

Efficacy of adalimumab in moderate to severe hidradenitis suppurativa: Real life data

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Abstract

Hidradenitis suppurativa (HS) is a relapsing, inflammatory disease characterized by painful nodules, abscesses, sinus track formation and scarring. HS has a great impact on patients' quality of life and its treatment may be really challenging. Adalimumab provides a new therapeutic option for HS. Our aim was to assess the therapeutic potential of adalimumab on patients with HS based on the data from the daily clinical practice of an HS Outpatient Clinic. 19 patients with clinically evident moderate to severe HS, under adalimumab treatment for at least 24 weeks, participated in this observational, retrospective study. The Hidradenitis Suppurativa Physician's Global Assessment scale, Modified Santorius scale and Dermatology Life Quality Index (DLQI) at baseline, week 4, week 12 and week 24 were retrieved from the records. Both Modified Santorius score and DLQI were significantly decreased during the weeks of evaluation (Friedman's test; $P < 0.001$). The proportion of patients who achieved clinical response was 10.5% ($n = 2$) at week 4, 42.1% ($n = 8$) at week 12 and 63.2% ($n = 12$) at week 24. Treatment with adalimumab was linked with both clinical remission of HS and improvement of patients' quality of life.

Introduction

Hidradenitis suppurativa (HS), which is also referred to as acne inversa, is a chronic, relapsing, inflammatory disease.¹ It presents with non-inflamed or inflamed nodules, abscesses, sinus track formation and scarring development mainly at the anguine and axilla.² It most commonly affects

women and it is highly associated with smoking and overweight.³

HS has a great impact on patients' quality of life.⁴ Apart from pain, malodor and discomfort, which can definitely cause, HS can lead to depressive symptoms, feelings of hopelessness and low self-esteem.⁵ Mild disease can be usually managed with topical agents; however, progression to moderate or severe disease requires the use of systemic therapies such as oral antibiotics, retinoids and immunosuppressant drugs.⁶ Even though there are therapeutic options, management of HS is challenging, since there are plenty of cases not responsive to treatment.⁷ Therefore, the approval of adalimumab for the treatment of moderate to severe HS enriched the therapeutic armamentarium and was proven to be promising for refractory HS cases.⁸

Despite the well-designed studies, real life data expressing the experience of adalimumab in HS cases are limited.⁹⁻¹³ Therefore, this study was designed to assess the therapeutic potential of adalimumab on patients with HS based on the data from the daily clinical practice of an HS Outpatient Clinic, located in a Tertiary Hospital in Northern Greece.

Materials and Methods

A single-center, observational, retrospective study was conducted to assess the efficacy of adalimumab on patients suffering from HS in daily practice. The records of HS patients who visited our department between February 2016 and May 2017 were used. Eligibility criteria were clinically evident moderate to severe HS, with the Hidradenitis Suppurativa Physician's Global Assessment (HS-PGA) scale \geq moderate, under adalimumab treatment for at least 24 weeks. Subject who had to discontinue treatment with adalimumab due to adverse event or had to receive an adjuvant therapeutic modality (except for topical agents) were excluded. Written informed consent from all patients was provided. The study design scheme is presented in Figure 1. All patients were treated with subcutaneous injections of adalimumab at a dose of 160 mg at baseline, 80 mg at week 2, 40 mg at week 4 and 40 mg weekly thereafter. Patients' age, gender, age at disease onset, time to final diagnosis, Body Mass Index (BMI), waist circumference, occupational and educational status, presence of arthritis, dyslipidemia, diabetes mellitus and hypertension, systolic and diastolic blood pressure, work absenteeism (yes/no), days of absence per year, treatment history and

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Hurley stage were recorded at baseline. The HS-PGA scale, Modified Santorius scale and Dermatology Life Quality Index (DLQI) at baseline, week 4, week 12 and week 24 were retrieved from the records. Roughly, HS-PGA scale assigns patients to one of six ordinal categories (clear, minimal, mild, moderate, severe, or very severe) based on the number of nodules (inflammatory and non-inflammatory), abscesses, and fistulas (draining and non-draining);⁸ the Modified Santorius Scale assesses the number of involved anatomical regions, the number and type of lesions and the extent of involvement,¹⁴ while DLQI measures dermatology specific health-related quality of life. The presence of clinical response, which was defined as an HS-PGA score of clear, minimal, or mild with at least a 2-grade improvement relative to baseline score, was assessed at week 4, week 12 and week 24.

