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The real-life efficacy and safety of secukinumab therapy (150 and 300 mg) in patients with moderate-to-severe plaque psoriasis: A twelve week, single center, retrospective study

Orta ve şiddetli plak tip psoriazis hastalarında sekukinumab (150 ve 300 mg) tedavisinin gerçek yaşam etkinliği ve güvenliği: On iki haftalık, tek merkezli, retrospektif bir çalışma

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Abstract

Background and Design: Secukinumab is an effective treatment option in moderate-to-severe plaque type psoriasis. However, there are a few real-life data studies comparing the efficacy of 150 mg and 300 mg dosages. The aim of this study was to evaluate the efficacy and safety of secukinumab at 150 mg and 300 mg in clinical practice in chronic plaque type psoriasis patients attending our center.
Materials and Methods: The medical records of 33 patients consecutively treated with secukinumab 150 mg or 300 mg for a minimum three-month period were analyzed retrospectively. Treatment response was defined as the achievement of a minimum psoriasis area and severity index (PASI) 75 response at week 12.
Results: Eighteen (55.5%) of the patients were men. The mean duration of the disease was 20±9.38 (1-40) years. Most (75.7%) patients had previously received at least one biological therapy. Seventeen patients were treated with 300 mg and 14 with 150 mg during the induction and maintenance periods. Two patients received induction therapy at 150 mg and maintenance therapy at 300 mg. At week 12, PASI 75, 90, and 100 responses were achieved in 78.8%, 66.7%, and 22.3% of patients, respectively. Treatment responses were similar between patients receiving 150 mg and 300 mg, and also between biologic naive and non-naive patients ($p>0.05$). Adverse events were observed in three patients, but these did not necessitate discontinuation of therapy.
Conclusion: Secukinumab at doses of 150 mg and 300 mg is a fast-acting, effective and safe treatment option in patients with chronic plaque type psoriasis, both biologic naive and non-naive.
Keywords: Anti-IL-17A, secukinumab, psoriasis, efficacy, side effects

Öz

Amaç: Sekukinumab orta ve şiddetli plak tip psoriaziste etkili bir tedavi seçeneğidir. Literatürde 150 mg ve 300 mg'nin etkinliğini karşılaştıran birkaç gerçek yaşam veri çalışması vardır. Bu çalışmanın amacı merkezimize başvuran kronik plak tip psoriazis hastalarında sekukinumab 150 mg ve 300 mg'nin klinik uygulamadaki etkinliğini ve güvenilirliğini değerlendirmektir.
Gereç ve Yöntem: En az üç ay boyunca ardışık olarak sekukinumab 150 mg veya 300 mg ile tedavi edilen 33 hastanın tıbbi kayıtları retrospektif olarak incelendi. Tedavi yanıtı, 12. haftada minimum psoriazis alan ve şiddet indeksi (PAŞİ) 75 yanıtının elde edilmesi olarak tanımlandı.
Bulgular: Hastaların 18'i (%55,5) erkekti. Hastalığın ortalama süresi 20±9,38 (1-40) yıl idi. Çoğu hasta (%75,7) daha önce en az bir biyolojik tedavi almıştı. İndüksiyon ve idame döneminde 17 hasta 300 mg, 14 hasta 150 mg ile tedavi edildi. İki hasta ise 150 mg ile indüksiyon tedavisi ve 300 mg ile idame tedavisi aldı. On ikinci haftada, hastaların %78,8, %66,7 ve %22,3'ünde sırasıyla PAŞİ 75, 90 ve 100 yanıtı elde edildi.

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Sekukinumab 150 mg ve 300 mg alan hastalar arasında ve biyolojik naif olan ve olmayan hastalar arasında tedavi yanıtları benzerdi (p>0,05). Üç hastada advers etkiler gözlendi ancak bunlar tedavinin kesilmesini gerektirmedi.
Sonuç: Sekukinumab 150 mg ve 300 mg, hem biyolojik naif hem de naif olmayan kronik plak tip psoriazis hastalarında hızlı, etkili ve güvenli bir tedavi seçeneğidir.
Anahtar Kelimeler: Anti-IL-17A, psoriazis, sekukinumab, etkinlik, yan etkiler

