EFFICACY OF AND SAFETY OF SECUKINUMAB IN PSORIASIS VULGARIS; A PROSPECTIVE STUDY

ABSTRACT

Objective: Psoriasis is an immune mediated inflammatory skin disorder that potentially requires lifelong management. Different therapies treating psoriasis have been recognized wherein Secukinumab is a fully humanized, IL-17A monoclonal antibody that has been approved by US Food and Drug administration for the treatment of moderate to severe plaque psoriasis. Therefore, this study targeted to assess the efficacy of Secukinumab in patients with moderate to severe psoriasis.

Methodology: This was a Prospective interventional multicenter study conducted by using consecutive sampling technique. The duration of study was about one year. The sample size was 138. Adult patients between 18-65 years of either gender with clinical diagnosis of psoriasis vulgaris involving scalp, face, hands, or genital areas, were include. Treatment initiated by the administration of a single dose of 300 mg Secukinumab subcutaneously for 4 weeks then monthly for 52 weeks. Paired t-test was applied to assess the difference in the PASI score at various follow ups.

Results: The study results showed thatout of 138 patients, 112(81.2%) were males and 26(18.8%) were females and their mean age was 40.47 ± 9.55 years. As far as distribution of disease is concerned, 117(84.8%) patients reported Plaque Psoriasis, 57(41.3%) patients reported Scalp Psoriasis, 9(6.5%) patients reported nail Psoriasis, 11(8.0%) patients reported Palmoplantar Psoriasis, and 5(3.6%) patients reported Erythrodermic psoriasis. For the comparison of Secukinumab treatment under PASI scores, there was statistically significant reduction observed from mean of baseline PASI scores till 1 week ($p<0.001$), till 2 week ($p<0.001$), till 4 week ($p<0.001$), till 8 week ($p<0.001$). The improvement in mean PASI score from baseline to 1 year was 91 %.

Conclusion: This study concluded that Secukinumab is a highly effective, rapid-acting biological therapy with no obvious adverse effects. Additionally, it was seen that secukinumab

significantly reduced the baseline PASI score till 8 week rapidly in moderate and severe psoriasis.

INTRODUCTION

Psoriasis is a chronic, immune mediated inflammatory skin disease with approximately 120-180 million people who are affected worldwide, and its occurrence is predicted between 2%-11.8% [1,2]. World Health Organization documented psoriasis as a serious non-transmissible disease in 2014 and the associated WHO report in 2016 put emphasized on better realization of the morbidity related to the disease, globally [3].

Previous research particularly estimated the occurrence of psoriasis in adults range between 0.27% [4] and 11.4%,[5] with gender, age, geographical location, ethnicity, environmental and genetic factors participating to the differences in the occurrence of the disease.[6] It has been reported that higher occurrence rates were observed at elevated latitude as well as in white population as compared to other racial groups [7]. The Global Burden of Disease group has predicted the occurrence of psoriasis for 21 regions worldwide [8].

It is characterized by the erythematosus, scaly plaques most commonly found on the scalp, elbows, knees, and back. [9] It is now regarded as a systemic disease which is related with metabolic, psychological, arthritic, and cardiovascular comorbidities [10]. Mostly, Psoriasis can arise at any age but frequently it is more prevalent under 35 years of age [11].

Psoriasis usually affects the skin, but joints may also be affected. Inflammation is not only limited to the psoriatic skin but also involve the other organ systems. Psoriasis patients show evidence of hyperlipidemia, hypertension, type 2 diabetes, coronary artery disease, and raised body mass index in comparison with the healthy subjects [12], these metabolic disturbances were two folds more prevalent in psoriasis patients than healthy individuals [13].

Presently, the impact of psoriasis on psychosomatic and mental wellbeing is an imperative concern due to the influence of the disease on social health and management. Psoriasis patients have an elevated incidence of depression, anxiety and low self esteem. Amazingly, psoriasis management diminishes anxiety symptoms [14].

