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OUTCOME OF SECUKINUMAB IN PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS

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Abstract
Objective: To determine the outcome of Secukinumab in the therapy of moderate to severe plaque psoriasis at a tertiary care hospital of Karachi, Pakistan.
Study design: Single arm non-randomized trial
Place and duration of study: Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi from 5th July 2021 to 10th July 2022.
Methodology: The study included moderate or severe plaque psoriasis patients aged 30 years or older receiving treatment with subcutaneous injections of Secukinumab 300mg at zero one two three and four weeks and then every month for five months. Patients were followed till week 25. Pre and post therapy photographs were taken. Psoriasis Area and Severity Index (PASI) was calculated before and after treatment. Outcome was assessed in terms of improvement in plaque psoriasis. All patients who were presented with 75% decline in the PASI at the end of the therapy as compared to baseline were labelled as improvement.
Results: Of 35 patients, the average age was 37.68 ± 9.89 years, with a majority of 22 (65.7%) males. The average duration of psoriasis was 10.42 ± 8.03 years, and psoriatic arthritis was observed in 15 (42.9%) patients. The PASI score decreased from 20.66 ± 3.09 to 4.22 ± 1.66 (p-value < 0.001, 95% CI 15.50 to 17.36), representing an average reduction of 79.73%. The treatment showed >75% decrease in PASI score post-treatment in 31 (88.57%) patients. Adverse events were reported in 2 patients.
Conclusion: Current study findings showed a good outcome and established the safety of secunkinumab in therapy of patients with moderate to severe plaque psoriasis.

Keywords: Outcome, Secukinumab, moderate to severe plaque psoriasis.

Introduction

Characterized by the formation of thick, scaly plaques on the surface of the skin, plaque psoriasis is a chronic autoimmune condition. It affects millions of individuals worldwide and significantly

impacts their quality of life.[1] While several treatment options exist, a substantial number of patients with moderate to severe plaque psoriasis fail to attain satisfactory results or experience intolerable side effects with conventional therapies.[2,3]

Proinflammatory cytokines mediated by T cells and dendritic ceels are the pathological driving force in psoriasis.[4] In recent years, the advent of biologic agents targeting specific immune pathways has revolutionized the management of psoriasis.Human monoclonal antibody secukinumab selectively inhibits interluekin 17 A and has shown promising results in random control trials and real world studies.[6-8] However, there remains a need to assess the real-world efficiency and safety of Secukinumab in routine clinical practice, particularly in moderate to severe plaque psoriasis patients who may have diverse characteristics and treatment histories.

This intervention study aims to evaluate the safety and efficacy of secukinumab in real world scenarios in moderate to severe plaque psoriaisis patients. By collecting data from a diverse patient population in routine clinical settings, we aim to provide valuable insights into the outcomes and experiences of patients receiving Secukinumab outside the controlled environment of clinical trials.

The prime objective of this study is to assess the outcome of Secukinumab in terms of psoriasis severity improvement, as measured by a scoring systems such as the Psoriasis Area Severity Index (PASI). We will analyze the proportion of patients achieving clinically significant improvement, defined as PASI 75. Additionally, we will evaluate the impact of Secukinumab on associated comorbidities, such as psoriatic arthritis, and nature of adverse events, serious infections, and other safety parameters associated with Secukinumab treatment.

The rationale of the study is that there is a dearth in the knowledge regarding the Secukinumab treatment for moderate to severe plaque psoriasis patients in the local literature.Demographic differences and characteristic from different ethnic and geographic backgrounds have been proposed to impact the effectiveness and safety of the available therapies. Hence data from this study would form the benchmark for improvement in current management of plaque psoriasis patients.

Methodology

This single arm non-randomized trial was conducted Dermatology Department at, Jinnah Postgraduate Medical Centre, Karachi from 5-july-2021… to 10-july2022… Consent from the institutional ethical review committee was undertaken prior to conduction of study **(IRB #NO.F.2-81/2021-GENL/252/JPMC)**, also approved on **ClinicalTrials.gov PRS with ID No NCT05974982**. Informed consent was obtained from all the patients for assigning them to sample and used their data in research.

