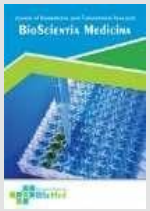
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Secukinumab Therapy on Psoriasis at Dr. Mohammad Hoesin General Hospital Palembang

Nopriyati[1*], Rio Tampubolon[1], Sarah Diba[1], M Athuf Thaha[1], Theresia L Toruan[1], Fitriani[1]

[1]Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sriwijaya/Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

ARTICLE INFO

Keywords:
Psoriasis
Biological agents
Secukinumab
Retrospective

***Corresponding author:**
Nopriyati

E-mail address:
nopriyati@fk.unsri.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v6i11.612

A B S T R A C T

Background: Psoriasis is a chronic inflammatory skin disease mediated by T lymphocytes. IL-17 or IL-22 plays an important role in the chronic inflammatory process. Secukinumab is an effective biological agent therapy with a molecular target, IL-17A. This study aimed to describe PASI improvement and safety of using secukinumab in psoriasis patients at the Dermatology and Venereology Clinic Dr. Mohammad Hoesin General Hospital Palembang. **Methods:** This study was a retrospective, descriptive-analytic study. The inclusion criteria of this study were all medical record data of patients diagnosed with cutaneous psoriasis through anamnesis, clinical and histopathology examination, treated with secukinumab from January 2018 to December 2020. **Results:** Psoriasis patients with secukinumab therapy were 15 people. The number of male patients was 8 people, the mean age (+ SD) was 40.4, + 12.34 years, and the age range was 19-64 years. A family history of psoriasis was present in 2 patients (13.4%). Psoriasis vulgaris was the most prevalent type of psoriasis and was treated with secukinumab in 8 patients (53.3%). Another type was pustular psoriasis (20%) and erythrodermic psoriasis (26,7%). The triggers of exacerbations obtained in this study include occupation, hypertension, diabetes mellitus, obesity, smoking, and infections. PASI 75 was achieved by 13 patients (86.7%) at week 12, and all patients achieved DLQI<5. There were no adverse events during the use of secukinumab. **Conclusion:** The improvement of PASI and DLQI scores were achieved at week 12 in accordance with previous studies. Risk factors do not reduce the therapeutic effect of secukinumab in achieving PASI 75.

1. Introduction

Psoriasis is a chronic inflammatory skin disease mediated by immunologic disorders.[1] The prevalence of psoriasis varies, ranging from 2-3% in Europe and the United States, 1.99% in Australia and Asia, and 0.14% in Southeast Asia.[2,3] This disease can affect both men and women, with the most common age range being 15-30 years.[1] Onset less than 40 years is related to the HLA gene and family history with psoriasis.[4]

T lymphocytes play an important role in the pathogenesis of psoriasis. CD8+ T cells are predominantly located in the epidermis, and CD4+ T cells are predominantly located in the upper dermis. CD8+ T cells convert Tc17 to Tc1 and Th17 to produce IL-17, IL-22, TNF-α, and IFN-α, while a subset of CD4+ T cells, Th 17 and Th 22 cells, also produce IL-17 and IL22. Innate lymphoid cell 3 (ILC3) in psoriatic lesions also produces IL-17 and IL-22 cytokines. Cytokines IL-17 and IL-22 have been shown to play a major role in chronic inflammation of psoriasis.[1]

The clinical features that are often found are papules to thick erythematous plaques and layered scales accompanied by itching.[1,5] Risk factors for psoriasis include obesity, smoking, infection, and drugs.[1,4] Symmetrical distribution of lesions is often found on the extensor, scalp, lumbosacral extremities,

buttocks, and genitalia.[6] Histopathological examinations can be used to support the diagnosis of psoriasis. Typical features that can be found are thickening of the epidermis, parakeratosis, and elongation of dermal capillaries. Infiltration of inflammatory cells in the epidermis causes accumulation in the stratum corneum parakeratosis called Munro's microabscess and in the spinosum layer called Kogoj spongiform pustules.[1,7]

