2]. Psoriasis vulgaris with skin lesions are scaling papules and plaques that can be seen in any sites of the body, usually affected the scalp and rubbed areas. Treatment of psoriasis depends on the severity of the disease. Topical therapy, phototherapy, and systemic agents (such as methotrexate (MTX), acitretin, cyclosporin A...) may control the disease[3]. However, these therapies have not been highly effective in treatment with a significant recurrence rate.

[1]Hanoi Medical University
[2]National Hospital of Dermatology and Venereology
** Correspondence: Email: lanphamthi009@gmail.com*
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Biologics target mediators in the pathogenesis of psoriasis, of which IL-17A is an important cytokine. Secukinumab is a recombinant human monoclonal immunoglobin G1 that selectively inhibits IL-17A[4]. In January 2015, secukinumab was approved by the Food and Drug Administration (FDA) to use the 300mg regimen and consider the 150mg regimen in some patients to treat plaque psoriasis. In March 2017, the Ministry of Health of Vietnam licensed secukinumab (Fraizeron) to treat moderate to severe plaque psoriasis. The effectiveness of secukinumab has been proven through many studies in Vietnam and all over the world[5,6]. However, the cost of treatment remained the major factor restraining biological therapy. Therefore, we conducted this study to evaluate the effectiveness and safety of the secukinumab 150mg regimen in the treatment of moderate to severe vulgaris psoriasis.

2. MATERIALS AND METHODS

2.1. Study population

The study population consisted of 32 adult patients diagnosed with moderate to severe psoriasis vulgaris in National Hospital of Dermatology and Venereology from August 2022 to June 2023. Included patients have never been treated with secukinumab before. In addition, we excluded patients with contraindications or warnings to secukinumab, such as drug hypersensitivity, active infections (bacterial, tuberculosis…), pregnancy, nursing mother and Crohn's disease.

2.2. Study design

This is a prospective clinical trial. The patient was examined and diagnosed with moderate to severe psoriasis vulgaris. Patients signed the informed consent form to participate in the study. They followed secukinumab 150mg subcutaneous injection at weeks 0, 1, 2, 3, 4, 8, 12, 16. The medicine product utilized in this study was Fraizeron (secukinumab 150mg in the form of a vial of powder for solution in subcutaneous administration). This material was approved by the Ministry of Health of Vietnam. We evaluated the effectiveness with psoriasis area and severity index (PASI), body surface area (BSA), investigator's global assessment 2011 (IGA2011), dermatology life quality index (DLQI), and recorded adverse events during 16 weeks.

2.3. Statistical analysis

Data entry and analysis were processed by SPSS software version 20.0. Frequency and descriptive statistics were used, combined with quantitative comparison statistical tests (T-Test for standard normal distribution variables and Mann - Whitney test, Wilcoxon test for non-standard normal distribution variables, standard distribution of quantitative variables was examined by Shapiro - Wilk test), frequency comparison (Chi-square or Fisher Exact test if ≥ 20% of expected frequency < 5). Linear regression analysis was utilized to identify the association between treatment effectiveness and patient characteristics.

2.4. Ethical approval

The study was approved by the Ethics Committee of the National Hospital of Dermatology and Venereology in August 2022.

3. RESULTS

3.1. Baseline characteristics

Table 1. Demographic and baseline clinical characteristics of the overall study population (N = 32)

Age (years)	39.1 ± 13.0 (22 - 77)	
Gender	Male	12 (37.5%)
	Female	20 (62.5%)
		p = 0.157
Disease duration (years)	9.3 ± 5.6 (2 - 25)	
Family history of psoriasis - Yes	3 (9.4%)	
Previous topical treatment - Yes	31 (96.9%)	
Previous MTX - Yes	10 (31.3%)	
Previous acitretin - Yes	3 (9.4%)	
Previous cyclosporin A - Yes	1 (3.1%)	
Previous phototherapy - Yes	1 (3.1%)	
Previous biologic - Yes	0	
HBsAg	Positive	0
	Negative	32 (100%)
Quantiferon (latent tuberculosis)	Positive	1 (3.1%)
	Negative	31 (96.9%)
Anti-HCV	Positive	0
	Negative	32 (100%)
Weight (kg)	56.8 ± 7.1 (43 - 78)	
Body mass index (BMI)	21.85 ± 1.92 (17.16 - 14.62)	
Baseline PASI	29.3 ± 10.4 (12.8 - 49.5)	
	Moderate	9 (28.1%)
	Severe	23 (71.9%)
Baseline BSA	Moderate	9 (28.1%)
	Severe	23 (71.9%)
Baseline DLQI	20.7 ± 4.7 (13-27)	
	Very large effect	13 (40.6%)
	Extremely large effect	19 (59.4%)