Generally, Psoriatic patients are divided into two groups: mild or moderate to severe psoriasis, based on the clinical severity of the inflammatory lesion, the proportion of affected area, and life expectancy [15].

Psoriasis is a multifaceted syndrome for which a variety of innovative treatment modalities have discovered in the earlier years. Despite of the discovery of novel therapies, psoriasis remains a treatable but still not curable disorder. According to mode of action, remedies treating psoriasis can be grouped into five classes: anti-interleukin-12/23 agents (anti-IL12/23), anti-interleukin-17 agents (anti-IL17), anti-metabolites (AM), anti-T-cell agent (ANT), and anti-tumor necrosis factor-α agent (anti-TNF-α) [16].

Until now, three human monoclonal antibodies targeting IL-17 are accessible. Secukinumab and ixekizumab selectively targets IL-17A causing inhibition of IL-17 receptor's contact with endothelial cells, keratinocytes, osteoblasts and chondrocytes [17].On the other hand, brodalumab is aimed in opposition to the IL-17 receptor A. Secukinumab was approved for psoriasis in 2015 as the first IL-17A inhibitor. Later on, it was also approved for the active psoriasis arthritic and ankylosing spondylitis [18]. Secukinumab's efficacy in psoriasis vulgaris has been proved to be superior to other numerous biological agents like etanercept and ustekinumab [19].

 A combination of glucocorticoids with vitamin D analogues topically along with phototherapy is used to treat mild to moderate psoriasis whereas systemic treatment frequently requires for moderate to severe type of psoriasis [16]. Biological factors targeting IL-17A have revealed higher effectiveness in treating moderate to severe psoriasis. Additionally, it has been reported that anti IL-17A agents has fast mode of action [20].

The targeted therapies demonstrated high clinical efficiency for the inhibition of IL-23 and IL-17. Some extent of a persistent antipsoriatic effect by these therapies could be established following discontinuation of drug [21,22].

Common undesirable effects due to IL-17 receptor inhibition are nasopharyngitis, headache, arthralgia, and upper respiratory tract infection. Moreover, IL-17 signaling is critical for the

acute defense in opposition to extracellular bacterial and fungal infections. Candidal infections are generally more reported in patients treating by anti-IL17 biological agents such as Secukinumab and ixekizumab than etanercept [18].

A number of researches have documented the recommendation of Secukinumab in treatment of psoriasis, but not any of the researches have been conducted in Pakistan, a South Asian country where the prevalence of moderate to severe psoriasis is highly observed. Therefore, it was imperative to assess the effectiveness and safety of Secukinumab in patients of psoriasis vulgaris.

MATERIAL AND METHODS

This was a Prospective interventional multicenter study conducted by using consecutive sampling technique. The duration of study was about one year after ethical approval of synopsis from the Institutional Review Board. A total of 138 adult patients between 18-65 years of either gender having psoriatic lesion involving scalp, face, hands, or genital areas, those patients who were treated only with Secukinumab for minimum four weeks, patients having PASI >10.0 at baseline were included in the study whereas those who were contra-indicated or intolerable to conventional treatment, on concomitant systemic therapy like methotrexate, acitretin or cyclosporine, on phototherapy (Ultraviolet B or psoralen plus ultraviolet A), were excluded.

Baseline demographics of patients for instance age, sex, height; weight, BMI, age at beginning of disease, duration of psoriasis, affected areas by psoriasis and Severity Index (PASI) at baseline and outcome of biological treatment, were documented. Treatment initiated by the administration of a single dose of 300 mg Secukinumab subcutaneously once a week for 4 weeks, followed up by once a month, for 52 weeks. Outcome measures of treatment were recorded clinically as PASI scores, with adverse effects both for moderate and severe psoriasis. Patients were followed up for 52 weeks. Data was analyzed using SPSS version 23.0. For quantitative variables mean and standard deviation were documented. Qualitative variables were recorded as frequency and percentages. Paired t-test was applied to assess the association between baseline and at various follow ups. P-value of <0.05 was considered as statistically significant.