The primary efficacy endpoints were i) the percentage of patients who achieved clinical response at week 4, week 12 and week 24 and ii) the proportion of patients at each stage of the HS-PGA scale at baseline, week 4, week 12 and week 24. Major secondary endpoints included i) the assessment of the Modified Santorius scale at baseline, week 4, week 12 and week 24, as well as the detection of possible, statistically significant differences in the Santorius scale through the evaluation period and ii) the assessment of DLQI at baseline, week 4,

week 12 and week 24 and the detection of possible, statistically significant differences in DLQI through the evaluation period.

Statistical analysis

The software Statistical Package for Social Sciences (SPSS), version 22.0 (SPSS, Inc., Chicago, IL, USA) was used for the statistical analysis of the data. Shapiro–Wilk test was performed to test the normality of continuous variables. Descriptive statistics were used to describe the study population's demographic and clinical characteristics. All continuous variables were expressed as the mean \pm standard deviation, median and range. The categorical variables were presented as frequencies and percentages. Friedman's ANOVA test was used to detect differences in the Modified Santorius scale and DLQI across the whole follow-up period, as well as the Bonferroni post hoc test. All tests were two sided and the significance level was $\alpha = 0.05$.

Results

In total, 19 patients participated in the study. Patients' demographic and clinical characteristics at baseline are summarized in Table 1.

Both Modified Santorius score and DLQI were significantly decreased during the weeks of evaluation (Friedman's test; $P < 0.001$). All data are presented in Table 2 and Figure 2. The proportion of patients who achieved clinical response was 10.5% ($n = 2$) at week 4, 42.1% ($n = 8$) at week 12 and 63.2% ($n = 12$) at week 24 (Figure 3). Data regarding the proportion of patients at each stage of the HS-PGA from baseline to week 24 are presented in Figure 4. At baseline, all patients suffered from moderate or severe disease, as this was assessed with the HS-PGA scale. At week 24, only 5.3% of the patients had moderate disease; the rest (94.7%) achieved an HS-PGA score of mild, minimal or clear.

Discussion and Conclusions

This study provided evidence that adalimumab is an efficient and safe treatment option for moderate to severe HS. Both Modified Santorius score and DLQI were significantly decreased during the weeks of evaluation, while 63.2% of patients achieved clinical response by week 24. HS is a chronic, painful, inflammatory, skin disease which is frequently refractory to treatment. Its pathogenesis is not completely understood but immunologic abnormalities

Table 1. Patients' demographic and clinical characteristics at baseline.

Characteristics	Statistics
Age (years)	
Mean \pm SD	39.05 \pm 11.65
Median (Min-Max)	40.0 (21.0-59.0)
Gender	
Male n (%)	14 (73.7)
Female n (%)	5 (26.3)
Age at disease onset (years)	
Mean \pm SD	28.11 \pm 8.13
Median (Min-Max)	27.0 (15.0-40.0)
Time to diagnosis (months)	
Mean \pm SD	63.82 \pm 78.57
Median (Min-Max)	24.0 (0.1-264.0)
BMI (kg/m ²)	
Mean \pm SD	32.74 \pm 9.92
Median (Min-Max)	29.41 (22.96-60.96)
Waist circumference (cm)	
Mean \pm SD	103.89 \pm 22.25
Median (Min-Max)	98.0 (67.0-150.0)
Occupational status	
Full time n (%)	13 (68.5)
On sick leave n (%)	2 (10.5)
On disability benefit n (%)	2 (10.5)
Retired n (%)	2 (10.5)
Educational status	
High school n (%)	13 (68.4)
University (4 years) n (%)	5 (26.3)
University (> 4 years) n (%)	1 (5.3)
Arthritis	
Yes n (%)	1 (5.3)
No n (%)	18 (94.7)
Dyslipidemia	
Yes n (%)	2 (10.5)
No n (%)	17 (89.5)
Diabetes mellitus	
Yes n (%)	3 (15.8)
No n (%)	16 (84.2)
Hypertension	
Yes n (%)	10 (52.6)
No n (%)	9 (47.4)
Systolic BP (mmHg)	
Mean \pm SD	130.26 \pm 15.23
Median (Min-Max)	130.0 (110.0-170.0)
Diastolic BP (mmHg)	
Mean \pm SD	77.37 \pm 7.14
Median (Min-Max)	75.0 (65.0-90.0)
Smoking status	
Yes n (%)	14 (73.7)
No n (%)	5 (26.3)
Work absenteeism	
Yes n (%)	11 (57.9)
No n (%)	8 (42.1)
Days of absence per year	
Mean \pm SD	4.68 \pm 6.92
Median (Min-Max)	4.0 (0.0-30.0)
Previous treatments	
Topical and systemic antibiotics n (%)	14 (73.7)
Systemic retinoid n (%)	2 (10.5)
Systemic antibiotics + retinoid n (%)	3 (15.8)
Hurley stage	
Stage II n (%)	14 (73.7)
Stage III n (%)	5 (26.3)

