

Secukinumab Treatment in Patients with Hidradenitis Suppurativa in Real-World Clinical Settings: A Multicenter Study

Ece Erbağcı¹, Özge Sevil Karstarlı Bakay², Fatma Aslı Hapa³

¹ Uşak University Training and Research Hospital, Department of Dermatology and Venereology, Uşak, Turkey

² Pamukkale University Faculty of Medicine, Department of Dermatology and Venereology, Denizli, Turkey

³ Izmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital, Department of Dermatology and Venereology, Izmir, Turkey

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Corresponding Author: Ece Erbağcı, Uşak University Training and Research Hospital, Department of Dermatology and Venereology, Uşak, Turkey. E-mail: ece.erbagci@gmail.com

ABSTRACT

Introduction: Treatment of hidradenitis suppurativa (HS) remains a challenge in clinical practice for dermatologists. Although the effectiveness and safety of secukinumab (SEC) in the treatment of HS have been demonstrated in phase III studies, real-world data is limited.

Objectives: We conducted a retrospective multicenter study to evaluate the effectiveness and safety of SEC treatment in HS patients in real-world settings.

Methods: Adult patients who were diagnosed with HS and used SEC for at least 3 months were included in the study.

Results: A total of 31 patients were included in the study; 14 of them (45.2%) were female. The mean age was 39.32 ± 10.26 years, and the mean disease duration was 11.77 ± 7.99 years. Nine (29%) patients were biologic-naïve and 10 (32.3%) were adalimumab-naïve. Disease severity was Hurley I in 7 patients (22.6%), Hurley II in 9 patients (29%), and Hurley III in 15 patients (48.4%). The Hidradenitis Suppurativa Clinical Response (HiSCR) was achieved in 20 patients (64.5%) in the third month of treatment. SEC treatment was discontinued due to primary ineffectiveness in 9 (29%)

patients, secondary ineffectiveness in 1 (3.2%) patient, adverse effects in 1 (3.2%) patient, and loss of follow-up in 1 (3.2%) patient. Paradoxical pyoderma gangrenosum was observed as an adverse effect in 1 patient that resolved after discontinuing SEC and starting infliximab.

Conclusions: SEC appears to be an effective and safe treatment option for HS, especially when used in the early and mild stages of the disease and in biologic-naive patients.

Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, and debilitating skin follicular disease that typically appears after puberty with painful deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillary, inguinal, and anogenital regions [1]. The underlying pathogenic mechanism of HS mainly involves the formation of follicular hyperkeratosis first, causing plugging and dilation that results in follicle rupture with subsequent inflammation, abscess, and sinus tract formation [1, 2]. HS immunopathogenesis is complex and still being studied, but several cytokines appear to be especially important. IL-17 levels are increased in serum and in damaged skin of HS patients compared with healthy control subjects, and they correlate with disease severity [3, 4]. Therefore, blockade of the IL-17 pathway may be a promising treatment for HS.

Secukinumab (SEC) is a monoclonal antibody targeting IL-17A, and its effectiveness and safety in the treatment of HS were demonstrated in the SUNSHINE and SUNRISE phase III randomized clinical trials [5]. Adalimumab, an anti-tumor necrosis factor (TNF)- α inhibitor, was the first biologic drug approved for the treatment of HS. Recently, the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) also approved SEC for use in adults with active moderate-to-severe HS [6, 7]. However, there are few real-world studies on the effectiveness and safety of SEC in HS treatment.

Objectives

In our study, we aimed to share our real-world data on the efficacy and safety of SEC treatment in HS patients.

Methods

We conducted a retrospective multicenter study to evaluate the effectiveness and safety of SEC treatment in HS patients in a real-world setting. SEC has been available in our country since 2018. Therefore, hospital electronic record systems were retrospectively scanned between 1.1.2018 and

1.3.2024 (end date of inclusion in the study). Adult patients (age ≥ 18 years) who were diagnosed with HS and used SEC for at least 3 months during the specified date range were included in the study.

