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Secukinumab in psoriasis: A single center experience

Psoriaziste sekukinumab: Tek merkez deneyimi

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Abstract

Background and Design: Several randomized clinical trials demonstrated the safety and efficacy of secukinumab in the systemic treatment of moderate-severe psoriasis, whereas real-life data is limited. The aim of our study is to assess efficacy and safety of the secukinumab in psoriasis patients.
Materials and Methods: Thirty-two patients treated with secukinumab were retrospectively reviewed in the study. The efficacy of secukinumab was evaluated as PASI 50, PASI 75, PASI 90 response rates at 16, 24 and 36 weeks. Side effects of secukinumab treatment were recorded.
Results: The mean PASI of the 32 patients before treatment was 12.38 ± 6.49 and lowered to 1.96, 1.85 and 3.01, after 16, 24 and 36 weeks, respectively. At the 16th week of the treatment, 83.3% of the patients reached PASI 50, 70.0% had PASI 75 and 50.0% had PASI 90 response rates. At 16, 24 and 36 weeks, PASI 50, 75 and 90 responses were generally higher in biologic-naive patients than non-naive to biologics, however the differences were not statistically significant ($p > 0.05$). Secukinumab was discontinued in 7 (21.9%) patients during the treatment. Of the 7 patients, 5 (15.6%) patients failed to respond to secukinumab and 2 (6.2%) developed various side effects. Oral candidiasis which observed in 4 (12.5%) patients was the most common side effect of secukinumab treatment.
Conclusion: Secukinumab can be effective and safe treatment option in psoriasis patients. The efficacy of secukinumab in clinical practice may be higher in bio-naive patients.
Keywords: Secukinumab, psoriasis, biologic treatment, efficacy, safety

Öz

Amaç: Birçok randomize klinik çalışma, orta-şiddetli psoriazisin sistemik tedavisinde sekukinumabın etkinliği ve güvenilirliğini ortaya koyarken, gerçek yaşam verileri sınırlıdır. Çalışmamızın amacı psoriaziste sekukinumabın etkinliği ve güvenilirliğini değerlendirmektir.
Gereç ve Yöntem: Çalışmada sekukinumab tedavisi alan 32 hasta retrospektif olarak incelendi. Sekukinumabın etkinliği tedavinin 16, 24 ve 36. haftalarında PAŞİ 50, PAŞİ 75, PAŞİ 90 yanıt oranları ile değerlendirildi. Sekukinumab tedavisinin yan etkileri kaydedildi.
Bulgular: 32 hastanın sekukinumab tedavisi öncesi PAŞİ ortalaması 12.38 ± 6.49 olup tedavinin 16, 24 ve 36. haftalarında sırasıyla 1.96, 1.85 ve 3.01'e geriledi. Tedavinin 16. haftasında hastaların %83.3'ü PAŞİ 50'ye ulaşırken % 70.0'ında PAŞİ 75 ve % 50.0'ında PAŞİ 90 yanıt oranları elde edildi. Tedavinin 16, 24 ve 36. haftalarında, PAŞİ 50, 75 ve 90 yanıtları, biyolojik-naif hastalarda, biyolojik-naif olmayanlara göre daha yüksekti, ancak istatistiksel olarak anlamlı bir fark saptanamadı ($p > 0.05$). Beş (%15.6) hastada yetersiz klinik yanıt, 2 (%6.2) hastada ise tedaviye bağlı yan etkiler nedeniyle toplam 7 (%21.9) hastada tedavi kesildi. Dört (%12.5) hastada görülen oral kandidiyazis sekukinumaba bağlı en sık yan etki olarak kaydedildi.
Sonuç: Sekukinumab, orta-şiddetli psoriazis hastalarında etkili ve güvenli bir tedavi seçeneğidir. Sekukinumabın gerçek yaşam verisi olarak etkinliği biyolojik-naif hastalarda daha yüksek olabilir.
Anahtar Kelimeler: Sekukinumab, psoriazis, biyolojik tedavi, etkinlik, güvenilirlik

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Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease that affects about 2-3% of the population[1]. As a T-cell-mediated inflammatory skin disease, therefore many targeted immunological therapeutic options have been tried recently in psoriasis. It is well documented that Interleukin (IL)-17 plays a substantial role in the immunopathogenesis of psoriasis. Secukinumab as an IL-17 receptor inhibitor has been applied in the treatment of moderate and severe plaque psoriasis in adult patients[2,3].