have been suggested to play a causal role in the disease.¹⁵ IL-1 β , TNF- α and IL-10 levels are elevated in HS skin providing data that biologics targeting these cytokines may be beneficial in HS.¹⁶

As treatment of HS can be really challenging, various therapeutic options have been suggested with multifarious results. Topical or systemic antibiotics, systemic steroids, antiandrogens, retinoids, biological drugs and surgical or laser excision of the affected areas are mainly the options in regard to the severity of the disease.¹⁷

Biological agents (adalimumab, infliximab, ustekinumab) could be a therapeutic option for patients suffering from moderate to severe HS.^{13,18} Partial responses are achieved in about 50% of patients, while the lack of response to one particular biologic agent does not preclude a potential efficacy to another one.¹⁸ Several biologic agents have been used for the treatment of severe or recalcitrant to treatment HS.^{19,20} However, adalimumab, which is a fully human, IgG1 monoclonal antibody specific for TNF- α , is the only biologic agent that has been approved for the treatment of moderate to severe HS.²¹

In a prospective, open study 15 patients suffering from moderate-to-severe HS, were treated with adalimumab at the indicated dose. Sartorius score was significantly reduced by week 24, as well as the VAS score and DLQI.²² Moreover, some case series have been published on the use of adalimumab (at the standard regime for psoriasis vulgaris) for the treatment of HS; all studies reported significant improvement in the number of affected regions, nodules, fistulas and DLQI after 4-6 weeks of treatment.²³⁻²⁵ Sbidian *et al.* conducted a national cohort study and reported that 71.4% of the patients receiving adalimumab achieved a partial response and none had a complete response after a median follow-up of 6.8 months.¹³ However, another prospective, open study with 6 patients with moderate to severe HS, treated with adalimumab failed to show statistically significant improvement of the both HS Severity Index (HSSI) and DLQI by week 12.⁹

In a prospective, randomized, double-

blind, placebo-controlled study, 21 patients with HS received adalimumab (80mg s.c. at baseline, followed by 40mg s.c. every other week for 12 weeks). A significant improvement in Santorius score was achieved at 2 weeks ($P<0.024$) but not at the end of treatment ($P=0.07$).²⁶ In a Phase 2, randomized, double-blind, placebo-controlled study, 17.6% of patients treated with 40mg adalimumab weekly, achieved clinical response

at week 16 and the drug was well-tolerated.⁸ These results were confirmed by two phase 3, multicenter, double-blind, placebo-controlled trials of adalimumab for HS, PIONEER I and PIONEER I.²¹ Clinical response rates were significantly higher in the adalimumab groups as compared to placebo at week 12; 41.8% versus 26.0% ($P = 0.003$) in PIONEER I and 58.9% versus 27.6% ($P < 0.001$) in PIONEER II.²¹ The

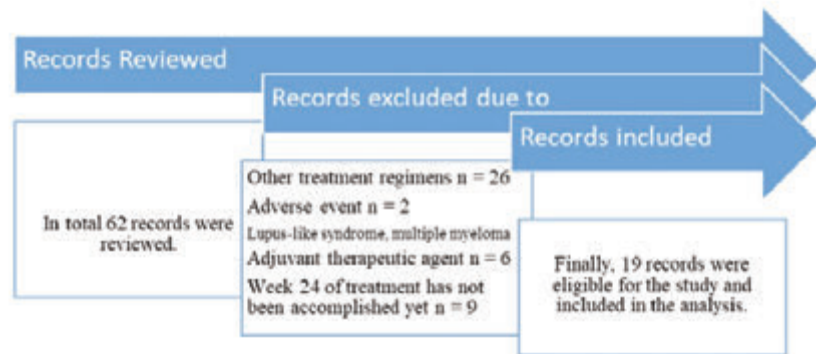


Figure 1. Study design scheme.