All patients were enrolled through non-probability consecutive sampling. Patients with known plaque psoriasis aged 30 years or above of either gender were included. However, patients with history of eczema, malignancy, hepatitis B, C or AIDS or any other known illness were excluded. In addition, patients who were immunocompromised were also excluded. Plaque psoriasis was defined as well circumscribed, erythematous, sharply demarcated, and scaly plaques with > 1 cm in diameter over the extensor surfaces and scalp for more than one month.

Estimation of sample using confidence interval at 95% was calculated using EpiInfo sample size calculator and PASI score 75 in previous study 54.5%[9]. The sample size came out to be 356 at 5% margin of error. However, as the samples were large and unachievable during the study period and the cost of the medicine was too high that was unaffordable for majority of the patients therefore, 35 patients who offered free of cost treatment with plaque psoriasis were included.

All included patients had moderate or severe plaque psoriasis despite receiving UV therapy, systematic therapy, or biological therapy. These patients were offered free of cost Secukinumab 300mg injections subcutaneously at week zero, one, two, three, four and then every month for five months. Patients were followed up till week 25. Before and after treatment photographs were taken. Moreover, PASI was calculated before and after treatment. Outcome was assessed in terms of >75% reduction in PASI score post treatment of injection Secukinumab. More than 75% decrease in the PASI at the termination of the therapy compared to baseline was noted as outcome. A pre-structured proforma was used to collect all this data along with demographic characteristics such as age, sex,

length of psoriatic disease, and previous therapy for plaque psoriasis. In addition, any adverse event during the treatment period was also observed.

Version 24 of the Statistical Package for Social Sciences (SPSS) was used for statistical analysis. Mean along with standard deviation was reported qualitative variables like age, duration of psoriasis, and PASI score before and after the treatment. Whereas gender, psoriatic arthritis, previous therapy, >75% reduction in PASI score post treatment, and adverse events were presented in the form of frequency and percentages. A dependent t-test was applied to calculate theaverage difference of PASI score before and after the treatment. Moreover, the Fisher-Exact test was applied to see the association of >75% reduction in PASI score post treatment of the treatment with general characteristics. Statistically significant p-value of less than equal to 0.05 was considered.

Results

The study was carried out on 35. The study found that the average age of the patients was 37.68 ± 9.89 years, with a majority of 22 (65.7%) males and 12 (34.3%) females. The mean duration of psoriasis among the patients was 10.42 ± 8.03 years, and psoriatic arthritis was observed in 15 (42.9%) patients. The majority of patients, 33 (94.3%), received systematic therapy, while 2 (5.7%) patients each received UV therapy and biological therapy. (Table 1)

Treatment with the therapy resulted in a significant decline in the PASI score from baseline to the termination of the therapy. The PASI score decreased from 20.66 ± 3.09 to 4.22 ± 1.66 (p-value < 0.001, 95% CI 15.50 to 17.36), representing an average reduction of 79.73%. Similar improvements were observed when analyzing the data based on age, gender, duration of psoriasis, and presence of psoriatic arthritis. (Table 2)

The treatment outcome reported >75% reduction in PASI score post treatment in 31 (88.57%) patients, indicating positive outcomes in the majority of the study population. (Figure 1) The study did not find a significant association between the PASI score and the general characteristics of the patients. (Table 3)

Adverse events were reported in 2 patients, representing a small proportion of the study population. One patient experienced a flare of the disease, while another patient developed an upper respiratory tract infection.