From the past medical records, patient age, sex, body weight (kg), height (cm), body mass index (BMI), smoking status, comorbidities, age at disease onset, duration of disease, duration of medication (SEC) use, additional treatments used for HS (if any), previous treatments (systemic antibiotics, immunosuppressants, acitretin, surgery, etc.), areas of HS involvement, disease severity (Hurley stage), and adverse effects (if any) with SEC treatment were noted.

The Hidradenitis Suppurativa Clinical Response (HiSCR), which is a validated treatment endpoint for HS, is defined as a $\geq 50\%$ reduction in inflammatory lesion count (sum of abscesses and inflammatory nodules) and no increase in abscesses or draining fistulas when compared with baseline [8]. The primary endpoint to evaluate the effectiveness of SEC in our study was to determine the proportion of patients who achieved a HiSCR response at 3 months of treatment. As a loading dose of SEC, 300 mg subcutaneously was administered to all patients once a week for 5 weeks, and then the maintenance dose was started.

The local ethics committee approved the study protocol. Statistical analyses were made in the SPSS for Windows Version 23.0 package program. Numerical variables were summarized as mean \pm standard deviation (SD), median, min-max values, and categorical variables were summarized as numbers and percentages. Appropriate parametric or non-parametric statistical tests were used according to the distribution and types of variables. The significance level was taken as $P < 0.05$.

Results

A total of 31 patients diagnosed with HS who used SEC for at least 3 months were included in the study; 14 (45.2%) were female. The mean age was 39.32 ± 10.26 years, the mean disease duration was 11.77 ± 7.99 years, and the mean body mass index (BMI) was 28.59 ± 5.83 kg/m². Thirteen (41.9%) patients were smokers, and 1 (3.2%) was an ex-smoker. The most common comorbidity was psoriasis (35.5%), followed

by arthritis (32.3%), diabetes (9.7%), and hypertension (9.7%). Nine (29%) patients were biologic-naive, and 10 (32.3%) were adalimumab-naive. Disease severity was Hurley I in 7 patients (22.6%), Hurley II in 9 patients (29%), and Hurley III in 15 patients (48.4%). The most common area of involvement was the pelvic (96.8%), followed by the axilla (93.5%) and inframammary (35.5%), respectively. Characteristics of the patients are shown in Table 1.

The dose of SEC was 150 mg/28 days in 1 patient (due to the accompanying diagnosis of ankylosing spondylitis), 300 mg/28 days in 19 patients, 300 mg/14 days in 10 patients, and 300 mg/28 days initially and then 300 mg/14 days (due to secondary ineffectiveness) in 1 patient. The mean duration of SEC use was 12.06 ± 10.51 (min: 3–max: 48) months. As additional treatment combined with SEC, 12 (38.7%) patients used oral antibiotics, 9 (29%) patients used methotrexate, and 2 (6.5%) patients used zinc gluconate. HiSCR was achieved in 20 patients (64.5%) in the third month of treatment. SEC treatment was discontinued due to primary ineffectiveness in 9 (29%) patients, secondary ineffectiveness in 1 (3.2%) patient, adverse effects in 1 (3.2%) patient, and loss of follow-up in 1 (3.2%) patient. Paradoxical pyoderma gangrenosum was observed as an adverse effect that caused treatment discontinuation in one patient. A 48-year-old man with HS developed pyoderma gangrenosum after 13 months of SEC treatment. The patient, who had no other disease that could explain the etiology of pyoderma gangrenosum, improved after SEC treatment was discontinued and infliximab was started.