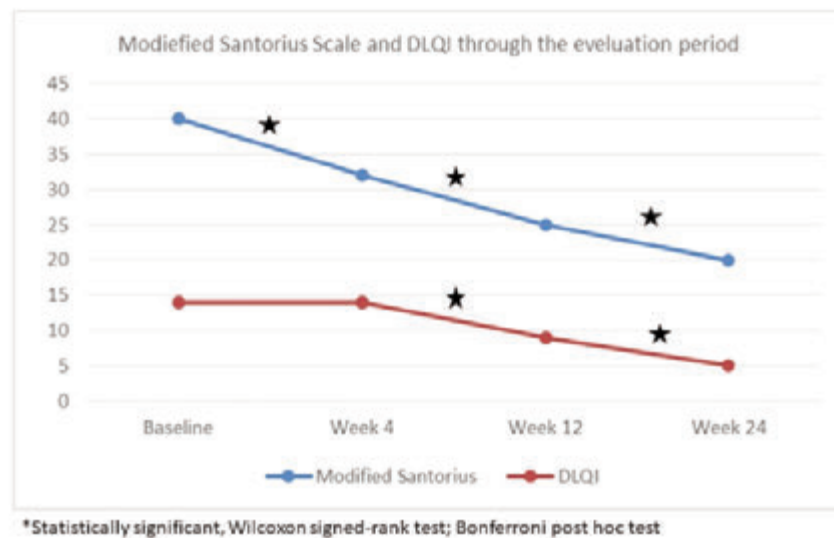


Figure 2. Modified Santorius Scale and Dermatology Life Quality Index (DLQI) through the evaluation period.

Table 2. Descriptive statistics for modified Santorius scale and Dermatology Life Quality Index (DLQI) during weeks of evaluation.

Variables	Baseline	Week 4	Week 12	Week 24	P value
Modified Santorius Scale					
Mean \pm SD	42.21 \pm 18.42	35.26 \pm 16.14	26.26 \pm 12.01	19.37 \pm 7.95	< 0.001*
Median (Min-Max)	40.0 (15.0-80.0)	32.0 (14.0-80.0)	25.0 (10.0-60.0)	20.0 (6.0-34.0)	
DLQI (0-30)					
Mean \pm SD	17.00 \pm 6.36	15.63 \pm 5.95	10.47 \pm 4.89	6.05 \pm 5.23	< 0.001*
Median (Min-Max)	14.0 (5.0-25.0)	14.0 (9.0-26.0)	9.0 (0.0-20.0)	5.0 (0.0-20.0)	

*Friedman's test; difference across the whole evaluation period.

rates of serious adverse events did not differ significantly in the study groups, suggesting the good safety profile of the drug.²¹ Moreover, the safety of the drug in treating HS is verified by a systematic review which has shown no significant difference in serious or infectious adverse effects compared with placebo.²⁷

It seems that reduction of adalimumab treatment frequency from every week to every other week, may lead to deterioration of HS in some patients.⁸ Moreover, serious adverse effects, which are not common, seem to have a similar pattern in both dosage groups. In patients with HS, the safety of adalimumab weekly and every other week has been proven to be comparable.¹¹ The safety of the weekly administered adalimumab in patients with dermatologic conditions is supported by data on other

non-dermatologic conditions, such as rheumatoid arthritis or Crohn's disease.¹¹ Therefore, adalimumab treatment for HS is recommended on a weekly basis.^{17,19,21}