The study was conducted on 32 adult patients with the mean age of 39.1 ± 13.0 years, no gender differences and the weight ranging from 43 to 78 kg, with the average body mass index of 21.85 ± 1.92. Duration of disease varied from 2 - 25 years. 1 case with latent tuberculosis (positive Quantiferon test) and no patient positive with HBsAg and HIV test. In the study population, only 3 patients had a family history of psoriasis (accounting for 9.4%), most patients had been treated with topical

therapy previously (96.9%), the most common oral systemic agent was MTX (31.3%) while only 1 patient was previously treated with cyclosporin A. Only 1 patient (3.1%) had ever been treated with phototherapy and none had been previously treated with any biologics.

Regarding the severity before treatment, the mean PASI at baseline score was 29.2 ± 10.4, of which severe level accounted for 71.95%, this proportion was also equal to the number of severe patients calculated according to the BSA index. The baseline DLQI index was 20.7 ± 4.7, with a large or extremely large effect on patients' life.

3.2. The changes of PASI score during 16 weeks of regimen

Table 2. The changes of PASI score during 16 weeks of regimen (N = 32)

Week	0	1	2	3	4	8	12	16
PASI	29.2 ± 10.4	28.3 ± 1.8	25.7 ± 1.6	18.5 ± 1.5	12.2 ± 1.3	6.6 ± 1.0	3.4 ± 0.7	2.5 ± 0.7
p(compared to week 0)		0.000[a]	0.000[a]	0.000[a]	0.000[a]	0.000[b]	0.000[b]	0.000[b]

[a]standard normal distribution variable, examined by paired T-Test.

[b]non-standard normal distribution variable, examined by Wilcoxon's signed-rank test.

The PASI score gradually decreased during 16 weeks of treatment, with p < 0.001 (99% confidence) from the 1st week. PASI score decreased dramatically at week 3 (18.5 ± 1.5), statistically significant up to week 16 (2.5 ± 0.7).

3.3. The effectiveness over time with PASI 50, PASI 75, PASI 90 and PASI 100 responses

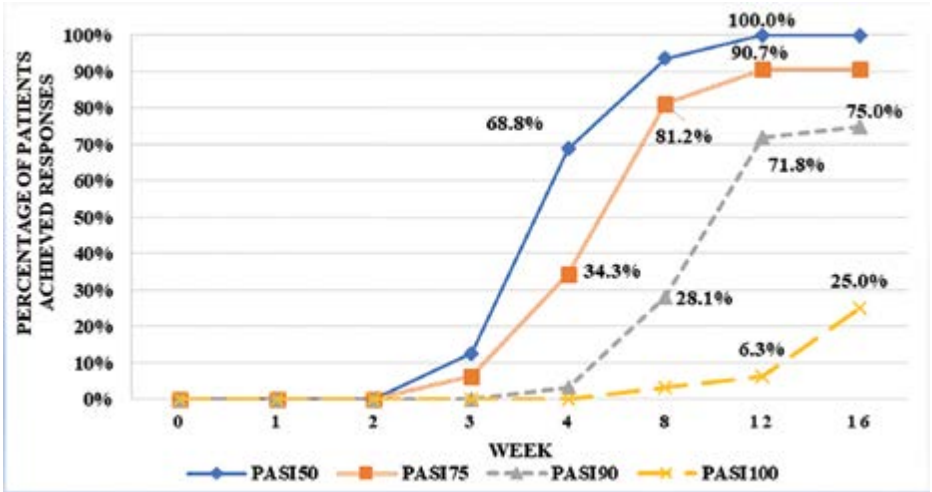
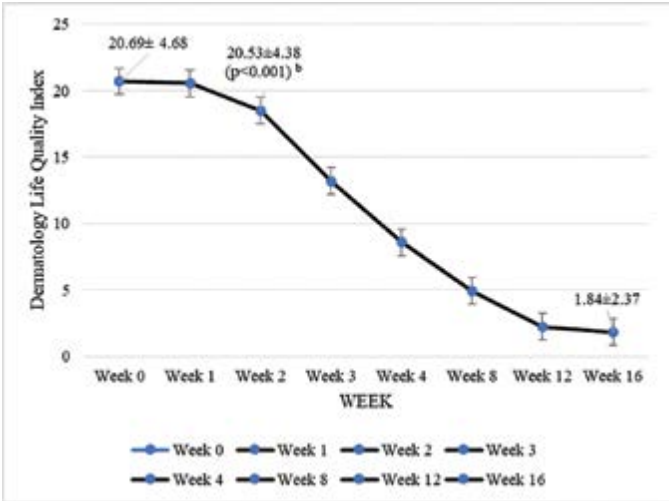