Management of psoriasis requires long-term therapy for optimal improvement.[8] Biological therapy was started as a treatment for moderate-to-severe psoriasis and psoriatic arthritis in early 2000.[6] This therapy is one of the treatments for psoriasis based on advanced molecular biology research. Biological agents are designed to inhibit an important molecular step in the pathogenesis of psoriasis. Three types of biological agents play a role in psoriasis therapy: recombinant human cytokines, fusion proteins, and monoclonal antibodies. Biological therapy has shown improvement in psoriasis area severity index (PASI) values up to 50-70%, quality of life, safety, and tolerability.[1] Biological agent has better antipsoriatic activity, with a lower risk of hepatotoxicity than methotrexate (MTX).[9] Secukinumab is one of the Effective biologic agents of therapy for psoriasis and is derived from human antibodies. The molecular target of secukinumab biologic therapy, IL-17A, plays a role in binding and neutralizing IL-17A.[1,10] This study aimed to describe the effect of risk factors on the therapeutic effect of secukinumab on psoriasis.

2. Methods

This study was a retrospective, descriptive-analytic study. The inclusion criteria of this study were all medical record data of patients diagnosed with cutaneous psoriasis through anamnesis, clinical and histopathology examination, treated with secukinumab from January 2018 to December 2020. This research was approved by the National Health Research and Development Ethics Commission (KEPK) Dr. Mohammad Hoesin General Hospital Palembang (No. 35/kepkrsmh/2021).

Medical records of psoriasis patients at Dr. Mohammad Hoesin General Hospital Palembang were collected to obtain the number of psoriasis patients treated with secukinumab and the profile of these patients. This psoriasis patient profile assesses gender, age, occupation, family history, psoriasis type, risk factors, PASI, and DLQI. Patients' age was grouped into three types, i.e., type I: onset under 40 years, type II: onset over 40 years.[1,11] Type of psoriasis was determined based on clinical features.[1] Severity is measured by PASI. The body areas assessed include the head, trunk, and upper and lower extremities. PASI parameters that must be considered are the degree of erythema, induration, and scale.[12] Quality of life is measured by the dermatology life quality index (DLQI), in the form of 10 questions about the patient's physical, psychological and social function of the disease.[13] The patient's risk factors were obtained from medical record data: obesity, smoking habit, hypertension, diabetes mellitus type 2, and infection.[1,14] Data collection technique in this study used total sampling. The data collected was cleaned, editing and coding, and processed using the Statistical Analysis Software Package (SPSS) software version 22.0 (IBM Corporation, United States of America, 2013) and displayed in the form of tables and narratives. The relationship of risk factors with improvement in PASI scores was assessed by the Chi-square test.

3. Results

The number of patients from January 2018 to December 2020 at the Dermatology and Venereology (DV) Clinic of Dr. Mohammad Hoesin General Hospital Palembang was 8532 people. The number of Dermatology Allergo-Immunology patients is 2472 people. The total number of psoriasis patients was 845 people. The most in 2018 were 323 people (38.2%). The number of psoriasis patients who met the inclusion criteria was 15 people.

In this study, 8 people (53.3%) are male patients. The mean age of psoriasis patients in this study was 40.4$\pm$12.34 years, with an age range of 19-64 years.

Data on psoriasis patients by gender, age group, and family history of psoriasis showed in table 1.

In this study, 4 people were overweight (26.7%) and 4 obese (26.7%) based on the patient's BMI. Between BMI and PASI improvement do not have a significant association (p=0.579) (Table 3). There was a family history of psoriasis in 2 patients (13.4%). Psoriasis vulgaris was the most common type found in 8 patients (53.3%). Other types of psoriasis are listed in table 1.

Housewives was the most prevalent occupation in this study (40%) followed by the employee (26.4%), the most common risk factor for exacerbations was an infection in 9 people (60%) and 5 with smoking habits (33.3%), other risk factors are listed in table 1. The association between risk factors and PASI improvement is measured and recorded in table 3.

Secukinumab 150 mg was the most prevalent dose, administered in 10 people (66.7%). The severity of psoriasis was measured using the psoriasis area and severity index (PASI). In this study, the mean value of PASI was 10.7±6.23, with a range of values from 2 to 21. Improvement 75% from baseline PASI was called PASI 75. In this study, PASI 75 was obtained in 13 people (86.7%), and 2 people (13.3%) achieved PASI 50 after week 12. All patients got DLQI improvement, mean DLQI 1.93±0.59 at week 12 (Table 2).