RESULTS

A total of 138 patients diagnosed with Psoriasis vulgaris were enrolled for the study wherein 112 (81.2%) were males and 26 (18.8%) were females; their mean age was 40.47±9.55 years. Mean duration of Psoriasis was 7.95±4.85 years. Mean age at onset of disease was 32.41±10.54 years. Mean baseline PASI scores was reported 54.20±13.49, 4.42±7.36 at 4 weeks, 0.28±2.07 at 12 weeks, 0.18±1.77 at 24 weeks, 0.04±0.51 at 36 weeks, and 0.0±0.0 at 52 weeks, as shown in Table 1.

Only six (4.3%) patients showed history of cardiovascular disease, 19 (13.8%) patients showed history of Diabetes mellitus. Thirty-two (23.2%) patients showed history of hypertension and30 (21.7%) patients were smokers (Table 2).

As far as distribution of disease is concerned, 117 (84.8%) patients reported Plaque Psoriasis, 57 (41.3%) reported Scalp Psoriasis, 9 (6.5%) reported nail Psoriasis, 11 (8.0%) reported Palmoplantar Psoriasis, and 5 (3.6%) reported Erythrodermic psoriasis while 137 (99.3%) reported Pustular psoriasis (Table 3).

There was statistically significant reduction observed in all patients from mean of baseline PASI scores untul week one ($p<0.001$), until week two ($p<0.001$), until week four ($p<0.001$), and until week eight ($p<0.001$) (Table 4). Additionally, no significant side effects were observed.

Table 1: Demographic characteristics of Psoriasis patients (n=138)

Variable	Mean±SD n(%)
Age (years)	40.47±9.55
Duration of Psoriasis (years)	7.95±4.85
Age at Onset of disease (years)	32.41±10.54
Baseline (Psoriasis Area and Severity Index scores)	54.20±13.49
At 4 weeks	4.42±7.36
At 12 weeks	0.28±2.07
At 24 weeks	0.18±1.77
At 36 weeks	0.04±0.51
At 52 weeks	0.0±0.0

Table 2: Frequency of gender and history

Variable		n	(%)
Gender	**Male**	112	81.2
	Female	26	18.8
Smoking	**Yes**	30	21.7
	No	108	78.3
Specify Severity	**Moderate**	55	39.9
	Severe	83	60.1
Co-morbids	**Diabetes Mellitus** **Yes**	19	13.8
	Diabetes Mellitus **No**	119	86.2
	Hypertension **Yes**	32	23.2
	Hypertension **No**	106	76.8
	Cardiovascular Disease **Yes**	6	4.3
	Cardiovascular Disease **No**	132	95.7

Table 3: Frequency of areas of involvement in psoriasis

Variable		n	(%)
Itching	**Yes**	120	87.0
	No	18	13.0
Joint Involvement	**Yes**	1	0.7
	No	137	99.3
Plaque Psoriasis	**Yes**	117	84.8
	No	21	15.2
Scalp Psoriasis	**Yes**	57	41.3
	No	81	58.7
Nail Psoriasis	**Yes**	9	6.5
	No	129	93.5
Palmoplantar Psoriasis	**Yes**	11	8.0
	No	127	92.0
Erythrodermic psoriasis	**Yes**	5	3.6
	No	133	96.4
Pustular psoriasis	**Yes**	137	99.3
	No	1	0.7
Psoriatic Arthritis	**Yes**	1	0.7
	No	137	99.3

Table 4: Association of comparison of baseline PASI scores with different weeksin psoriasis patients.

Variable	Mean±SD vs Mean±SD	p-value
Baseline vs At 4 weeks	54.20±13.49vs4.42±7.36	<0.001
Baseline vs At 12 week	54.20±13.49vs 0.28±2.07	<0.001
Baseline vs At 24 weeks	54.20±13.49vs0.18±1.77	<0.001
Baseline vs At 36 weeks	54.20±13.49vs0.04±0.51	<0.001
Baseline vs At 52 weeks	54.20±13.49vs0.0±0.0	<0.001

DISCUSSION

The present study demonstrated that Secukinumab treatment led to rapid and sustained improvement in PASI scores with 90% response rate. The safety profile of Secukinumab remained favorable through one year with no adverse event.