Although the efficacy and safety of secukinumab in psoriasis patients have been demonstrated in randomized clinical trials, the results may differ from those enrolled in daily practice. In this study, we aimed to evaluate efficacy and safety of the secukinumab in psoriasis patients in our tertiary hospital.

Materials and Methods

Moderate to severe plaque psoriasis patients older than 18 years old of age who received at least 16 weeks of secukinumab between May 2018-March 2020 were retrospectively evaluated in the study. No patient received any systemic conventional therapy concurrent with secukinumab. Topical treatments were allowed to be used with secukinumab. Erythrodermic, guttate, pustular, and palmoplantar psoriasis patients were not included in the study. Sociodemographic features of the patients, previous systemic and biologic treatments, presence of coexisting psoriatic arthritis (PsA) and nail involvement were recorded. Response to treatment was assessed with the Psoriasis Area and Severity Index (PASI) score (at baseline, 16th, 24th and 36th weeks). Duration and side effects of the treatment were recorded. The efficacy of treatment was evaluated by PASI 50, PASI 75 and PASI 90 response rates. Ethical approval was received from the Eskişehir Osmangazi University, Non-interventional Clinical Research Ethics Committee (approval number: 31, date: 10.09.2019).

Statistical Analysis

Descriptive statistics are given as number, percentage (%), mean and standard deviation (SD). Pearson Chi-Square and Pearson Exact Chi-Square analyzes were used in the analysis of the cross tables. IBM SPSS Statistics 21.0 (Armonk, NY: IBM Corp.) was used for the analysis. For statistical significance, $p < 0.05$ was accepted as the criterion.

Results

A total of 32 patients diagnosed with psoriasis were included in this study. Twenty-two (68.7%) of the patients were males, 10 (31.3%) were females. The median age of the patients was 45.68 ± 14.09 years. Four (12.5%) patients had accompanying PsA and 7 (21.9%) had nail involvement.

When the previous treatments were evaluated, all of the patients had received methotrexate, 13 (40.6%) of the patients received narrow-band ultraviolet B (Nb-UVB), 18 (56.3%) patients cyclosporine, 17 (53.1%) patients acitretin, 12 (37.5%) patients adalimumab, 8 (25.0%) patients infliximab, 7 (21.9%) patients ustekinumab and 1 (3.1%) patient certolizumab before secukinumab at different times. Fourteen (43.8%) patients had not previously received biological treatment (Table 1).

We evaluated the response to secukinumab at the 16th, 24th and 36th weeks of the treatment. At the 16th week of the treatment, PASI 50, PASI 75 and PASI 90 response rates were reached in 83.3%, 70.0% and 50.0% of the patients, respectively. At 24th week of the treatment, PASI 50, PASI 75 and PASI 90 responses were reached in 81.5%, 77.5% and 51.9% of the patients, respectively. At the 36th week of the treatment, PASI 50, PASI 75 and PASI 90 responses were reached in 76.0%, 72.0% and 44.0% of the patients, respectively. At 16th, 24th and 36th weeks, PASI 50, PASI 75 and PASI 90 response rates were generally higher in patients naive to biologics than in non-naive to biologics, however the differences between these groups were not statistically significant (Table 2).

Table 1. Baseline demographic and disease characteristics of the patients

Characteristic		Number (%) of patients
Gender, n (%)	Male	22 (68.3%)
	Female	10 (31.3%)
Age (years), mean ± SD		45.68±14.09
Psoriatic arthritis, n (%)		4 (12.5%)
Nail psoriasis, n (%)		7 (21.9%)
PASI baseline, mean ± SD		12.38 ± 6.49
Previous conventional systemic therapy, n (%)		
Methotrexate		32 (100.0%)
Cyclosporine		18 (56.3%)
Acitretin		17 (53.1%)
Phototherapy		13 (40.6%)
Previous biologic treatment, n (%)		
Adalimumab		12 (37.5%)
Ustekinumab		7 (21.9%)
Infliximab		8 (25.0%)
Certolizumab		1 (3.1%)
Mean duration of secukinumab (month), mean ± SD		10.52 ± 4.49

SD: Standard deviation

The mean duration of secukinumab treatment was 10.52 ± 4.49 months. Secukinumab was ceased during the treatment in 5 (15.6%) patients due to lack or loss of clinical response and all of these patients were non-naive to biologics. At the 16th week of the treatment, 3 (60%) of the patients did not reached to PASI 50 response rate and secukinumab was ceased. Two (40%) patients had PASI 50 response (PASI > 50% of initial value) rates at the 16th week initially, however this response was lost in the following time of treatment and secukinumab was ceased.