Table 1. General characteristics.

	Number (n=15)	**Percentage (%)**
Gender		
Male	8	53.3
Female	7	46.7
Age group		
<40	6	40
>40	9	60
Family history with psoriasis		
Mother	1	6.7
Children	1	6.7
None	13	86.6
BMI		
Normal (18.5-24.99)	7	46.6
Overweight (≥25)	4	26.7
Obesity (≥30)	4	26.7
Psoriasis type		
Psoriasis vulgaris	8	53.3
Pustular psoriasis	3	20
Sebopsoriasis	0	0
Inverse psoriasis	0	0
Erythrodermic psoriasis	4	26.7
Occupation		
Housewife	6	40
Employee	4	26.4
Chef	1	6.7
Sport teacher	1	6.7
Driver	1	6.7
Student	1	6.7
Policeman	1	6.7
Risk factors		
Hypertension	2	13.3
DM type 2	2	13.3
Smoking	5	33.3
Gangrene radix dentis	5	33.3
Pulpa necrosis	1	6.7
Pulpitis	1	6.7
Blepharitis	1	6.7
Tonsilopharingitis	1	6.7
Secukinumab dose		
150 mg	10	66.7
300 mg	5	33.3
PASI at week 12		
PASI 75	13	86.7%
PASI 50	2	13.3%

Table 2. PASI and DLQI score before and after secukinumab therapy.

	Mean (±SD)		p-value*
	Baseline	**Week 12**	
PASI	10.7±6.23	2.2±2.24	0.001
DLQI	17.07±4.68	1.93±0.59	0.001

*Wilcoxon test, p=0.05

Table 3. Risk factors on PASI 75.

Risk factors	**PASI at week 12**		**Total**	**p-value**
	PASI 75 n(%)	**PASI 50 n(%)**		
BMI				
Normal (18.5-24.99)	6(85.7)	1(14.3)	7	0.579*
Overweight (≥25)	4(100)	0	4	
Obesity (≥30)	3(75)	1(25)	4	
Hypertension				
No	11(84.6)	2(15.4)	13	1.000**
Yes	2(100)	0	2	
DM type 2				
No	11(84.6)	2(15.4)	13	1.000**
Yes	2(100)	0	2	
Smoking				
No	9(90)	1(10)	10	1.000**
Yes	4(80)	1(20)	5	
Infection				
No	6(100)	0	6	0.486**
Yes	7(77.8)	2(22.2)	9	

*Pearson Chi-Square test, p=0.05.
**Fisher's exact test, p=0.05.

4. Discussion

Psoriasis is one of the most common chronic inflammatory skin diseases, with prevalence varying by region.[14] Global prevalence ranges from 0.1-5.1%, and in Southeast Asia, 0.14%.[2] Psoriasis vulgaris is the most common type, with 90% of total psoriasis patients.[15] In this study, the number of psoriasis patients was 845, 9.9% of patients at the DV Clinic of Dr. Mohammad Hoesin General Hospital Palembang period 2018-2020. The number of psoriasis patient visits has decreased in the last 2 years, most prevalent in 2018, which was 323 people. The most common type of psoriasis in the DV Clinic of Dr. Mohammad Hoesin General Hospital Palembang in 2018-2020 was psoriasis vulgaris, with a total of 671 people (74% psoriasis patients).

Secukinumab was the first anti-IL17A therapy approved by the US Food and Drug Administration (FDA) also European Medicines Agency for moderate-to-severe psoriasis and psoriatic arthritis management since 2015.[10] This biologic agent has been included in the Indonesian dermatologist and venereologist association (PERDOSKI) clinical practice guidelines (PPK) since 2017. Secukinumab has been used at the DV Clinic of Dr. Mohammad Hoesin General Hospital Palembang since 2018 for psoriasis therapy. This study recorded psoriasis patients receiving secukinumab therapy at the DV Clinic of Dr. Mohammad Hoesin General Hospital Palembang from 2018 to 2020. The number of patients at the DV Clinic of Dr. Mohammad Hoesin General Hospital Palembang who were treated with secukinumab was 16 people, but 1 person was excluded due to a diagnosis of cutaneous T-cell lymphoma (CTCL). The clinical picture of CTCL can be similar to psoriasis, and the histopathological examination of early-stage CTCL also shows psoriasiform dermatitis.[16] The number of patients treated with secukinumab is 1.8% of the total psoriasis patients at the DV Clinic of Dr. Mohammad Hoesin General Hospital Palembang. Patients receiving secukinumab therapy must meet the following restriction criteria: severe psoriasis, psoriatic arthritis, the patient does not respond well to at least 2 therapies (e.g., cyclosporine, methotrexate, or