Table 1: General characteristics of the patients (n=35)

	n	**%**
Age, years	*37.68 ±9.89*	
≤40	25	71.4
>40	10	28.6
Gender		
Male	22	65.7
Female	12	34.3
Duration of Psoriasis, years	*10.42 ±8.03*	
≤10	24	68.6
>10	11	31.4
Psoriatic Arthritis		
Yes	15	42.9
No	20	57.1
Previous therapy		
UV Therapy	2	5.7
Systematic therapy	33	94.3
Biological therapy	2	5.7

UV: Ultraviolet *mean ±SD

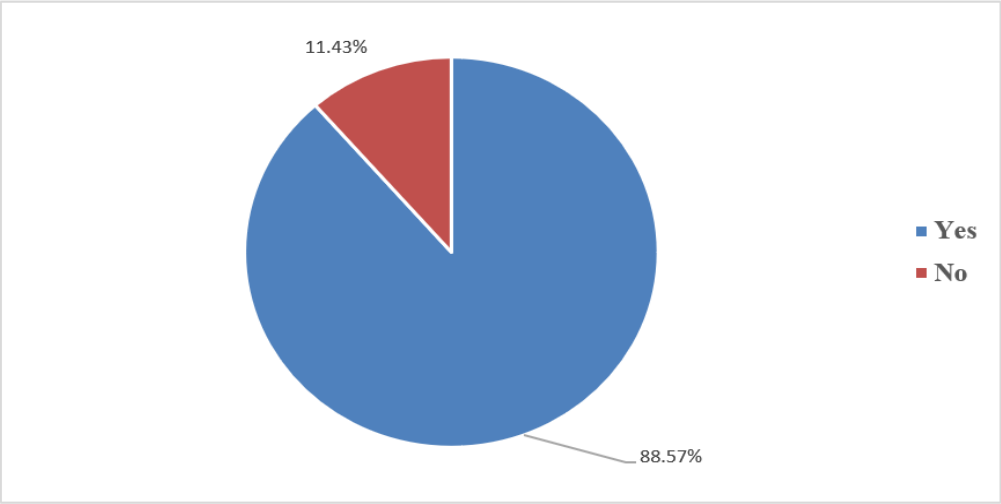


Figure 1: Reporting frequency of >75% reduction in PASI score post treatment (n=35)

Table 2: Mean difference of PASI score at baseline and at the end of therapy (n=35)

	PASI		p-value	95% CI	Average Percentage Reduction
	Baseline	End of therapy			
Total (n=35)					
Mean ±SD	20.66 ±3.09	4.22 ±1.66	<0.001	15.50 to 17.36	79.73%
Age, years					
≤40	21.08 ±2.69	4.48 ±1.81	<0.001	15.51 to 17.69	78.83%
>40	19.61 ±3.87	3.60 ±1.07	<0.001	13.87 to 18.15	81.97%
Gender					
Male	20.25 ±2.18	4.26 ±1.78	<0.001	15.04 to 16.94	79.11%
Female	21.44 ±4.35	4.17 ±1.47	<0.001	15.09 to 19.46	80.91%
Duration of Psoriasis, months					
≤10	20.63 ±3.16	4.29 ±1.87	<0.001	15.14 to 17.53	79.46%
>10	20.72 ±3.07	4.09 ±1.14	<0.001	14.93 to 18.35	80.32%
Psoriatic Arthritis					
Yes	20.06 ±2.91	3.80 ±1.32	<0.001	14.96 to 26.85	81.21%
No	21.12 ±3.21	4.55 ±1.84	<0.001	15.16 to 17.97	78.61%

CI: Confidence Interval, PASI: Psoriasis Area and Severity Index, SD: Standard Deviation, dependent t-test applied, p-value ≤0.05 considered as significant

Table 3: Comparison of PASI Score >75% reduction with general characteristics (n=35)

Variables	PASI Score >75% reduction*		
	Yes (n=31)	No (n=4)	p-value
Age, years			
≤40	21 (84.0)	4 (16.0)	0.303
>40	10 (100)	0 (0)	
Gender			
Male	20 (87.0)	3 (13.0)	>0.999
Female	11 (91.7)	1 (8.3)	
Duration of Psoriasis, months			
≤10	21 (87.5)	3 (12.5)	>0.999
>10	10 (90.9)	1 (9.1)	
Psoriatic Arthritis			
Yes	14 (93.3)	1 (6.7)	0.619
No	17 (85.0)	3 (15.0)	