A Prospective, cross-sectional study conducted in Lahore analyzed the study wherein sample size involved 56 males (64.4%) and 31 females (35.6%) thereby proved the male predilection in their study [23]. These findings were similar with our study and showed that 112 (81.2%) were males and 26 (18.8%) were females thereby proved male predominance.

Similarly, another research reported gender distribution of Psoriasis patients that was 71% males and 29% females [24]. Further researches conducted in Pakistan have revealed unpredictable statistics. One research from Jinnah Hospital, Lahore has reported 42% females and 58% males [25]. One more study from Liaquat University of Medical and Health Sciences has revealed 56%

males and 44% females [26]. As far as our study is concerned, male predominance was obvious and showed that 112 (81.2%) were males and 26(18.8%) were females.

Likewise, one study reported the mean age of affected patients was 39.8 years [24]. Further analysis based on Pakistani population have shown similar findings [26,27]. Another current research conducted in Korea has also revealed analogous findings [28]. Iran Research, the reported mean age was 33.3 years at onset of disease [29]. Our study was inconsistent with the above mentioned researches and observed the mean age of affected Psoriasis patient was 40.47±9.55 years.

Concerning area of involvement, one more study observed 46% patients involved joints whereas another study from Jinnah hospital Lahore proved joint involvement was observed in 35% patients [30]. On the other hand, an Iranian studyincluded 150 patients that reported joint involvement in 73% cases [27]. The present study was not in agreement with the above cited studies as there was only one (0.7%) patient involved joints. Similarly, one research found involvement of nail in 29% psoriasis patients [24]. Likewise, another small sample size study based completely on nail involvement has reported a rate of occurrence of 54% [27]. Our study was not supported by above studies and showed that Nail Psoriasis was found only in nine (6.5%) patients.

Globally, a number ofassociated comorbidities with psoriasis have been reported. Hypertension, Diabetes, psychologicaldisorder of varying degree and cardiovascular diseases have been related with psoriasis although in low frequency as shown in some study [24]. As far as our study is concerned, 19 (13.8%) psoriasis patients showed history of Diabetes mellitus along with 32 (23.2%) patients showed history of hypertension. Interestingly, one of the studies conducted in Japan analyzed the efficacy of secukinumab in psoriasis vulgaris and psoriatic arthritis using Psoriasis Area and Severity Index score (PASI). It was observed that mean PASI score was enhanced from baseline (14.7±12.3) to week 12 (1.78 ± 3.3), which was sustained until week 24(1.59 ±3.0). [31] As far as our study is concerned, it was found that mean PASI score was significantly improved from baseline (54.20±13.49) to week 8 (1.20±5.77) and sustained until 52 weeks.

Furthermore, above mentioned research demonstrated the Absolute PASI score and proposed that absolute PASI score of less than or equal to three [32,33] and less than or equal to two [34]

shows success of treatment by secukinumab, regardless of baseline PASI score. In our study, it was reported that reduction in PASI score from baseline to week eight in moderate and severe psoriasis patients indicated the successful treatment by the administration of secukinumab.

Many biological agents are accessible for management of plaque psoriasis, but these remedies differ in effectiveness and safety profile. Generally, IL-23 and IL-17 inhibitors reveal superior effectiveness as compared to TNF-α inhibitors, whereas further analysis on the mode of action of biologic agents revealed that IL-17, a inhibitors, work rapidly as compared to TNF-α inhibitors and ustekinumab [35]. Importantly, secukinumab caused PASI 75 rapid response in 25% of cases in duration of three weeks, therefore proving accomplishment of 50% reduction in PASI score [36]. Our study was consistent with the above study and showed that quick reduction in PASI score was achieved from baseline 54.20 ± 13.49 to week 8 1.20 ± 5.77 under treatment of secukinumab in psoriasis patients whereas our study did not compare the secukinumab with other IL-17 inhibitors.