Seven (21.9%) patients experienced adverse events during the course of the treatment. The most common adverse event was oral candidiasis which developed in 4 (12.5%) patients, while nasopharyngitis and external otitis was observed in 1 (3.1%) patient. Secukinumab was discontinued in 2 (6.2%) patients due to the adverse events; one patient because of erectile dysfunction and another patient for weight gain problem.

Discussion

Psoriasis is a papulosquamous skin disorder which occurs with complex interactions between immune system, hereditary and environmental

Table 2. Results of PASI responses of patient groups according to weeks

	Total	Naiv	Non-naive	p
Total patients, n (%)	32 (100%)	14 (43.8%)	18 (56.3%)	-
Number of patients at week 16	30	13	17	-
PASI 50, n (%)	25 (83.3%)	13 (100%)	12 (70.6%)	0.09
PASI 75, n (%)	21 (70.0%)	13 (100%)	8 (47.1%)	0.006
PASI 90, n (%)	15 (50.0%)	9 (69.2%)	6 (35.3%)	0.14
Number of patients at week 24	27	10	17	-
PASI 50, n (%)	22 (81.5%)	10 (100%)	12 (70.6%)	0.16
PASI 75, n (%)	21 (77.8%)	10 (100%)	11 (64.7%)	0.09
PASI 90, n (%)	14 (51.9%)	8 (80.0%)	6 (35.3%)	0.06
Number of patients at week 36	25	8	17	-
PASI 50, n (%)	19 (76.0%)	8 (100%)	11 (64.7%)	0.15
PASI 75, n (%)	18(72.0%)	8(100%)	10(58.8%)	0.09
PASI 90, n (%)	11 (44.0%)	6 (75%)	5 (29.4%)	0.08

factors. Although the precise pathogenesis of psoriasis is not fully understood, it is considered as a T cell mediated inflammatory disease[4]. Recently, the key role of T helper (Th)-17 cells which produces cytokines such as IL-17A, IL-17F, IL-22, IL-26 was documented in the inflammatory response of the disease. Higher cytokines have been observed in both psoriatic lesion and non-affected skin of the patients with psoriasis[3,5].

Secukinumab is a recombinant human immunoglobulin G1 monoclonal antibody that specifically binds to IL-17A. In 2015, it was approved for the treatment of moderate-to-severe plaque psoriasis and in 2016 for the psoriatic arthritis[3,6]. According to the randomized placebo-controlled clinical trials, secukinumab has shown higher PASI 75, 90 and 100 response rates compared to placebo at the 12th week[7-9].

Looking into real-world data, several studies have demonstrated a promising efficacy of secukinumab in clinical practice[10-15]. However, in our study, PASI 75 and PASI 90 clinical response rates were found lower than the previous real-life studies[10,11,13,16,17] while similar with the study of Notario et al.[18], at week 16.

At the 24th week of secukinumab, previous studies[19-21] reported similar PASI 75 response rates with our study, while lower PASI 90 responses was found in our study compared to the other studies[19,20]. In a study conducted by Chiricozzi et al.[21], they reported similar PASI 75 and PASI 90 response rates with our study at week 24. Additionally, the rate of their bio-naive patients were found similar with our results. Recently, Galuzzo et al.[11] retrospectively evaluated the efficacy of secukinumab in a real-world setting and reported higher PASI 75 and PASI 90 response rates at week 24, compared to our study. The number of bio-naive patients in their study was higher than our study.

Several studies showed that previous biologic treatments may affect the response to secukinumab and bio-naive patients reached higher PASI response rates[10,11,18]. A retrospective study in which 51.4% of the patients had previously received biological treatment revealed that bio-naive patients tended to achieve PASI 75 faster than non-naive patients at week 4[19]. Similarly, Ger et al.[22] suggested that number of prior biologic failures were significantly associated with decrease response rate of secukinumab treatment.

In our study, PASI 75 and 90 response rates were found lower as compared to the other studies[19,22] at the 36th week. This may be explained by the lower rate of bio-naive patients in our study. However, there was no statistically significant difference between patients with naive to biologics and non-naive to biologics in our study.