Figure 1. The effectiveness over time with PASI 50, PASI 75, PASI 90 and PASI 100 responses (N = 32)

The response began to occur at week 4, 68.8% of patients achieved PASI50 and 34.3% achieved PASI75. The PASI50 and PASI75 responses increased continuously until week 12 and remained constant, 100% and 90.7% of patients achieved PASI50 and PASI75 after 12 weeks, respectively. Regarding the PASI90 and PASI100 responses, there was a substantial increase from

the 8th week of treatment, and these continued to increase until the 16th week, with 25% of patients achieving PASI100 and 75% of patients achieving PASI90.

3.4. The changes in DLQI during 16 weeks of regimen



b : non-standard normal distribution variable, examined by Wilcoxon's signed-rank test

Figure 2. The changes in DLQI during 16 weeks of regimen (N = 32)

The change in the DLQI showed that the patient's quality of life gradually improved during the 16-week regimen. The DLQI decreased with statistical significance from week 2 ($p < 0.001$, 99% confidence level). By weeks 12 and 16, the mean DLQI was 2.25 and 1.84, respectively.

3.5. The percentage of IGA 2011 0/1 response over time

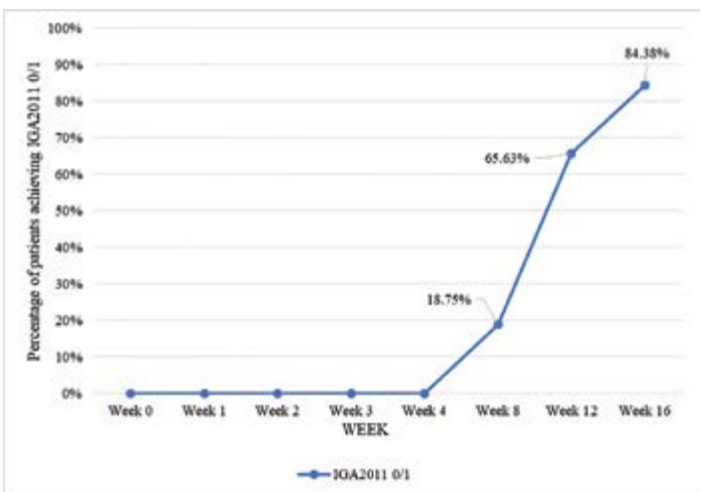


Figure 3. The percentage of IGA 2011 0/1 response over time (N = 32)

Patients were seen to achieve the IGA 2011 0/1 response (clear or almost clear lesions) from week 8, 18.75% of patients achieved IGA2011 0/1. This rate continued to increase until week 16 with 84.38% of patients achieving IGA 2011 response.