Although the most fast-acting IL-17 inhibitor, brodalumab had a distressing effect such as depression, despite the definitive factor for depression with its use is vague [37]. On the other hand, Secukinumab has no alarming sign for depression and suicidal tendency. Hence, patients are occasionally more willing to initiate secukinumab treatment, instead of brodalumab or TNF-α inhibitors [36]. Our study demonstrated that there were no reported adverse effects of secukinumab therapy, thereby proved its superior clinical efficacy and effectiveness over the other biological therapies.

About 40% of psoriasis patients might grow psoriatic arthritis in their lifespan. Therefore, it is imperative to treat symptoms related to joints along with skin to prevent irreparable joint destruction. Hence, Secukinumab is one of six biological agents (that includes etanercept, adalimumab, infliximab, ustekinumab, and ixekizumab) recently accepted for the management of psoriatic arthritis along with psoriasis vulgaris. Secukinumab gives superior effectiveness following 52 weeks of treatment, but this biological agent might impede radiographic joint injury in psoriatic arthritis patients until two years.[38] Consequently, secukinumab presents an enduring treatment alternate for psoriatic arthritis patients that not only slow the damage to the joints but also prevents further damaging as well. Our study was inconsistent with the above cited studies and reported that there was only one (0.7%) patient showed the joint involvement thereby our study comprehensively focused the skin symptoms associated with psoriasis. The

large sample size of the study has assured that we have treated extensive range of psoriatic patients. However the study might not be immune from selection bias due to non probability sampling technique. Further studies with probability sampling technique are recommended to generalize the results

CONCLUSION

Secukinumab has superior efficacy with excellent skin clearance. Thus it offers the potential for equal or improved therapeutic effects as compared to other biological agents? and is a valuable addition to our current antipsoriatic armamentarium. Additionally, it was seen that secukinumab significantly reduced the baseline PASI score until eight weeks and sustained clearance till 52 weeks.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFERENCES

1. Dogra S, Yadav S. Psoriasis in India: Prevalence and pattern. Indian JDermatol VenereolLeprol. 2010 Nov-Dec;76(6):595-601. doi: 10.4103/0378-6323.72443.

2. Gelfand JM, Weinstein R, Porter SB, Neimann AL, Berlin JA, Margolis DJ. Prevalence and treatment of psoriasis in the United Kingdom: a population-based study. Arch Dermatol. 2005 Dec;141(12):1537-41. doi: 10.1001/archderm.141.12.1537.

3. World Health Organization. Global report on psoriasis, 2016. https://apps.who.int/iris/handle/10665/204417

4. Li R, Sun J, Ren LM, Wang HY, Liu WH, Zhang XW, et al. Epidemiology of eight common rheumatic diseases in China: a large-scale cross-sectional survey in Beijing. Rheumatology (Oxford). 2012 Apr;51(4):721-9. doi: 10.1093/rheumatology/ker370.

5. Parisi R, Symmons DPM, Griffiths CEM, Ashcroft DM, Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol2013 Feb;133(2):377-85. doi: 10.1038/jid.2012.339.

6. Enamandram M, Kimball AB. Psoriasis epidemiology: the interplay of genes and the environment. J Invest Dermatol2013 Feb;133(2):287-9. doi: 10.1038/jid.2012.434.

7. Alexis AF, Blackcloud P. Psoriasis in skin of color: epidemiology, genetics, clinical presentation, and treatment nuances. J ClinAesthetDermatol. 2014 Nov;7(11):16-24.

8. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. J Invest Dermatol. 2014 Jun;134(6):1527-1534. doi: 10.1038/jid.2013.446.

9. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet. 2007 Jul 21;370(9583):263-271. doi: 10.1016/S0140-6736(07)61128-3.