phototherapy), has a history of hypersensitivity to systemic therapy, contraindications to conventional therapy. Secukinumab can also be given to psoriasis patients with special conditions, such as there are extensive lesions on the scalp that do not respond to topical drugs, involvement of visible areas (such as hands and face), and resistance to topical drugs.[17]

In this study, the number of male patients (53.3%) was more than female, and the mean age (±SD) of the patients was 40.4±12.34 years. The multicenter study of Ger et al. on 118 psoriasis patients who were treated with secukinumab during the period December 2015-March 2018 consisted of 88 men and 30 women, with a mean age (±SD) 48.0+13.8 years.[18] Multicenter study Galluzo et al., on 107 psoriasis patients treated with secukinumab during the period September 2015-May 2017, 75% were men with a mean age of 47.5 years.[10] Torres et al. also have 68% of 330 psoriases with secukinumab therapy were male, with mean age (±SD) 51.9+14.6 years.[19] Psoriasis has the same prevalence in men and women.[1]

Psoriasis can occur at any age. The onset <40 can be influenced by genetic factors.[1,14] In this study, there were 9 patients (60%) aged >40 years, all patients ranging from 19-64 years. Previous studies have shown that secukinumab can be used for psoriasis in children and the elderly. Dogra et al. reported a case of erythrodermic psoriasis in a 13-year-old child treated with secukinumab, achieved complete remission at week 8, and there were no adverse effects.[20,21] Henderson et al. found that secukinumab had a lower incidence of injection site reactions in pediatric patients than adalimumab, etanercept, and ixekizumab.[21,22] Elderly psoriasis patients (>65 years) reported good efficacy and safety with secukinumab therapy, although they often had comorbid diseases such as hypertension and type 2 diabetes mellitus (DM). Korber et al. compare secukinumab efficacy in young and old patients. PASI 75 obtained at week 52 of therapy were 81.8% and 79.4%, respectively.[21,23]

Genetic factors play a role in psoriasis onset <40 years and family history of psoriasis. Ger et al. found that 24.6% of patients had a family history of psoriasis.[18] Solmaz et al, showed that 31.9% of patients had a family history of psoriasis. In this study, there were 2 people (13.4%) with a family history of psoriasis. The genetic factor of human leukocyte antigen (HLA) class 1, HLA-Cw6, can trigger psoriasis and is prone to become more severe.[11,14]

In this study, 8 people (53.4%) with BMI >25 consisted of 4 overweight (26.7%) and 4 obese (26.7%). Table 3 showed that secukinumab response therapy does not affect BMI (p=0,579). Kiltz et al. obtained more overweight patients than in this study, who were 361 people (26.3%) and 519 obese (37.8%).[24] Galluzo et al. also obtained obesity was the most prevalent comorbid and showed there was no significant association with secukinumab response therapy.[10] Imafuku et al. also supported these findings and showed no significant relationship between PASI improvement in obese patients. Imafuku et al. stated that sex, age, and weight did not affect the efficacy and safety of secukinumab therapy.[25, 26]

The types of psoriasis receiving secukinumab therapy in this study included: 8 psoriasis Vulgaris patients (53.3%), 3 pustular psoriases (20%), and 4 erythrodermic psoriases (26.7%). Secukinumab has been clinically tested in phase III and is widely used for the treatment of psoriasis vulgaris, while in pustular psoriasis and erythrodermic psoriasis, it has also been reported to have good efficacy. Georgakopoulos et al. recorded the administration of secukinumab in 41 patients with plaque psoriasis. All patients achieved PASI 75 at week 12.[27] Imafuku et al. conducted a clinical trial of secukinumab therapy in 12 generalized pustular psoriasis patients, and showed that 10 patients (83.3%) achieved PASI 75 at week 16, 2 patients discontinued therapy because increasing liver function due to alcohol consumption.[25] Damiani et al. also conducted a clinical trial on 13 erythrodermic psoriasis patients, which showed 5 patients (38,5%) achieved PASI 75, 3 PASI 90 (23.1%), and 4 PASI 100 (30.8%).[28]