3.6. The correlation between PASI 90 response at week 16 and some factors

Table 3. The correlation between PASI 90 response at week 16 and some factors (N = 32)

Week 16	Weight	BMI	PASI before treatment
Achieved PASI 90 (n = 24)	55.21 ± 1.18	22.73 ± 0.58	27.42 ± 1.93
Does not reach PASI90 (n = 8)	61.50 ± 3.13	21.55 ± 0.40	34.89 ± 4.09
p	**0.027**	0.138	0.077

In the 16th week, there were 24 patients achieving PASI90 and 8 patients not achieving PASI90. Analysis showed that there was a difference in weight between the two groups (with p = 0.027, 95% confidence level), no difference in body mass index (BMI) and baseline severity of disease (PASI0).

3.7. The correlation between weight and efficacy

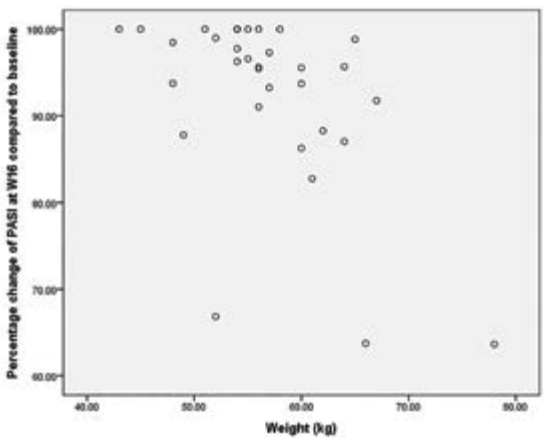


Figure 4. The scatter graph demonstrating the correlation between weight and efficacy

Regression analysis showed that weight and the percentage decrease of PASI at week 16 were strongly correlated with r = -0.513 and p = 0.003. The linear regression equation was formulated as % reduction in PASI at week 16 = - 0.758 x weight + 135.42.

3.8. The correlation between weight and PASI 90 response

Table 4. The correlation between weight and PASI 90 response at week 16 (N = 32)

	Weight < 60kg	Weight ≥ 60kg	p
Achieved PASI 90 T16	21 (87.5%)	3 (37.5%)	**0.012**
Does not meet PASI T16	3 (12.5%)	5 (62.5%)	
Total	24	8	

The Fisher Exact test showed that the group weighing less than 60kg had a statistically significantly higher rate of achieving PASI90 at week 16 (87.5%) than the group weighing 60kg or more (37.5%).

3.9. The safety of secukinumab 150mg regimen in patients with moderate-severe psoriasis vulgaris

Table 5. Adverse events over time (N = 32)

Adverse events	n	%
Fatigue and nasopharyngitis	2	6.3%
Shingles	1	3.1%
Total	3	9.4%

The percentage of patients experiencing complications during treatment was 9.4%, including 2 cases (6.3%) manifesting fatigue and nasopharyngitis and 1 case (3.1%) diagnosed with shingles on the left abdominal and lumbar region.

4. DISCUSSION

Secukinumab is a biologic that selectively targets IL-17A, an interleukin that has been proven to play a key role in the pathogenesis of psoriasis. Secukinumab 150mg regimen was recommended by the FDA and the manufacturer for use in some patients. Our study on 32 patients showed the average baseline PASI of 29.2 ± 10.4, of which the severe level was major with 71.9%, treated with the 150mg regimen. The baseline PASI of patients in our study is higher than in some clinical trials, suggesting that the severity of Vietnamese patients is higher when they find the biologic for treatment of psoriasis[6,7]. Results during the first 16 weeks showed that the PASI score gradually decreased but was significantly from week 0 to week 16, and DLQI gradually decreased but statistically significant from week 2. Patients achieved the highest PASI50 and PASI75 at week 12 and maintained the response until week 16, with the percentage at 100% and 90.7% of patients, respectively. Meanwhile, the proportion of patients achieving PASI90 and PASI100 continued to increase until week 16, with 75% and 25% of patients, respectively. A real-life cohort study in China on 47 patients with moderate-severe psoriasis showed that the highest percentage of patients achieving PASI75, PASI90 and PASI100 at week 12 and maintained until week 24 with 100%, 97.8% and 95.7%, respectively[7]. The patients in this study had a mean weight (61.89 ± 11.06 kg) higher than ours and the baseline PASI (14.34 ± 10.04) lower than ours[7]. A phase-3 clinical trial (ERASURE) on 245 patients with moderate-severe psoriasis treated with secukinumab 150mg regimen showed that the percentages of patients achieving IGA 0/1, PASI75, PASI90 and PASI100 responses at week 12 were respectively 51.2%, 71.6%, 39.1% and 12.8%, these outcomes are lower than our results[6]. The FIXTURE - phase-3 clinical trial also reported similar results to ERASURE, with the superior effectiveness of secukinumab 150mg regimen over etanercept, a biological drug in the TNF-α inhibitor group[6]. However, these 2 clinical trials were conducted on patients with higher weight and BMI than ones of our study population, despite lower baseline PASI. Another clinical trial