10. Springate DA, Parisi R, Kontopantelis E, Reeves D, Griffiths CEM, Ashcroft DM. Incidence, prevalence and mortality of patients with psoriasis: a U.K. population-based cohort study. Br JDermatol. 2017 Mar;176(3):650-658. doi: 10.1111/bjd.

11. Langley RG, Krueger GG, Griffiths CE. Psoriasis: epidemiology, clinical features, and quality of life. Ann Rheum Dis. 2005 Mar;64Suppl 2(Suppl 2):ii18-23; discussion ii24-5. doi: 10.1136/ard.2004.033217.

12. Furue K, Ito T, Tsuji G, Kadono T, Nakahara T, Furue M. Autoimmunity and autoimmune co-morbidities in psoriasis. Immunology.2018 May;154(1):21-7.

13. Gerdes S, Mrowietz U, Boehncke WH. Comorbidity in psoriasis. Hautarzt2016 Jun;67(6):438-44. doi: 10.1007/s00105-016-3805-3.

14. Fleming P, Bai JW, Pratt M, Sibbald C, Lynde C, Gulliver WP. The prevalence of anxiety in patients with psoriasis: A systematic review of observational studies and clinical trials. J. Eur. Acad. Dermatol. Venereol. 2017 May;31(5):798-807. doi: 10.1111/jdv.13891.

15. Mrowietz U, Kragballe K, Reich K, Spuls P, Griffiths CE, Nast A, et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res. 2011 Jan;303(1):1-10. doi: 10.1007/s00403-010-1080-1.

16. Lv J, Zhou D, Wang Y, Zhao J, Chen Z, Zhang J, et al. Quantitative evaluation to efficacy and safety of therapies for psoriasis: A network meta-analysis. Mol Pain. 2018 Jan-Dec;14:1744806918762205. doi: 10.1177/1744806918762205.

17. Galluzzo M, Talamonti M, De Simone C, D'Adamio S, Moretta G, Tambone S, et al. Secukinumab in moderate-to-severe plaque psoriasis: a multi-center, retrospective, real-life study up to 52 weeks observation. Expert opinion on biological therapy. 2018 Jul 3;18(7):727-35.

18. Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CE, Papp K, et al. Secukinumab in plaque psoriasis—Results of two phase 3 trials. N. Engl. J. Med. 2014 Jul 24;371(4):326-38. doi: 10.1056/NEJMoa1314258.

19. Kawalec P, Holko P, Moćko P, Pilc A. Comparative effectiveness of abatacept, apremilast, secukinumab and ustekinumab treatment of psoriatic arthritis: a systematic review and network meta-analysis. Rheumatology international. 2018 Feb 1;38(2):189-201.

20. Frieder J, Kivelevitch D, Menter A. Secukinumab: a review of the anti-IL-17A biologic for the treatment of psoriasis. Therapeutic advances in chronic disease. 2018 Jan;9(1):5-21.

21. Papp KA, Blauvelt A, Bukhalo M, Gooderham M, Krueger JG, Lacour JP,et al. Risankizumab versus ustekinumab for moderate-to-severe plaque psoriasis. N. Engl. J. Med. 2017 Apr 20;376(16):1551-1560. doi: 10.1056/NEJMoa1607017.

22. Bagel J, Duffin KC, Moore A, Ferris LK, Siu K, Steadman J, et al. The effect of secukinumab on moderate-to-severe scalp psoriasis: Results of a 24-week, randomized,

double-blind, placebo-controlled phase 3b study. J Am AcadDermatol. 2017 Oct;77(4):667-674. doi: 10.1016/j.jaad.2017.05.033.

23. Khawaja AR, Bokhari SM, Tariq R, Atif S, Muhammad H, Faisal Q, et al. Disease Severity, Quality of Life, and Psychiatric Morbidity in Patients With Psoriasis With Reference to Sociodemographic, Lifestyle, and Clinical Variables: A Prospective, Cross-Sectional Study From Lahore, Pakistan. Prim Care Companion CNS Disord. 2015 Jun 25;17(3):10.4088/PCC.14m01629. doi: 10.4088/PCC.14m01629.