The risk factors for psoriasis exacerbations are divided into extrinsic factors and intrinsic factors. Extrinsic factors include mechanical stress, air

pollution, drugs, vaccines, infections, smoking, and alcohol consumption. Intrinsic factors include metabolic syndrome, obesity, diabetes mellitus, dyslipidemia, hypertension, and mental stress.[14] Work can induce new lesions and psoriasis exacerbations. Occupational trigger factors include mechanical stress, UV light, and mild irritation.[29] In this study, the most prevalent occupations were housewives (40%) and 4 employees (26.4%). Chiriac et al.'s research, in 1236 psoriasis patients, the most frequent patient occupation data were retirees on 149 people (12.6%), while housewives were 4.37% people and employees 8.74%.[30]

Another extrinsic factor that was the most common in this study was an infection, consisting of 5 gangrene radix dentist (33.3%), 1 pulp necrosis (6.7%), 1 pulpitis (6.7%), 1 blepharitis (6.7%), and 1 tonsillopharyngitis (6.7%). Fujita et al. found that there were 6 fungal infections (2%) and tuberculosis (0.7%). These diseases did not affect the safety and therapeutic effect of secukinumab on psoriasis.[31] Similar to this study, the infection does not affect the response therapy of secukinumab on psoriasis (p=0.486).

Smoking can reduce the therapeutic effect of TNF-α and IL-17 inhibitory biologic agents because the nicotine in cigarettes activates nicotinic acetylcholine receptors, thereby increasing Th-1/Th-17 polarization and the production of pro-inflammatory cytokines, including TNF-α, IL-12, IL-17, IL-23, IL-1β, and IFN-α.[28] Ger et al., on 118 psoriasis patients, patients with smoking habits was obtained in 41.5% of patients.[18] Damiani et al., in patients with erythrodermic psoriasis who were treated with secukinumab, 7 patients have smoking habits (53.8%).[28] In this study, 5 patients (33.3%) have smoking habits. However, in this study, smoking habits did not affect the response to secukinumab treatment. There was no significant association between PASI improvement and smoking habits (p=1.000).

Hypertension and type 2 diabetes are also risk factors for psoriasis exacerbations. These comorbid can affect therapy to achieve a cure.[8,14] Ger et al., obtained 33% patients with hypertension and 17,8% type 2 DM.[18] Megna et al., study on 385 moderate-severe plaque psoriasis with secukinumab therapy, obtained the most frequent comorbid 32.1% hypertension, 14.8% dyslipidemia, and 13.9% type 2 diabetes.[32] In this study, obtained 2 patients hypertension (13,3%) and 2 type 2 diabetes (13,3%). Secukinumab has been reported to be effective in patients with the comorbid disease and who have failed previous biologic agents such as ustekinumab. Secukinumab is also used as a biological agent of choice in patients with chronic psoriasis with multiple comorbidities, including psoriatic arthritis, obesity, and congestive heart failure.[8] According to this study, comorbid hypertension and type 2 diabetes did not affect the response to therapy (p=1.000, respectively).

In this study, secukinumab 150 mg per injection was given to 10 patients (66.7%). Schwensen et al. compared secukinumab 150 mg per injection in 33 people with PASI 2-5 and 300 mg in 36 people with a higher PASI (5-12.5); the results, clinical remission was higher in the secukinumab 150 mg group. After 3 months of therapy with secukinumab, 150 mg was found to be PASI <2 in 82.6% of patients compared to 43.3% of patients with secukinumab 300 mg.[33] Imafuku et al., secukinumab 150 mg was given to PPG patients at initial loading dose at week 8, doses was increased to 300 mg. The results at week 16 of PASI 75 were achieved by 10 people (83.3%).[25] Langley et al. showed secukinumab 300 mg and 150 mg were faster in achieving PASI 50 (3 weeks and 3.9 weeks, respectively) compared to etanercept on 7 weeks (p<0.001). Psoriasis patients who achieved PASI 75 at week 12 of secukinumab therapy at a dose of 300 mg were 81.6%, while the dose of 150 mg was 71.6%.[10,18,34]