Introduction

Psoriasis is a chronic inflammatory disease that affects 2%-3% of the population[1]; it is believed to occur in genetically predisposed individuals through the interaction of environmental and immunological factors. New discoveries on the pathogenesis of psoriasis have led to the development of biological treatments involving complex molecules, such as monoclonal antibodies or receptor fusion proteins that target specific inflammatory pathways. These drugs target two pathways of importance in the occurrence and chronicity of psoriatic plaques, namely, tumor necrosis factor- signaling and the interleukin (IL)-23/T helper 17 (Th17) axis. IL-17A may potentially act as a master cytokine in the pathogenesis of psoriasis and stimulate keratinocytes to secrete chemokines and other proinflammatory mediators that recruit additional inflammatory cells, including neutrophils, Th17 cells, dendritic cells, and innate lymphoid cells[2]. The cytokine is primarily produced by Th17 cells, but also secreted by natural killer cells, mast cells, and neutrophils. Secukinumab is a recombinant human monoclonal antibody that neutralizes IL-17A regardless of its source. The drug was approved by the U.S. Food and Drug Administration in 2015 for the treatment of patients with moderate-to-severe plaque psoriasis with inadequate response to systemic conventional therapies or with contraindications for these treatments[3]. Secukinumab is a novel biological agent that has been used in Turkey since 2018. The purpose of this study is to evaluate demographic and clinical features, responses to treatment, and side-effects among psoriasis patients receiving secukinumab therapy by using our center's real-life data.

Materials and Methods

This retrospective, single-center, observational study involved consecutive adult patients with moderate-to-severe plaque psoriasis treated with secukinumab between April 2018 and December 2019. The study protocol was approved by the Ankara University Faculty of Medicine Ethics Committee (approval number: I1-56-20). Patients receiving secukinumab therapy for at least 3 months were included in the study. Subcutaneous secukinumab was administered at doses of 150 or 300 mg once weekly for 5 weeks for induction therapy and then every 4 weeks thereafter as maintenance therapy. The dose administered was based on the clinical decision of the evaluating physician prior to treatment.

Data regarding patients' demographic characteristics, including age, gender, comorbidities, duration of disease, co-presence of psoriatic arthritis, previous systemic and/or biological therapies, and adverse events reported during treatment, were collected from file records. psoriasis area and severity index (PASI) values were recorded at baseline (pretreatment) and at week 12. Treatment efficacy was defined as a 75% or greater reduction in PASI values (PASI75, PASI90, and PASI100) compared with the baseline at week 12.

Statistical Analysis

SPSS software (SPSS for Windows, Version 15.0, SPSS Inc., USA) was used for statistical analysis. Qualitative variables were expressed as numbers and percentages, while quantitative variables were expressed as mean ± standard deviation (SD). The chi-squared and Fisher's exact tests were used to compare categorical variables, and the Mann-Whitney U test and Student's t-tests were used to compare parametric values. A p-value of <0.05 was considered statistically significant.

Results

Patient characteristics

The demographic and clinical features of the 33 patients included in this study are summarized in Table 1. The mean (±SD) age of the patients was 46.7±11.7 years, and 18 (55.5%) of the patients were male. The mean disease duration was 20±9.38 years (range: 1-40 years), and the mean pretreatment PASI score of the entire study population was 16.7±4.04 (range: 8-27). Joint involvement was present in nine patients (27.3%). The mean body weight of all patients was 78.1±15.2 kg (range: 52-110 kg). The most common comorbidities were hypertension (11, 33.3%) and diabetes mellitus (7, 21.2%). According to the Quantiferon-TB Gold test result and chest X-Ray scanning, latent *Mycobacterium tuberculosis* infection was detected in 15 (48%) patients, and isoniazid treatment was started as prophylaxis. Five (15.2%) patients showed latent hepatitis B virus (HBV) infection following serological testing (i.e., anti-HBs, anti-HBc, and HBV-DNA) and received antiviral therapy during treatment for up to 1 year. All of the patients had received at least one conventional systemic therapy for psoriasis; methotrexate was the most common drug administered (84%), followed by acitretin (51%) and cyclosporine (48%). The majority of the patients (75.7%) had also previously received biological therapy, including adalimumab (18, 51.5%), ustekinumab (16, 48.5%), etanercept (8, 24.3%), and infliximab (7, 21.2%). Only eight (24.3%) patients were biologically naive. Secukinumab was, on average, the fifth line therapy received, and the mean duration of secukinumab therapy was 5.6±2.6 months (range: 3-12 months).