Patients who achieved HiSCR were compared with those who did not achieve it in terms of their clinical characteristics. In patients who achieved HiSCR, disease severity was milder ($P = 0.044$), disease duration was shorter ($P = 0.04$), duration of SEC use was longer (due to discontinuation of treatment in those who did not achieve HiSCR) ($P = 0.032$), use of additional combined oral antibiotics was less ($P = 0.007$), and naivety to previous biologic drugs ($P = 0.012$) and adalimumab ($P = 0.005$) was higher. While all biologic-naive patients achieved HiSCR, 11/22 (50%) of biologic-experienced patients achieved HiSCR. Although our number of cases in the study was very limited, we did not detect any statistically significant difference in terms of clinical and demographic data between biologic-experienced patients and biologic-naive patients (statistics are not shown). No statistically significant relationship was found between HiSCR achievement and age, sex, BMI, smoking status, age at disease onset, areas of involvement, and SEC dose. To further analyze the relationships with HiSCR, a multivariate analysis was performed using logistic regression with a model including all clinical and demographic variables. The multivariate analysis was then repeated with a second model that included only those variables that showed a significant

or near-significant association ($P \leq 0.25$) with HiSCR response in univariate analysis (smoking status, Hurley stage, disease duration, biologic and adalimumab naivety). However, no significant relationship was found between variables and HiSCR in both models, probably due to the small number of patients. Therefore, the linear analysis results are shown in Table 1.

Conclusions

The results of our study support the idea that SEC is an effective treatment option for HS in real-world clinical settings. HiSCR was achieved in 20 (64.5%) of our 31 cases. We observed that the response to treatment was better in the early stages of the disease, in those with less severe disease, and in biologic-naive patients.

In the SUNSHINE and SUNRISE phase III studies, SEC treatment in adult patients with HS was compared with placebo at doses of 300 mg/4 weeks and 300 mg/2 weeks. The proportion of patients with HiSCR at the 16th week of treatment was 45% in the SEC 300 mg/2 weeks group, 42% in the SEC 300 mg/4 weeks group, and 34% in the placebo group in the SUNSHINE study. In the SUNRISE study, this proportion was 42% in the SEC 300 mg/2 weeks group, 46% in the SEC 300 mg/4 weeks group, and 31% in the placebo group. The proportion of patients achieving HiSCR in the SEC treatment groups was sustained, with a trend toward improvement up to week 52 in both studies. In both trials, treatment with both SEC regimens was well tolerated. The most frequently reported adverse events were headache, nasopharyngitis, and worsening of HS. No new treatment-emergent adverse events were identified up to week 52 [5].

In the SUNSHINE and SUNRISE studies, when subgroup analysis was performed according to the patients' biological experience, it was found that biologic-naive patients tended to show greater treatment effectiveness, similar to our study [9]. However, this analysis also noted that biologic-experienced patients had more severe Hurley stage, longer disease duration, and a higher rate of previous HS surgery than biologic-naive patients [9]. Additionally, in real-world experience, biological agents tend to be preferred for more severe disease that is unresponsive to conventional treatment. Therefore, when interpreting the difference in clinical response, it is necessary to consider that this may be related to the biological experience as well as HS severity, disease duration, previous treatment history, or a mixture of all these.

Case series, case reports, and retrospective studies on the real-world effectiveness and safety of SEC in HS are available in the literature. In the open-label pilot study of Prussick et al, 9 patients with moderate to severe HS were administered

Table 1. Demographic and Clinical Characteristics of Patients According to HiSCR.