It was suggested that variation of PASI responses in clinical practice comparing randomized controlled trials can be explained by differences in baseline characteristics of the study population[18]. In a retrospective study, it is reported that patients aged 55 and older were less responsive to secukinumab treatment, where 50.0% of the patients reached PASI 75 at week 12[23]. However, when our patients were evaluated in a 16-week treatment period, 62.5% (5/8) of the patients aged 55 and older achieved PASI 75 and PASI 90 response rates. Megna et al.[24] evaluated the efficacy of secukinumab in patients with psoriasis aged ≥ 65 years. In this study, mean PASI score was 11.4 at baseline and reduced to 2.1, at week 24. Our results confirmed the high effectiveness of secukinumab in patients aged ≥ 65 years, with a mean PASI score at baseline was 12.7 and reduced to 1.08, at week 24.

Rompoti et al.[12] reported that patients with accompanying PsA showed lower clinical responses to secukinumab. Similarly, Chiricozzi et al.[21] suggested that the higher rate of patients with PsA may decrease the clinical response in terms of absolute PASI scores. In our study, although we have fewer patients with PsA compared to the reported studies[12,21], 75% (3/4) of the patients reached PASI 90 responses at the 16th, 24th and 36th weeks of the secukinumab.

Secukinumab was ceased in 5 (15.6%) patients due to lack of clinical response in our study. In recent studies[10,21] with a 52-week treatment duration, the rate of bio-naive patients were higher than our patients, while lower discontinuation rates were reported than our study. Moreover, Notario et al.[18] reported that 26.5% of patients discontinued secukinumab due to lack of efficacy by week 52, which was higher than our study. In this study, 28% of the patients had not previously received biological treatment. These results confirm that the prior biologic treatments can affect the continuation rates of secukinumab.

The most frequently reported adverse events of secukinumab are pharyngitis, diarrhea, and upper respiratory infections[3]. Blockage of the mediators of adaptive and innate immune systems induced by biologic therapies can predispose to opportunistic infections. Additionally, it is also well known that IL-17A has a substantial role in immune

defense against mucocutaneous infections such as *Candida albicans*[25]. Georgakopoulos et al.[23] evaluated the safety of secukinumab and found that Candida infections was observed in 9 (4.2%) of 47 patients. In a study conducted by Özçelik et al.[13], oral candidiasis was detected in only one (3.8%) patient who received secukinumab. In our study, oral candidiasis developed in 4 (12.5%) patients which was higher than the previous studies[13,23,16], however all patients responded to oral and topical antifungal therapies without discontinuation of secukinumab treatment.

In our study, secukinumab was discontinued in 2 (6.2%) patients due to the adverse events. One (3.1%) of the patients had significant weight gain and the patient refused to continue treatment. Several studies assessed the body weight changes in psoriasis patients who treated with anti-TNF agents and significant weight gain was observed with adalimumab and infliximab treatments[26-28]. Takamura et al.[29] retrospectively reviewed the impact of infliximab, ustekinumab and secukinumab treatments on the body weight and significant weight gain was reported only with infliximab after 7 months of the treatment, however no gain was reported in patients who received ustekinumab and secukinumab. However, in a recent study conducted by Topaloğlu et al.[15], weight gain was reported more common in patients treated with ustekinumab and secukinumab than anti-TNF agents.

One (3.1%) of our patients developed erectile dysfunction after the 10th injection of secukinumab. Dastoli et al.[30] reported the first case of secukinumab-induced erectile dysfunction which developed 60 days after the initiation of treatment which disappeared with substituting secukinumab with ixekizumab. To our best knowledge, our patient is the second case of secukinumab-induced erectile dysfunction and treatment discontinued for this reason.

Study Limitations

Limitations of this study are being a retrospective design and the small number of the patients who had completed 16th, 24th and 36th weeks of the treatment with secukinumab.

Conclusion

Secukinumab may be considered as an effective and safe biologic treatment option in moderate-to-severe psoriasis patients however, wider scale studies are required to assess its safety and effectiveness in real clinical practice.

Ethics

Ethics Committee Approval: Ethical approval was received from the Eskişehir Osmangazi University, Non-interventional Clinical Research Ethics Committee (approval number: 31, date: 10.09.2019).

Conflict of Interest: No conflict of interest was declared by the authors.

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