Seventeen patients (51.5%) were treated with 300 mg of secukinumab while 14 (42.4%) received 150 mg of secukinumab during the induction and maintenance periods. Only moisturizers were applied to psoriatic lesions during the treatment period. The dose of two patients receiving 150 mg of secukinumab in the induction period (weeks: 0-4) was increased to 300 mg during the maintenance period (week: 8) because of unresponsiveness. These two patients who required a dose increase were also those with a history of biological therapy. The baseline mean PASI score of the patients receiving 150 mg of secukinumab was 15.9±4.2 (range: 10-24), and six were biologically naive. Only two of the patients receiving 300 mg of secukinumab were biologically naive. The baseline mean PASI score in the 300 mg group was 17.2±4 (range: 8-27). Although the baseline mean PASI score was lower in the 150 mg

group than in the 300 mg group, the difference between groups was not statistically significant (p>0.05). No significant differences in terms of baseline clinical and demographic features were observed between the subgroups, except in terms of body weight (Table 1). Specifically, the mean body weight of patients in the 300 mg group was statistically higher than that of patients in the 150 mg group (p=0.021).

Treatment results and adverse events

PASI75, PASI90, and PASI100 responses were achieved in 78.8% (n=26), 66.7% (n=22), and 22.3% (n=9) of the patients, respectively, at week 12. The mean PASI score at week 12 was 2.9±3.2 (range: 0-12). The improvement in mean PASI scores compared with the baseline was statistically significant (p<0.001). However, no statistically significant association was observed between treatment efficacy and gender or age (p>0.05). A PASI75 response was achieved in 91.3% (n=21) of the patients with nail involvement and in 88.9% (n=8) of those with joint involvement. No statistically significant relationship was observed between PASI75 response and joint or nail involvement (p>0.05).

PASI75, PASI90, and PASI100 responses were respectively achieved in 85.7% (n=12), 78.5% (n=11), and 28.4% (n=4) of the patients receiving 150 mg of secukinumab, as well as in 70.6% (n=12), 64.7% (n=11), and 29.4% (n=5) of those receiving 300 mg of secukinumab. The mean PASI scores after 12 weeks of treatment were 3.2±3.5 (range: 0-12) in the 300 mg group and 2.6±3.1 (0-12) in the 150 mg group. No statistically significant difference was determined between the 150 and 300 mg groups in terms of PASI75, PASI90, and PASI100 responses or mean PASI scores after treatment (p>0.05).

Table 1. Patient demographic and clinical characteristics and treatment responses according to secukinumab dosage

	All patients (n=33)	Patients receiving 150 mg (n=14)*	Patients receiving 300 mg (n=17)*	p-value
Male/female	15/18	8/6	6/11	0.224
Age	46.7±11.7 (21-66)	48.4±12.3 (21-66)	47.4±10 (29-64)	0.814
Duration of disease	20±9.38 (1-40)	20.3±11.4 (1-40)	20.6±7.9 (10-35)	0.934
PASI score at baseline	16.7±4.04 (8-27)	15.9±4.2 (10-24)	17.2±4 (8-27)	0.387
Psoriatic arthritis	9 (27.3%)	3 (21.4%)	6 (35.2%)	0.456
Body weight (kg)	78.1±15.2	69.3±3.4	84.3±4.6	0.021
Comorbidities				
Hypertension	11 (33.3%)	4 (28.4%)	7 (41.1%)	-
Diabetes mellitus	7 (21.2%)	2 (14.2%)	5 (29.4%)	
Hyperlipidemia	4 (12.1%)	1 (7.1%)	3 (17.6%)	
Hypo/hyperthyroidism	4 (12.1%)	1 (7.1%)	3 (17.6%)	
Previous systemic treatment				
Methotrexate	26 (84%)	13 (92.8%)	13 (76.4%)	-
Cyclosporine	16 (48%)	7 (50%)	9 (47.6%)	
Acitretin	17 (51%)	8 (57.1%)	6 (35.2%)	
Phototherapy	15 (48.4%)	8 (57.1%)	7 (41.1%)	
Previous biological treatment	25 (75.7%)	8 (57.1%)	15 (88.2%)	0.097
Etanercept	8 (24.3%)	3(21.4%)	5 (29.4%)	-
Infliximab	6 (18.8%)	3 (21.4%)	3 (17.6%)	
Adalimumab	18 (54.5%)	6 (42.8%)	12 (70.5%)	
Ustekinumab	15 (45.4%)	5 (35.7%)	10 (58.8%)	
Number of biologic agents				
1	9 (27.2%)	5 (35.7%)	3 (17.6%)	-
2	7 (21.2%)	0	7 (41.1%)	
3	6 (18.8%)	3 (21.4%)	3 (17.6%)	
4	2 (6%)	1 (7.1%)	1 (5.8%)	
PASI score after treatment	2.9±3.2 (0-12)	2.6±3.1 (0-12)	3.2±3.5 (0-12)	0.823
Treatment response at week 12				
PASI75	26 (78.8%)	12 (85.7%)	12 (70.6%)	0.185
PASI90	22 (66.7%)	11 (78.5%)	11 (64.7%)	0.707
PASI100	9 (22.3%)	4 (28.4%)	5 (29.4%)	1.000