Treatment was successful if PASI 75 was achieved at week 12.[17] Galluzo et al. recorded that PASI improvement at week 12 consisted of PASI 75 by 64 patients (80%), 54 PASI 90 (67.5%), and 44 PASI 100 (55%).[10] Georgakopoulos et al. found that 41 patients (100%) with moderate-to-severe plaque psoriasis reached PASI 75 at week 12 of therapy.[27] This study

obtained data for PASI 75 at week 12 achieved by 13 patients (86.7%), while the other 2 patients had not been categorized as a failure of therapy because they could reach PASI 50. Secukinumab significantly reduced mean PASI at week 12 compared to the baseline (p=0.001).

The mean baseline DLQI (±SD) of the patients in this study was 17.07±4.68. This score means psoriasis is a very large effect on a patient's life (score: 11-20).[13] Psoriasis vulgaris patients with lesions in visible areas of the body, such as the face, arms, and legs, have low self-confidence. It puts high emotional stress that impacts work, activities, and relationships with other people. Psoriasis patients are more likely to avoid activities in public places because there is a feeling of stigmatization and social rejection.[35] PASI 50-75 are in the success criteria if the patients have a DLQI score <5.[17] In this study, all patients had DLQI scores significantly reduced at week 12 (p=0.001), mean DLQI (±SD) 1.93±0.59, the range 1-3. Megna et al. support this study. Mean DLQI at baseline is 11.7+2.8, achieved significant improvement at week 4, with mean DLQI (±SD) 4.0±3.6.[32]

Clinical trial data regarding the safety of secukinumab are still low.[8] Secukinumab adverse events reported in the previous study are respiratory tract infections, nasopharyngitis, arthralgia, and diarrhea.[18,25,31] Imafuku et al., in 12 pustular psoriasis patients, the most prevalent adverse events after secukinumab therapy were nasopharyngitis in 6 patients (50%).[25] Ger et al., in 118 psoriasis patients, the most prevalent adverse event reported is upper respiratory tract infections at 16.1% of patients and 7.6% of nasopharyngitis.[18] Phung et al. found no adverse events of secukinumab therapy in 12 patients with plaque psoriasis.[37] In this study, according to Phung et al. there are no adverse events in psoriasis patients.

The limitation of this study is that the health insurance only covers the cost of 6 doses of 150 mg of secukinumab therapy, so secukinumab therapy in patients with low socioeconomic status was discontinued. Data was only recorded until week 12 because 10 patients did not continue secukinumab therapy. Some patients were discontinued after initial therapy to avoid hospital visits due to the COVID-19 pandemic. The patient was satisfied with 6 times the initial treatment of secukinumab and then given continued therapy with methotrexate or cyclosporine. During the 2018-2020 period, there were no relapse data among these patients. Another limitation is that only research at one health center and research in several health centers is recommended to reduce the error rate of data on psoriasis patients with secukinumab therapy. Further research with more research subjects can support better research results.

5. Conclusion

The number of psoriasis patients receiving secukinumab therapy in the DV Clinic of Dr. Mohammad Hoesin General Hospital Palembang is increasing. Exacerbation precipitating factors such as obesity, hypertension, type 2 DM, smoking, and infection did not affect the response to therapy. Improvements in PASI and DLQI values were achieved at week 12 in accordance with previous studies. There are no adverse events during therapy.