	HiSCR (+) (N = 20, 64.5%)	HiSCR (-) (N = 11, 35.5%)	P	Total (N = 31, 100%)
Age, years Mean \pm SD Min - max	37.05 \pm 9.11 20-54	43.45 \pm 11.36 25-68	0.97	39.32 \pm 10.26 20-68
Sex Female, N (%) Male, N (%)	11 (55) 9 (45)	3 (27.3) 8 (72.7)	0.258	14 (45.2) 17 (54.8)
Body weight, kg Mean \pm SD Min - max	87.1 \pm 21.67 55-130	85 \pm 16.34 65-120	0.782	86.35 \pm 19.68 55-130
Height, cm Mean \pm SD Min - max	173.65 \pm 11.05 155-191	173.55 \pm 6.56 161-186	0.977	173.61 \pm 9.58 155-191
Body mass index (BMI), kg/m ² Mean \pm SD Min - max	28.8 \pm 6.3 19-40.8	28.2 \pm 5.12 22.6-37.9	0.887	28.59 \pm 5.83 19-40.8
Smoking status No, N (%) Yes, N (%) Ex-smoker, N (%)	13 (65) 7 (35) -	4 (36.4) 6 (54.5) 1 (9.1)	0.153	17 (54.8) 13 (41.9) 1 (3.2)
Hurley stage I, N (%) II, N (%) III, N (%)	7 (35) 6 (30) 7 (35)	- 3 (27.3) 8 (72.7)	0.044	7 (22.6) 9 (29) 15 (48.4)
Age of the disease onset, years Mean \pm SD Min - max	27.55 \pm 9.19 13-51	27.82 \pm 9.29 15-46	0.939	27.65 \pm 9.07 13-51
Duration of the disease, years Mean \pm SD Min - max	9.6 \pm 6.4 2-30	15.73 \pm 9.34 3-37	0.04	11.77 \pm 7.99 2-37
Duration of secukinumab use, months Mean \pm SD Min - max	15.15 \pm 11.75 3-48	6.45 \pm 3.96 3-14	0.032	12.06 \pm 10.51 3-48
Secukinumab (SEC) dosage 150 mg/28days, N (%) 300 mg/28days, N (%) 300 mg/14days, N (%) 300mg/28 days and then 300 mg/14 days, N (%)	1 (5) 13 (65) 5 (25) 1 (5)	- 6 (54.5) 5 (45.5) -	0.452	1 (3.2) 19 (61.3) 10 (32.3) 1 (3.2)
Areas of involvement Scalp, N (%) Axillary, N (%) Inframammary, N (%) Trunk, N (%) Pelvic, N (%)	1 (5) 19 (95) 7 (35) 1 (5) 20 (100)	2 (18.2) 10 (90.9) 4 (36.4) 3 (27.3) 10 (90.9)	0.281 1 1 0.115 0.355	3 (9.7) 29 (93.5) 11 (35.5) 4 (12.9) 30 (96.8)
Comorbidities Arthritis, N (%) Ankylosing spondylitis, N (%) Psoriatic arthritis, N (%) Rheumatoid arthritis, N (%) Psoriasis, N (%) Diabetes mellitus, N (%) Hypertension, N (%)	7 (35) 3 (15) 2 (10) 2 (10) 10 (50) 1 (5) 2 (10)	3 (27.3) 2 (18.2) 1 (9.1) - 1 (9.1) 2 (18.2) 1 (9.1)	1 0.121 0.281 1 - - -	10 (32.3) 5 (16.1) 3 (9.7) 2 (6.5) 11 (35.5) 3 (9.7) 3 (9.7)

Table 1. Demographic and Clinical Characteristics of Patients According to HiSCR. (continued)

	HiSCR (+) (N = 20, 64.5%)	HiSCR (-) (N = 11, 35.5%)	P	Total (N = 31, 100%)
Chronic obstructive pulmonary disease, N (%)	1 (5)	-	-	1 (3.2)
Chronic spontaneous urticaria, N (%)	2 (10)	-	-	2 (6.5)
Familial mediterranean fever, N (%)	2 (10)	-	-	2 (6.5)
Multiple sclerosis, N (%)	1 (5)	-	-	1 (3.2)
Alopecia universalis, N (%)	-	1 (9.1)	-	1 (3.2)
Additional treatments combined with SEC				
Oral antibiotics, N (%)	4 (20)	8 (72.7)	0.007	12 (38.7)
Zinc gluconate, N (%)	2 (10)	-	-	2 (6.5)
Methotrexate, N (%)	8 (40)	1 (9.1)	0.106	9 (29)
Previous treatments				
Adalimumab, N (%)	10 (50)	11 (100)	0.005	21 (67.7)
Oral antibiotics, N (%)	8 (40)	7 (63.6)	0.208	15 (48.4)
Intralesional steroid, N (%)	1 (5)	2 (18.2)	0.281	3 (9.7)
Surgery, N (%)	-	2 (18.2)	-	2 (6.5)
Acitretin, N (%)	-	1 (9.1)	-	1 (3.2)
Isotretinoin, N (%)	1 (5)	2 (18.2)	0.281	3 (9.7)
Methotrexate, N (%)	8 (40)	1 (9.1)	0.106	9 (29)
Dapsone, N (%)	-	1 (9.1)	-	1 (3.2)
Cyclosporine, N (%)	1 (5)	-	-	1 (3.2)
Etanercept, N (%)	4 (20)	-	-	4 (12.9)
Infliximab, N (%)	2 (10)	3 (27.3)	0.317	5 (16.1)
Golimumab, N (%)	1 (5)	-	-	1 (3.2)
Previous exposure to biologics				
Naive, N (%)	9 (45)	-	0.012	9 (29)
Non-naive, N (%)	11 (55)	11 (100)	-	22 (71)
SEC discontinued				
No, N (%)	19 (95)	-	-	19 (61.3)
Primary ineffectiveness, N (%)	-	9 (81.8)	-	9 (29)
Secondary ineffectiveness, N (%)	1 (5)	-	-	1 (3.2)
Adverse effects, N (%)	-	1 (9.1)	-	1 (3.2)
Loss of follow-up, N (%)	-	1 (9.1)	-	1 (3.2)