*Patients receiving 150 mg of secukinumab in the induction period and 300 mg of secukinumab in the maintenance period were excluded from the statistical analysis
PASI: Psoriasis area and severity index

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Among the biologically naive patients, 87.5% (n=7) achieved PASI75 responses, 37.5% (n=3) achieved PASI90 responses, and 37.5% (n=3) achieved PASI100 responses. PASI75, PASI90, and PASI100 response rates among patients who had previously received biological agents were 76% (n=19), 68% (n=17), and 24% (n=6), respectively. No statistically significant difference was found between the biologically naive and non-naive groups in terms of PASI75, PASI90, and PASI100 responses (p>0.05).

Adverse events were observed within 3 months in three (9%) patients. Upper respiratory tract infection was determined in one patient receiving 150 mg of secukinumab, and pruritus and urticaria that responded to antihistamine therapy were observed in two patients receiving 300 mg of the drug. No adverse events requiring discontinuation of treatment occurred.

Discussion

Secukinumab is a human monoclonal antibody that selectively targets and neutralizes IL-17A. Phase III studies have demonstrated that secukinumab is a highly efficacious, fast-acting biological therapy for psoriasis with a favorable safety profile that could be considered for patients requiring rapid clearance and those presenting with psoriatic arthritis or plaques in difficult-to-treat areas, such as the scalp, palms, and soles[4-7]. The average reported rates of PASI75, PASI90, and PASI100 responses induced by secukinumab at week 12 in a real-world evidence-based meta-analysis of the results of 43 studies were 79%, 50%, and 36%, respectively[8]. The results of the present study showed that 78.7% and 66.7% of the patients respectively achieved PASI75 and PASI90 responses in a real-life setting after 12 weeks of secukinumab therapy.

Secukinumab at 150 mg has been shown to be superior to placebo and etanercept in terms of inducing PASI90 responses at week 12 in phase III studies[6]. Moreover, 300 mg of secukinumab has been shown to exhibit statistically significantly higher efficacy compared with a drug dose of 150 mg in patients with moderate-to-severe-psoriasis[4,9,10]. A pooled subanalysis of five phase III clinical trials (i.e., Feature, Fixture, Erasure, Juncture, and Sculpture) showed that PASI75 response rates at week 12 ranged from 76% to 91% in patients treated with 300 mg of secukinumab and from 67% to 71% in those receiving 150 mg. A PASI90 response at week 12 was achieved by 39.1%-41.9% of the patients in the 150 mg group and 54.2%-73% of the patients in the 300 mg dose group[4,10-12]. Although real-life data-based studies comparing the efficacy of 150 and 300 mg of secukinumab are scarce, a drug dose of 300 mg is widely preferred in routine clinical practice. Secukinumab at 150 mg is primarily recommended for psoriasis patients with low PASI scores and low body weight[13]. A retrospective multicenter study comparing the efficacy of 150 and 300 mg of secukinumab reported higher treatment responses (i.e., PASI <2 and PASI <5) at week 12 in the 150 mg group, which was attributed to lower PASI scores prior to treatment[14]. In the present study, the proportion of patients achieving PASI75 and PASI90 responses under 300 mg of secukinumab at week 12 were 70.6% and 64.7%, respectively; by comparison, the proportion of patients achieving PASI75 and PASI90 responses under 150 mg of secukinumab at the same time point were 87.5% and 78.5%, respectively. No statistically significant difference in PASI75, PASI90, and PASI100 responses between the 150 and 300 mg groups was observed at week 12, but PASI75 and PASI90 response rates were generally higher in patients receiving 150 mg than in those receiving 300 mg. Patients given 150 mg of secukinumab had lower PASI scores before therapy, as well as a higher proportion of biologically naive patients, compared with the 300 mg group. This result may be related to the patient selection protocol adopted by the physician who evaluated the patients prior to treatment at our center.