6. References

1. Gudjonsson JE, Elder JT. Psoriasis. In: Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, eds. Fitzpatrick's Dermatology Vol 1 9ed. New York: McGraw Hill. 2019; 77:457-97.
2. Burden AD, Kirby B. Psoriasis and related disorders. In: Griffiths C, Barker J, Bleiker J, Bleiker T, Chalmers R, Creamer D. Rook's Textbook of Dermatology. 9th ed. New York: Wiley Blackwell. 2016; 4(35):1-48.
3. Parisi R, Iskandar IY, Kontopantelis E, Augustin M, Griffiths CE, et al. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modeling study. Br Med J. 2020; 369:1-10.
4. James WD, Elston DM. Treat JR, Rosenbach MA, Neuhaus IM. Seborrheic dermatitis,

psoriasis, recalcitrant palmoplantar eruption, pustular dermatosis, and erythroderma. In: James WD, Elston DM. Treat JR, Rosenbach MA, Neuhaus IM. Andrews Diseases of the skin. New York: Elsevier. 2020; 10:191-200.

5. Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis. Can Fam Physician. 2017;63(4): 278-85.
6. Van de Kerkhof PC, Nestle FO. Psoriasis. In: Bolognia JL, Scaffer JV, Cerroni L, eds. Dermatology. 4th ed. New York: Elsevier. 2018; 3(8):158-9.
7. Kim BY, Choi JW, Kim BR, Youn SW. Histopathological findings are associated with the clinical types of psoriasis but not with the corresponding lesional psoriasis severity index. Ann Dermatol. 2015; 27(1):26-31.
8. Augustin M, Jullen D, Peralta C. Real-world of secukinumab in psoriasis treatment-a meta-analysis of 43 studies. J Eur Acad Dermatol Venereol. 2020; 34:1174-85.
9. Gizondi P, Bellinato F, Bruni M, Angelis GD, Girolomoni G. Methotrexate vs secukinumab safety in psoriasis patients with metabolic syndrome. Dermatol Ther. 2020; 14281:1-5.
10. Galluzo M, Talamonti M, Simone CD, D'Adamio S, Moretta G, et al. Secukinumab in moderate to severe plaque psoriasis: a multicenter, retrospective, real-life study up to 52 weeks observation. Expert Opin Biol Ther. 2018: 1-33.
11. Solmaz D, Bakirci S, Kimyon G, Gunal EK, Dogru A, et al. Impact of having family history of psoriasis or psoriasis arthritis on psoriatic disease. J Am Coll Rheumatol. 2020; 72(1):63-9.
12. Otero ME, van Geel MJ, Hendriks JC, van de Kerkhof PC, Seyger MM, de Jong EM. A pilot study on the psoriasis area and severity index (PASI) for small areas: presentation and implications of low PASI score. J Dermatol Treat. 2014: 1-4.
13. Finlay AY. Principles of measurement and assessment in dermatology. In: Griffiths C, Barker J, Bleiker J, Bleiker T, Chalmers R, Creamer D. Rook's Textbook of Dermatology. 9th ed. New York: Wiley Blackwell. 2016; 16.1-8.
14. Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk factors for the development of psoriasis. Int J Mol Sci. 2019; 20(4347):1-14.
15. Berg SH, Balogh EA, Ghamrawi RI, Feldman SR. A review of secukinumab in psoriasis treatment. Immunother. 2020; 195:1-16.
16. De A, Raychaudury T, Rajagopalan M, Sarda A, Sharma M. A case of cutaneous T-cell lymphoma, masquerading as psoriasis, was given etanercept and secukinumab: Emphasizing the need for biopsy confirmation before starting biologics. Indian J Dermatol. 2017; 62(5):533-5.
17. Widaty S, Soebono H, Nilasari H, Listiawan MY, Siswati AS, et al. A clinical practice guide for dermatologists and venereal specialists in Indonesia. Jakarta: Perhimpunan Dokter Spesialis Kulit dan Kelamin Indonesia. 2017; 9:230-40.
18. Ger TY, Huang YH, Hui RC, Tsai TF, Chiu HY. Effectiveness and safety of secukinumab for psoriasis in real world practice: analysis of subgroups stratified by prior biologic failure or reimbursement. Ther Adv Chronic Dis. 2019; 10:1-9.
19. Torres T, Balato A, Conrad C, Conti A, Dapavo P, et al. Secukinumab drug survival in patients with psoriasis: a multicenter, real world, retrospective study. J Am Acad Dermatol. 2019; 81(1):273-5.
20. Dogra S, Bishnol A, Narang T, Handa S. Long term remission induced by secukinumab in a 13-years old boy having recalcitrant chronic erythrodermic psoriasis. Dermatol Ther. 2018; 31(4):1-2.