HiSCR = Hidradenitis Suppurativa Clinical Response; SD = standard deviation; SEC = secukinumab.

300 mg/4 weeks of SEC following a loading dose. Six of nine patients (67%) achieved HiSCR at 24 weeks. No serious adverse effects were observed [10]. In the open-label study of Casseres et al, following the loading dose, SEC was administered to 9 patients at a dose of 300 mg/4 weeks and to 11 patients at a dose of 300 mg/2 weeks. Seventy percent (14/20) of all patients achieved HiSCR by week 24. No serious adverse effects were observed [11]. These results were similar to our study.

In the single-center study of Reguiat et al, SEC was used in 20 patients with HS at a dose of 300 mg/4 weeks following the loading dose. HiSCR was achieved in 75% (15/20) of patients at the 16th week of treatment. After SEC treatment, no recurrence was observed after a mean follow-up of 14 months (range 3 to 36 months). No patient required rescue

therapy. In this study, it was observed that smoking status, weight, and HS severity did not affect the treatment results. Two patients with no personal or family history of inflammatory bowel disease developed Crohn disease after 3 and 5 months of treatment, respectively [12].

In the single-center studies reported by Melgosa Ramos et al from Spain, SEC was used at a dose of 300 mg every 14 or 28 days in 23 patients with HS. Considering only patients who reached the different follow-up evaluation periods, 17/21 (73.9%) reached HiSCR at week 16, 15/21 (71.4%) at week 24, 10/14 (71.4%) at week 36, and 10/12 (83.3%) at week 52. No severe adverse effects were reported [13].

In their single-center study, Martora et al used SEC at a dose of 300 mg/4 weeks following the loading dose in the treatment of moderate to severe HS in 4 biologic-naive

patients (adalimumab was contraindicated) and 17 patients who were secondary unresponsive to adalimumab. Seven of 21 patients failed to complete 52 weeks of treatment. Of the 14 patients who completed 52 weeks of treatment, 57.1% (8/14) achieved HiSCR at week 16 and 71.4% (10/14) at week 52 [14]. In the retrospective multicenter study reported by Ribero et al from Italy, SEC was used at a dose of 300 mg/4 weeks following the loading dose in 31 patients with HS (Hurley II or III) who were contraindicated or unresponsive to anti-TNF. 17 patients completed 28 weeks of target therapy. The HiSCR was achieved only by 10% of patients (3/31) at week 5, by 26% of patients (8/24) at week 16, and by 41% of patients (7/17) at week 28 [15]. In the study of Rocuzzo et al, 24 adult patients with HS (Hurley II or III) who were switched from adalimumab to SEC due to primary or secondary failure and/or unacceptable adverse effects. Six (25%) patients achieved HiSCR at 3 months and 13 (56.5%) at 6 months of treatment. Patients with Hurley stage II had a better response to treatment than those with Hurley III [16]. These results supported the effectiveness of SEC in cases unresponsive or contraindicated to adalimumab.