*75% reduction in the PASI score at the end of therapy from baseline was noted.
Fisher-Exact test applied, p-value ≤0.05 considered as significant

Discussion

The findings of the study reported that administration of Secukinumab led to a notable decrease in the PASI score, reflecting a substantial improvement in psoriasis severity from the beginning of the therapy to its conclusion. PASI 75 response is considered a clinically meaningful outcome and is often used as a primary efficacy endpoint in clinical trials evaluating the effectiveness of psoriasis treatments. The treatment demonstrated effectiveness in 88.57% of patients, underscoring favorable outcomes observed in the majority of individuals included in the current study. Achieving a PASI 75 response indicates a considerable improvement in the symptoms and signs of psoriasis and is indicative of a positive treatment response. Previous study findings revealed that in week five, a total of 54.5% patients demonstrated a PASI 50 response, indicating a significant improvement in their psoriasis severity. Moreover, at the twenty-five-week, 36.36% patients achieved an even higher level of improvement with a PASI 75 response. Additionally, seven patients were able to sustain a PASI 50 response, demonstrating the durability of the treatment effect over time.The study found compelling evidence in the improvement of psychosocial and physical well being of patients with psoriasis on Secukinumab,the study also found evidence of reduced disease severity along with a favourable safety profile.[9] Various other international studies as well as from Pakistan also reported higher efficacy of Secukinumab with no or very limited adverse effects.[10-12]

These results suggest that Secukinumab has a substantial impact on reducing psoriasis severity in a significant proportion of patients. It underscores the efficacy of Secukinumab as a treatment option for plaque psoriasis, providing patients with a meaningful improvement in their condition.(Figure 1).

It is worth mentioning that additional factors such as the study design, sample size, duration of treatment, and patient characteristics may influence the frequency of achieving a PASI 75 response. Therefore, consideration of these factors when understanding the findings of the study and implementing them to clinical practice.

Beyond the physical benefits, various studies have highlighted the positive impact of Secukinumab on the psychosocial aspects of patients' lives.[13-15] Psoriasis often leads to psychological distress, social stigma, and decreased quality of life.[16-18] However, Secukinumab treatment not only alleviates the physical symptoms but also contributes to an improved psychosocial well-being.[15] Patients experience enhanced self-esteem, reduced psychological burden, and improved overall quality of life, enabling them to engage in daily activities and social interactions more confidently.[19,20]

The current study also reinforces the favorable safety profile of Secukinumab. The treatment was well-tolerated by the majority of the patients, with minimal adverse events reported. This information is crucial for healthcare providers and patients alike, as ensuring the safety of a treatment is paramount in the management of chronic conditions such as psoriasis.

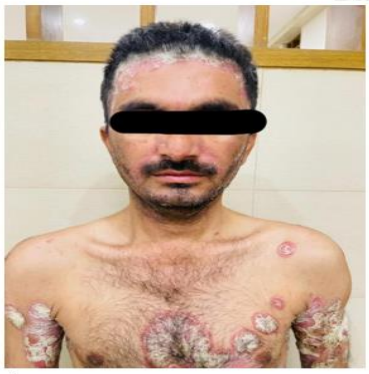
This interventional study aims to contribute to the better understanding of the efficacy and safety profile of Secukinumab. Ultimately, this study bridged the gap between controlled clinical trial settings and routine clinical practice, providing valuable evidence to inform treatment decisions and optimize patient care for individuals with psoriasis.

The current study has certain limitations. One of the major drawbacks of this study was that it is a single arm study without a control group. The lack of comparison makes it challenging to determine whether any improvements observed are due to the treatment itself or could have occurred spontaneously or as a result of other factors. Another limitation of our study is that the stock of the medicine Secukinumab was limited. Due to the very high costs of Secukinumab, the number of patients was also limited, which can affect the representativeness of the population being studied. The limited stock may also result in a selective or biased sample, as only a subset of eligible participants may have access to the medication. High costs associated with Secukinumab can have several consequences as this may result in non-adherence or discontinuation of treatment, potentially impacting the validity of the study results.