21. Wu JJ, Merola JF, Feldman SR, Menter A, Lebwohl M. Treatment of psoriasis with secukinumab in challenging patient scenarios: a review of the available evidence. Dermatol Ther. 2020; 10:351-64.
22. Berg MH, Carrasco D. Injection site reactions to biologic agents used in psoriasis and psoriatic arthritis. J Drugs Dermatol. 2017; 16(7):695-8.
23. Korber A, Pappavassilis C, Bhosekar V, Reinhart M. Efficacy and safety of secukinumab in elderly subjects with moderate to severe plaque psoriasis: a pooled analysis of phase III studies. Drugs Aging. 2018; 35(2):135-44.
24. Klitz U, Sfikakis P, Gaffney K, Sator P, Kiedrowski R, et al. Secukinumab use in patients with moderate to severe psoriasis, psoriasis arthritis, ankylosing spondylitis in real world setting in Europe: Baseline data from SERENA study. Adv Ther. 2020; 37:2865-83.
25. Imafuku S, Honma M, Okubo Y, Komine M, Ohtsuki M, et al. efficacy and safety of secukinumab in patients with generalized pustular psoriasis: a 52-week analysis from phase III open label multicenter Japanese study. J Dermatol. 2016; 43:1011-7.
26. Ohtsuki M, Morita A, Abe M. Secukinumab efficacy and safety in Japanese patients with moderate to severe plaque psoriasis: sub-analysis from ERASURE, a randomized, placebo-controlled, phase III study. J Dermatol. 2014; 41:1039-46.
27. Georgakopoulos JR, Igbani A, Phung M, Yeung J. Drug survival of secukinumab in real-world plaque psoriasis patients: a 52-week, multicenter, retrospective study. J Am Acad Dermatol. 2017; 78(5):1019-20.
28. Damiani G, Pacifico A, Russo F, Pigatto P, Bragazzi N, et al. Use of secukinumab in a cohort of erythrodermic psoriatic patients: a pilot study. J Clin Med. 2019; 8(6):770.
29. Mahler V, Diepgen T, Skudlik C, Becker D, Dickel H, et al. Psoriasis predisposition and occupational triggering factors in the appraisal of occupational medical expertises. J Dtsch Dermatol Ges. 2014: 12(6):519-29.
30. Chiriac A, Solovan C, Pinteala T, Chiriac AE, Brzezinski P, et al. The relationship between psoriasis and specific professional activities or occupationa-induced skin diseases. Shiraz E-Med J. 2015; 15(2):1-6.
31. Fujita H, Ohtsuki M, Morita A, Nagao R, Seko N, et al. safety and effectiveness of secukinumab in psoriasis vulgaris and psoriatic arthritis: real-world evidence in Japan. J Dermatol. 2021; 48(2):173-83.
32. Megna M, Di Costanzo L, Argenziano G, Balato A, Colasanti P, et al. Effectiveness and safety of secukinumab in Italian patients with psoriasis: an 82-week, multicenter retrospective real-world study. Expert Opin Biol Ther. 2019; 19(8):8555-61.
33. Schwensen JF, Clemmensen A, Sand C, Gniadecki R, Skov L, et al. Effectiveness and safety of secukinumab in 69 patients with moderate to severe plaque psoriasis: A retrospective multicenter study. Dermatol Ther. 2017: 30(6):1-3.
34. Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths C, et al. Secukinumab in plaque psoriasis-results of two phases 3 trials. N Engl J Med. 2014; 371:326-38.
35. El-Moselhy, Hagrass SA, Mohammed AS, Abd-Alrhman T, Alnabawy A, et al. Psychosocial impact and quality of life among adult Egyptian patients with psoriatic arthritis. Egypt J Hosp Med. 2017; 66:237-47.
36. Yang EJ, Beck KM, Liao W. Secukinumab in treatment of psoriasis: patients selection and perspectives. Psoriasis (Auckl). 2018; 8:875-82.

37. Phung M, Georgakopoulos JR, Ighani A, Giroux L, Yeung J. Secukinumab dose optimization in adult psoriasis patients: a retrospective, multicenter case series. J Am Acad Dermatol. 2018; 4:310-3.