on 61 patients with an average weight of 93.7 ± 31.71 kg, significantly higher, also resulted in the rates of PASI75, PASI90 and PASI100 response at 71.7%, 40.0% and 16.7%, respectively[8]. The difference in our study results compared to the above clinical trials was an important reason for the research team to analyze factors related to treatment effectiveness.

Our study chose the PASI90 response at week 16 for analysis, due to the continuously significant decrease of PASI percentage from week 12 to week 16. The results showed that the patient's weight was associated with the rate of achieving PASI90 response at week 16, while other factors such as BMI and baseline PASI demonstrated no difference between the two groups achieving and not achieving PASI90 at week 16. In terms of patients' weight, there have been reports showing the correlation between weight and secukinumab blood concentrations or treatment response[9,10]. Another study showed that patients weighing 90 kg or more responded better to a maintenance regimen of 300mg every 2 weeks[11]. Our study found no difference in BMI between the response and non-response groups. This is unlike the results of Rompoti et al., the response of regimen and BMI have a statistically significant association[12]. Another study on 136 patients also found that BMI ≥ 30 was associated with poor treatment response to secukinumab[13]. These differences may be due to the sample size in our study not large enough, it is necessary to investigate this association with a larger number of patients.

During the 16-week follow-up period, we recorded 3 cases (9.4%) of adverse events. 2 patients (6.3%) manifested signs of fatigue and nasopharyngitis immediately after the first dose of the regimen. These symptoms worsened after each injection. After 3 - 4 weeks, the patients tolerated the therapy and the symptoms were absent. 1 case (3.1%) had shingles in the left abdominal and lumbar region at week 9, he was treated with acyclovir 800mg 5 times per day for 7 days and the skin lesion then was recovered without post-herpetic neuralgia. The study by Yan et al showed that the overall rate of adverse effects was 48.9%, of which nasopharyngitis was most common (8.5%), herpes simplex infection had a lower rate (2.1%), and many other manifestations such as skin infections, respiratory infections, pruritus, diarrhoea...[7] Another review on 692 patients showed diverse adverse events, the rate of patients treated with secukinumab 150mg regimen with symptoms of nasopharyngitis was 23.7%, higher than our results[14]. It is necessary to conduct a study with a larger sample size to evaluate adverse events and identify a more reliable rate.

Regarding the development of anti-drug antibody (ADA), there have been no report or evidence stated that use the 150mg regimen increase the risk of drug resistance. According to a systemic review, 0.2% of patients treated with secukinumab by any regimens detected ADA but the efficacy of treatment was not reduced. And no correlation was found between dosing and immunogenicity.[15] FIXTURE and ERASURE clinical trial also showed that the prevalence of anti-drug antibodies were detected in 0.3 - 0.4% but this phenomenon was not associated with adverse events or reduced efficacy[6].

However, to investigate the efficacy and safety of the 150mg regimen, we should conduct randomized controlled trial to compare this regimen to the 300mg regimen and placebo, in order to have more strong recommendations.

5. CONCLUSIONS

Secukinumab 150mg subcutaneous injection regimen at weeks 0, 1, 2, 3, 4, and repeated every 4 weeks in patients with moderate-severe psoriasis vulgaris showed the significant efficacy with minor adverse events. Patients' weight is a factor related to treatment effectiveness.

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Conflicts of interest: The authors commit to have no conflict of interest in this topic.

REFERENCES

1. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. *J Invest Dermatol*. Feb 2013;133(2):377-85. doi:10.1038/jid.2012.339.