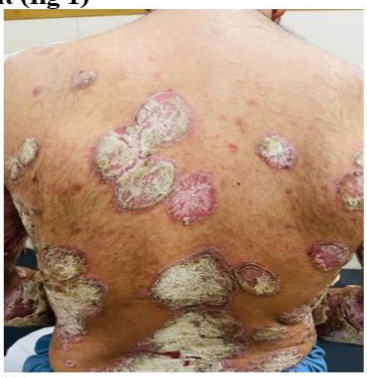
The study could be strengthened by extending the follow-up period and addressing certain limitations mentioned in the study. A longer follow-up period allows for the assessment of outcomes

over an extended period of time, providing a more comprehensive understanding of the treatment's effects. Some treatments may have delayed effects or show differences in efficacy over time. Moreover, by extending the follow-up period, researchers can observe the persistence of treatment effects, identify potential relapses or recurrences, and evaluate the long-term benefits and risks associated with the intervention. Lastly, a longer follow-up period often results in a larger dataset, which can increase the statistical power of the study. This enhanced power enables researchers to detect smaller or more subtle treatment effects and enhances the reliability of the study findings.

Before Treatment (fig 1)

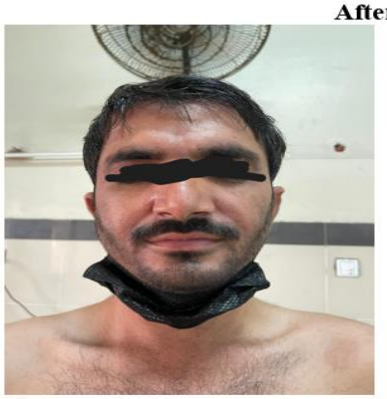


A



B

After 4th Dose



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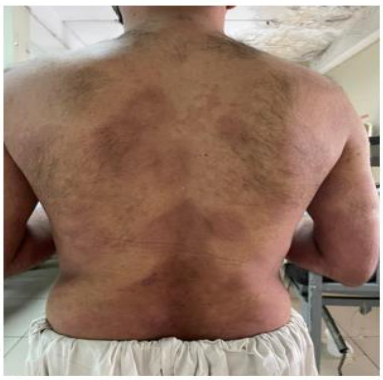

D

Conclusion

The findings of the study have concluded a major improvement and safety of Secukinumab in patients. By incorporating real-world data, the study has complemented existing clinical trial evidence and provided clinicians with valuable insights into the outcomes and considerations associated with Secukinumab treatment.

References

1. Pariser D, Frankel E, Schlessinger J, Poulin Y, Vender R, Langley RG et al. Efficacy of secukinumab in the treatment of moderate to severe plaque psoriasis in the North American Subgroup of Patients: Pooled Analysis of Four Phase 3 Studies. Dermatol Ther (Heidelb). 2018; **8(1)**:17-32.
2. Alexis AF, Blackcloud P. Psoriasis in skin of color: epidemiology, genetics, clinical presentation, and treatment nuances. J Clin Aesthet Dermatol. 2014; **7**:16–24.
3. Ohtsuki M, Morita A, Abe M, Takahashi H, Seko N, Karpov A, et al. Secukinumab efficacy and safety in Japanese patients with moderate-to-severe plaque psoriasis: subanalysis from ERASURE, a randomized, placebo-controlled, phase 3 study. J Dermatol. 2014; **41**:1039–46.
4. Asahina A, Torii H, Ohtsuki M, Tokimoto T, Hase H, Tsuchiya T, et al. Safety and efficacy of adalimumab treatment in Japanese patients with psoriasis: results of SALSA study. J Dermatol. 2016; **43**:1257–66.