In the multicenter real-world study of Haselgruber et al, 28 of 67 patients with moderate-severe HS (41.79%) achieved HiSCR at 24 weeks with SEC treatment. SEC was used at a dose of 300 mg/4 weeks or 300 mg/2 weeks following the loading dose. They defined therapeutic burden as the cumulative sum of previous systemic treatment cycles (whether biological or not) plus the total number of previous surgical interventions that the patient had undergone for HS before initiating SEC. They observed a negative correlation between therapeutic burden and achieving HiSCR at week 24 with SEC [17]. This correlation, similar to the results of our study, drew attention to the concept of a window of opportunity in the management of HS in the early stages of the disease.

In the single-center study reported by Abu Rached et al from Germany, 13 of 42 patients with moderate-severe HS (41.9%) achieved HiSCR response at 16 weeks with SEC treatment. SEC was used at a dose of 300 mg/4 weeks, increased to 300 mg/2 weeks if necessary. Adverse events were reported in 6 patients (14.3%), and treatment discontinuation occurred in 3 patients (7.1%). Median tobacco pack years and HS inguinal involvement was significantly lower in patients who achieved HiSCR [18].

Data on the effectiveness and safety of SEC in patients with HS have been reported in several case reports [19-23]. However, information on real-world data is still limited.

The most common comorbidity in our study population was psoriasis (35.5% of cases). This is, of course, due to the fact that SEC is given priority in treatment selection in cases where HS and psoriasis occur together. Large population studies have shown that the prevalence of HS in patients with psoriasis is higher than in controls, and the prevalence

of obesity and smoking is higher in patients with the coexistence of psoriasis and HS than in patients with psoriasis alone [24]. Therefore, this association may be an indicator of increased inflammatory burden. The other most common comorbidities in our study population were arthritis (32.3%), diabetes (9.7%), and hypertension (9.7%). HS has been associated with many comorbid diseases, such as diabetes, metabolic syndrome, cardiovascular diseases, mental illnesses, inflammatory bowel disease, spondylo-arthropathies and other immune-mediated diseases [25]. Therefore, it is important to question patients about these common comorbidities and take them into consideration in treatment selection.

In our study, paradoxical pyoderma gangrenosum as an adverse effect that caused discontinuation of treatment with SEC was observed in one case. Apart from this, no serious adverse effects were observed. Drug-induced paradoxical pyoderma gangrenosum is a very rare adverse effect. In the literature, paradoxical pyoderma gangrenosum induced by SEC has been reported in only two cases with HS [26, 27], and there are a few case reports reported in cases where SEC was used for psoriasis [28-31]. The clinical condition of the cases generally improved with SEC discontinuation and anti-inflammatory drug changes, as in our case. Upregulation of IL-23 is observed in pyoderma gangrenosum lesions, and targeted treatments with ustekinumab, an IL-12/23 antibody, have resulted in beneficial clinical outcomes [29, 32, 33]. IL-23-induced activation of plasmacytoid and dermal dendritic cells results in T helper 17 cells releasing IL-17A, which then acts on epidermal keratinocytes, resulting in a feed-forward inflammatory response. However, inhibiting IL-17A may paradoxically increase IL-23 production, triggering the development of pyoderma gangrenosum [34].

Limitations of our study include small sample size, lack of a control group, and open-label design. In addition, due to the retrospective design of our study, we could not use other commonly used scoring systems such as the dermatological quality of life index, Sartorius scoring, and the international hidradenitis suppurativa severity scoring system other than Hurley staging and HiSCR. However, despite its limitations, our study is valuable because it is one of the most comprehensive studies on the real-world experience of SEC treatment in patients with HS.

In line with the data of our study and previous literature, SEC appears to be an effective and safe treatment option for HS, especially when used in the early and mild stages of the disease and in biologic-naive patients.

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