24. EjazA, Suhail M,Iftikhar A. Psoriasis in Pakistani population: associations, comorbidities, and hematological profile.JPAD-Journal of Pakistan Association of Dermatologists. 2013;23 (1): 42-46.

25. Khan GA, Malik LM, Jahangir M. Prevalence of smoking, alcohol, and comorbid conditions in psoriasis. J Pak AssocDermatol.2010;20(4):212-6.

26. Bajaj DR, Mahesar SM, Devrajani BR, Iqbal MP. Lipid profile in patients with psoriasis presenting at Liaquat University Hospital Hyderabad. *J Pak Med Assoc*. 2009 Aug;59(8):512-5.

27. Ahmed I, Nasreen S. Frequency and pattern of nail changes in patients with psoriasis vulgaris. J Pak AssocDermatol. 2009;19:149-9.

28. Kim GW, Park HJ, Kim HS, Kim SH, Ko HC, Kim BS, et al. Analysis of cardiovascular risk factors and metabolic syndrome in korean patients with psoriasis. Ann Dermatol. 2012 Feb;24(1):11-5. doi: 10.5021/ad.2012.24.1.11.

29. Moghaddassi M, Shahram F, Chams-Davatchi C, Najafizadeh SR, Davatchi F. Different aspects of psoriasis: analysis of 150 Iranian patients. Arch Iran Med. 2009 May;12(3):279-83.

30. Saeed M, Zaman T, Rashid T, Jahangir M. Evaluation of joint involvement in patients of psoriasis: an observational study. J Pak AssocDermatol.2008;18(1):6-8.

31. Fujita H, Ohtsuki M, Morita A, Nagao R, Seko N, Matsumoto K, et al. Safety and effectiveness of secukinumab in psoriasis vulgaris and psoriatic arthritis: Real-world evidence in Japan. J Dermatol. 2021 Feb;48(2):175-183. doi: 10.1111/1346-8138.15655.

32. Zheng J. Absolute psoriasis area and severity index: an additional evaluation for clinical practice. Br J Dermatol.2017 Mar;176(3):576. doi: 10.1111/bjd.15216.

33. Gladman DD, Poulin Y, Adams K, Bourcier M, Barac S, Barber K, et al. Treating psoriasis and psoriatic arthritis: Position paper on applying the treat-to-target concept to Canadian daily practice. J Rheumatol 2017; 44(4): 519–534.

34. Mahil SK, Wilson N, Dand N, Reynolds NJ, Griffiths CEM, Emsley R, et al. Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, populationbased cohort study (the British Association of Dermatologists Biologics and Immunomodulators Register, BADBIR). Br J Dermatol. 2020; 182(5): 1158–1166.

35. Papp KA, Lebwohl MG. Onset of Action of Biologics in Patients with Moderate-to-Severe Psoriasis. J Drugs Dermatol. 2017;17(3):247–250.

36. Yang EJ, Beck KM, Liao W. Secukinumab in the treatment of psoriasis: patient selection and perspectives. Psoriasis (Auckl). 2018 Oct 17;8:75-82. doi: 10.2147/PTT.S146004.

37. Lebwohl MG, Papp KA, Marangell LB, Koo J, Blauvelt A, Gooderham M, et al. Psychiatric adverse events during treatment with brodalumab: Analysis of psoriasis clinical trials. J Am AcadDermatol. 2018;78(1):81–89.

38. Kavanaugh A, Mease PJ, Reimold AM, Tahir H, Rech J, Hall S, et al. Secukinumab for Long-Term Treatment of Psoriatic Arthritis: A Two-Year Followup From a Phase III, Randomized, Double-Blind Placebo-Controlled Study. Arthritis Care Res. 2017;69(3):347–355.