5. Galica K, Lesiak A, Ciążyńska M, Noweta M, Bednarski I, Narbutt J. Effectiveness and safety of secukinumab in patients with moderate-to-severe plaque psoriasis - a real life retrospective study. Postepy Dermatol Alergol. 2021; **38(6)**:973-78.
6. Shaukat S, Khan S, Hussain I. IL-17 and its role in psoriasis. J Pak Assoc Dermatol. 2017; **27 (1)**:1-3.
7. Griffiths CE, Reich K, Lebwohl M, van de Kerkhof P, Paul C, Menter A, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. Lancet. 2015; **386(9993)**:541-51. doi: 10.1016/S0140-6736(15)60125-8.
8. 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; **371(4)**:326-38. doi: 10.1056/NEJMoa1314258.
9. Tariq H, Basharat M, Javed S, Aman S. Efficacy and safety of secukinumab in treatment of moderate to severe psoriasis. J Pak Ass Derm 2022; **32(1):**9-14
10. Tirmizi SS. Efficacy of Secukinumab in Moderate to Severe Psoriasis Vulgaris: A Prospective Study. Pak J Med Health Sci. 2022; **16(09):**983-6.
11. Papp KA, Langley RG, Sigurgeirsson B, Abe M, Baker DR, Konno P, et al. Efficacy and safety of secukinumab in the treatment of moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled phase II dose-ranging study. Br J Dermatol. 2013; **168(2):**412-21. doi: 10.1111/bjd.12110.
12. Rich P, Sigurgeirsson B, Thaci D, Ortonne JP, Paul C, Schopf RE, et al. Secukinumab induction and maintenance therapy in moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled, phase II regimen-finding study. Br J Dermatol. 2013; **168(2):**402-11. doi: 10.1111/bjd.12112.
13. Foley P, Spelman L, Murrell DF, Mate E, Tronnberg R, Lowe PM. Secukinumab treatment showed improved quality of life in patients with chronic plaque psoriasis in Australia: Results from the HOPE study. Australas J Dermatol. 2022; **63(3):**312-20. doi: 10.1111/ajd.13893.
14. Augustin M, Dauden E, Mrowietz U, Konstantinou MP, Gerdes S, Kingo K, et al. Secukinumab treatment leads to normalization of quality of life and disease symptoms in psoriasis patients with or without prior systemic psoriasis therapy: the PROSE study results. J Eur Acad Dermatol Venereol. 2021; **35(2)**:431-40. doi: 10.1111/jdv.16632.
15. Blair HA. Secukinumab: A Review in Moderate to Severe Pediatric Plaque Psoriasis. Paediatr Drugs. 2021 Nov;23(6):601-608. doi: 10.1007/s40272-021-00476-w. Epub 2021. Erratum in: Paediatr Drugs. 2022; **24(1):**91.
16. Jankowiak B, Kowalewska B, Krajewska-Kułak E, Khvorik DF. Stigmatization and Quality of Life in Patients with Psoriasis. Dermatol Ther (Heidelb). 2020; **10(2):**285-296. doi: 10.1007/s13555-020-00363-1.
17. Esposito M, Saraceno R, Giunta A, Maccarone M, Chimenti S. An Italian study on psoriasis and depression. Dermatology. 2006; **212(2):**123-7. doi: 10.1159/000090652.
18. Homayoon D, Hiebler-Ragger M, Zenker M, Weger W, Unterrainer H, Aberer E. Relationship Between Skin Shame, Psychological Distress and Quality of Life in Patients with Psoriasis: a Pilot Study. Acta Derm Venereol. 2020; **100(14):**adv00205. doi: 10.2340/00015555-3563.
19. Elewski BE, Puig L, Mordin M, Gilloteau I, Sherif B, Fox T, et al. Psoriasis patients with psoriasis Area and Severity Index (PASI) 90 response achieve greater health-related quality-of-life improvements than those with PASI 75-89 response: results from two phase 3 studies of secukinumab. J Dermatolog Treat. 2017; **28(6):**492-9. doi: 10.1080/09546634.2017.1294727. Epub 2017 Mar 7. Erratum in: J Dermatolog Treat. 2017; **28(6)**:571.
20. Bardowska K, Krajewski PK, Tyczyńska K, Szepietowski JC. Safety evaluation of secukinumab in pediatric patients with plaque psoriasis. Expert Opin Drug Saf. 2022; **21(7):**867-72. doi: 10.1080/14740338.2022.2073349.