Phase III trials and studies based on real-life data have reported higher treatment responses with secukinumab in biologically naive patients compared with non-naive individuals[13,15,16]. Notario et al.[13], for example, reported PASI75 and PASI90 responses of 84.2% and 76.3%, respectively, for biologically naive patients at week 16; PASI75 and PASI90 responses of 66.6% and 43.3%, respectively, were also noted for non-naive patients at the same time point. Secukinumab has been described to be highly effective in biologically naive patients without the accompanying psoriatic arthritis[17]. Huang et al.[18] reported that all of the patients in their study who ceased secukinumab treatment because of unresponsiveness had previously received biological treatment. The probability of secondary loss of the effectiveness of secukinumab appears to increase in line with the number of prior biological failures. Galluzzo et al.[19] also showed that the proportions of patients achieving PASI75, PASI90, and PASI100 responses were inversely proportional to the number of biological drugs received by the patients prior to secukinumab therapy. However, Leman and Burden[20] suggested that the failure of one biological agent does not necessarily preclude a patient's response to another. One 84-week, retrospective multicenter study reported that secukinumab exhibits comparable effectiveness in biologically naive and non-naive patients[21]. In the present study, no statistically significant difference was observed in terms of PASI75, PASI90, and PASI100 responses between the biologically naive and non-naive groups, although PASI75 and PASI100 responses were higher in the former. In addition, two patients who received biological treatment but did not respond to induction treatment of 150 mg of secukinumab achieved a PASI75 response at week 12 after the drug dose was increased to 300 mg at week 8. Secukinumab at 300 mg may be considered for patients who had previously received biological treatment, and treatment may be maintained at a dosage of 150 mg after achieving PASI75 or PASI90 responses in selected patients.

In addition to its efficacy, secukinumab is also associated with a rapid clinical response. PASI50 and PASI75 responses were observed within 4 weeks in one study, and maintained or improved responses were documented through week 52[4]. A recent multicenter study conducted in Europe reported that improvements in PASI scores continued through week 52 with secukinumab therapy in 330 patients with moderate-to-severe psoriasis[22]. The Sculpture extension study demonstrated that 300 mg of secukinumab delivers strong and long-lasting sustained efficacy in patients with moderate-to-severe plaque psoriasis over 5 years[23]. The findings of the present study revealed the fast-acting efficacy of secukinumab therapy in psoriasis patients at week 12; however, the patients' long-term results were not evaluated.

Secukinumab is generally well tolerated and has a safety profile comparable with that of other antipsoriatic biological agents. The most common side-effects reported in randomized controlled studies are nasopharyngitis, headache, and upper respiratory tract infection

at weeks 12-52[24]. The risk of serious infection is very low, and reactivation of tuberculosis has not been reported[24]. Close follow-up is recommended for mucocutaneous candidiasis, especially in patients receiving a treatment dose of 300 mg[6]. A meta-analysis evaluating the results of 10 phase III studies revealed no increase in adverse event rates per year at the end of the first year, and no new safety signal was detected at the end of the fifth year of secukinumab therapy. A similar safety profile has been observed in patients groups receiving 150 and 300 mg of secukinumab over a 52-week period in phase III trials[8,25]. The results of a real-world evidenced-based meta-analysis involving 1,226 patients showed that the proportion of patients who experienced adverse events was consistent with the rates reported in randomized controlled trials; moreover, no new safety signals were observed[8]. Forty-eight percent of the patients in the present study had latent tuberculosis, and 15.2% had a history of hepatitis B infection, although no reactivation was observed. Upper respiratory tract infection, pruritus, and urticaria were observed in three patients, but no serious side-effects requiring discontinuation of treatment were detected.

Study Limitations

The main limitations of the study include the small patient group recruited, the short follow-up time (12 weeks), and the retrospective design.

Conclusion

Consistent with the previous literature, the present study findings reveal that 150 or 300 mg of secukinumab is an effective and safe treatment option for chronic plaque-type psoriasis patients. According to our clinical experience, induction and maintenance treatment at 150 mg may be recommended for biologically naive patients with low PASI scores when considering efficiency and treatment costs. Further studies are necessary to establish whether efficiency could be sustained under a 150 mg dosage during maintenance treatment in patients achieving PASI90 and PASI100 responses at 300 mg.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ankara University Faculty of Medicine Ethics Committee (approval number: I1-56-20).
Informed Consent: This is a retropsective study.
Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.K.Y., N.K., Concept: İ.K.Y., M.A., Design: İ.K.Y., N.K., Data Collection or Processing: İ.K.Y., M.A., Analysis or Interpretation: İ.K.Y., N.K., Literature Search: İ.K.Y., M.A., Writing: İ.K.Y.
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