Since HS has a great psychological impact and is associated with pain, depression and anxiety,²⁸ evaluation of therapeutic interventions for HS should not only focus on objective assessments, but also on subjective patient-reported outcomes.²⁹ It has been shown that adalimumab 40mg s.c. weekly, apart for the HS lesions, improves both pain and depressive symptoms.^{8,29} A recent systematic review suggests that adalimumab 40 mg weekly improves quality of life compared with placebo, with a reduction in DLQI score of 4.0 points.²⁷ Concerning the dynamic evaluation of a treatment response, the most commonly used measures are the Modified Sartorius

Score¹⁴ and the HS-PGA.⁸ Recently, Hidradenitis Suppurativa Clinical Response (HiSCR) has been developed to simplify the evaluation process and increase the sensitivity to detect HS-specific lesions.³⁰ HiSCR has been shown to be more responsive in detecting changes in response to treatment than HS-PGA.³¹ However, the use of HiSCR as the primary end point in clinical trials has been questioned, since this score only measures the inflammatory component of HS (nodules and abscesses) which is obviously reduced by anti-inflammatory medication.¹⁰

This study showed the high efficacy of adalimumab in a series of Greek patients with moderate to severe HS, through a 24-week period. Treatment with adalimumab was linked with both clinical remission of HS, as this was measured by Modified Santorius score and HS-PGA scale, and improvement of patients' quality of life. Moreover, the good safety profile of the drug, which is well-displayed in literature, was verified. To achieve healing in HS, adalimumab may need to be combined with other treatments such as antibiotics and surgical excision of persisting lesions.^{17,19} Either as monotherapy or adjuvant therapy, adalimumab enriches the therapeutic armamentarium for HS, the treatment of which may be really challenging.

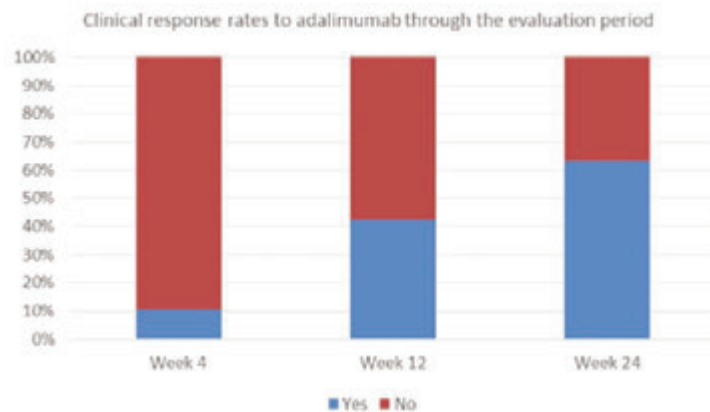


Figure 3. Clinical response rates to adalimumab through the evaluation period.

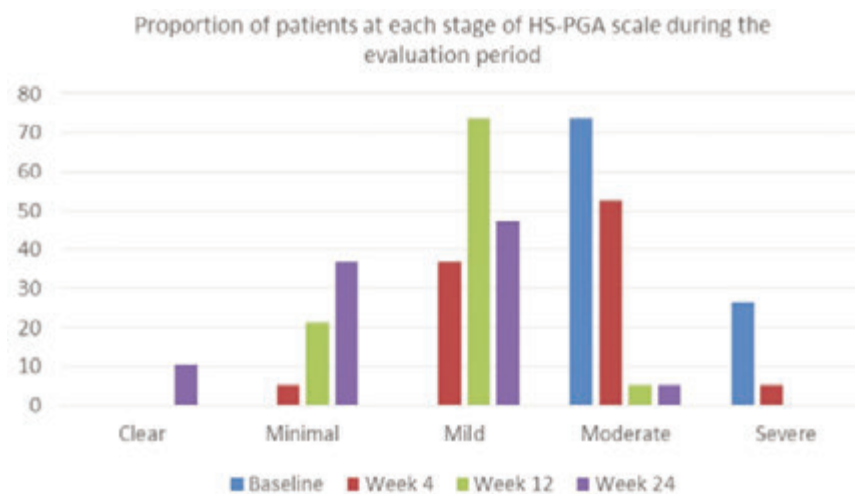


Figure 4. Proportion of patients at each stage of the Hidradenitis Suppurativa Physician's Global Assessment (HS-PGA) scale during the evaluation period.

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