2. Vanderpuye-Orgle J, Zhao Y, Lu J, Shrestha A, Sexton A, Seabury S, Lebwohl M. Evaluating the economic burden of psoriasis in the United States. *J Am Acad Dermatol*. Jun 2015;72(6):961-7.e5. doi:10.1016/j.jaad.2015.02.1099.

3. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. Feb 2021;84(2):432-470. doi:10.1016/j.jaad.2020.07.087.

4. Ahmed SS, De A, Das S, Manchanda Y. Biologics and Biosimilars in Psoriasis. *Indian J Dermatol*. May-Jun 2023;68(3):282-295. doi:10.4103/ijd.ijd_421_23.

5. Nguyen HT, Pham NTU, Tran TNA, Pham NN, Bui YT, Vu TTP. Long-Term Effectiveness and Drug Survival of Secukinumab in Vietnamese Patients with Psoriasis: Results from a Retrospective ENHANCE Study. *Dermatol Ther (Heidelb)*. Feb 2023;13(2):465-476. doi:10.1007/s13555-022-00867-y.

6. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis--results of two phase 3 trials. *N Engl J Med*. Jul 24 2014;371(4):326-38. doi:10.1056/NEJMoa1314258.

7. Zhao Y, Cai L, Liu XY, Zhang H, Zhang JZ. Efficacy and safety of secukinumab in Chinese patients with moderate-to-severe plaque psoriasis: a real-life cohort study. *Chin Med J (Engl)*. May 4 2021;134(11):1324-1328. doi:10.1097/cm9.0000000000001510.

8. Paul C, Lacour JP, Tedremets L, et al. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). *J Eur Acad Dermatol Venereol*. Jun 2015;29(6):1082-90. doi:10.1111/jdv.12751.

9. Lee JE, Wang J, Florian J, Wang YM, Kettl D, Marcus K, Woitach A. Effect of Body Weight on Risk-Benefit and Dosing Regimen Recommendation of Secukinumab for the Treatment of Moderate to Severe Plaque Psoriasis. *Clin Pharmacol Ther*. Jul 2019;106(1):78-80. doi:10.1002/cpt.1478

10. Bruin G, Loesche C, Nyirady J, Sander O. Population Pharmacokinetic Modeling of Secukinumab in Patients With Moderate to Severe Psoriasis. *J Clin Pharmacol*. Jul 2017;57(7):876-885. doi:10.1002/jcph.876.

11. Reich K, Puig L, Szepietowski JC, et al. Secukinumab dosing optimization in patients with moderate-to-severe plaque psoriasis: results from the randomized, open-label OPTIMISE study. *Br J Dermatol*. Feb 2020;182(2):304-315. doi:10.1111/bjd.18143.

12. Jiang C, Zhou H, Zhang W, et al. Efficacy, Safety and Pharmacokinetics of IL-17 Monoclonal Antibody Injection (AK111) in Patients with Moderate-to-Severe Plaque Psoriasis: A Randomized, Double-Blinded, Placebo-Controlled Phase Ib Multidose Escalation Clinical Study. *Dermatol Ther (Heidelb)*. Feb 2023;13(2):555-567. doi:10.1007/s13555-022-00880-1.

13. Notario J, Deza G, Vilarrasa E, et al. Treatment of patients with plaque psoriasis with secukinumab in a real-life setting: a 52-week, multicenter, retrospective study in Spain. *J Dermatolog Treat*. Aug 2019;30(5):424-429. doi:10.1080/09546634.2018.1528000.

14. Kircik L, Fowler J, Weiss J, Meng X, Guana A, Nyirady J. Efficacy of Secukinumab for Moderate-to-Severe Head and Neck Psoriasis Over 52 Weeks: Pooled Analysis of Four Phase 3 Studies. *Dermatol Ther (Heidelb)*. Dec 2016;6(4):627-638. doi:10.1007/s13555-016-0139-0.

15. Thomas LW, Lee EB, Wu JJ. Systematic review of anti-drug antibodies of IL-17 inhibitors for psoriasis. *J Dermatolog Treat*. Mar 2019;30(2):110-116. doi:10.1080/09546634.2018.1473552.