Hindawi
Dermatologic Therapy
Volume 2023, Article ID 3640285, 8 pages
https://doi.org/10.1155/2023/3640285

Research Article

Employing Adalimumab in Treatment of Moderate-to-Severe Hidradenitis Suppurativa: Real-Life Multicenter Data from the Czech Republic

Alzbeta Smetanova,[1] **Emanuel Marques**,[1] **Martina Kojanova**,[2] **Petr Arenberger**,[1] **Daniela Strosova**,[3] **Jorga Fialova**,[2] **and Monika Arenbergerova**[1]

[1]*Department of Dermatovenereology, Charles University, Third Faculty of Medicine and University Hospital of Kralovske Vinohrady, Prague, Czech Republic*
[2]*Department of Dermatovenereology, Charles University, First Faculty of Medicine and General University Hospital, Prague, Czech Republic*
[3]*Value Outcomes, Prague, Czech Republic*

Correspondence should be addressed to Alzbeta Smetanova; alzbeta.smetanova.derm@gmail.com

Received 3 November 2022; Revised 3 January 2023; Accepted 17 February 2023; Published 15 March 2023

Academic Editor: Qiuning Sun

Adalimumab is the only approved biologic treatment for moderate-to-severe hidradenitis suppurativa, nonetheless, long-term data from real-life setting are still limited. The objective of this observational multicenter study was to evaluate the effectiveness, safety, and drug survival of adalimumab in patients with hidradenitis suppurativa included in the BIOREP registry. A total of 299 patients who initiated adalimumab therapy for hidradenitis suppurativa from 2011 to November 2021 were included. The Dermatology-Life-Quality-Index (DLQI), pain scale, the number of abscesses, inflammatory nodules and draining tunnels, and International Hidradenitis Suppurativa Severity Score System (IHS4) were recorded in the 0^{th}, 3^{rd}, and 6^{th} months; then every 6 months during the ongoing adalimumab treatment. Studied patients underwent treatment for up to 48 months, with the average duration of treatment lasting 2.3 years. The mean age of the patients was 44.9 years, 79% were smokers or ex-smokers, 54.8% were obese, and 26.4% were overweight, the mean BMI was 30.8. The mean time from diagnosis to initiation adalimumab therapy was 9.1 years. The number of patients with severe IHS4 dropped from the initial 249 (83.3%) to 65 (30.1%) after 12 months and this trend was maintained up to the 48^{th} month. A decreasing number of inflammatory lesions were rapid and sustained and correlated to the improvement of patients' quality of life, the mean DLQI score dropped from 17.6 to 8.5 after 3 months and to 5, 7 after 48 months. No unexpected risk signals were observed. Our long-term study demonstrates the effectiveness and safety of adalimumab in a real-life setting.

1. Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that severely impairs patients' quality of life. It is characterized by recurrent painful nodules, abscesses, and draining sinus tracts most commonly in the axillary, inguinal, and anogenital regions Reference [1]. Chronic inflammation and dysregulated epithelial differentiation, especially of hair follicle keratinocytes, which leads to follicular hyperkeratosis, dilatation, and rupture, have been involved in the pathogenesis of HS [2]. Cardiovascular diseases risk factors including central obesity, history of smoking, metabolic syndrome, dyslipidemia, and hypertension are more prevalent among HS patients compared to the general population [3]. At the same time, HS is associated with other immune-mediated diseases, such as inflammatory bowel disease and spondyloarthropathy (Nguyen TV, Damiani G) and high rates of depression and anxiety have been reported in HS patients [4].

In a recent review, the prevalence of HS in the American and European populations varies from 0.7% to 1.2% [5]. The onset of the disease is usually shortly after puberty, and HS is more common in women compared to men (>2 : 1). It is not clear whether menopause induces remission [1, 6]. Delayed diagnosis led to irreversible scarring and significantly impacted patient's physical and mental health and his ability to integrate into everyday work and social life [7]. In a recent multicenter study, the therapeutic delay correlated to lack of response to adalimumab [8].

According to the recommendations of the Czech State Institute for Drug Control, fully human monoclonal antibody blocking tumor necrosis alfa-adalimumab, is the only approved biological drug for the treatment of moderate-to-severe HS. Treatment is reimbursed only for adult patients and adolescents over 12 years of age who have active moderate-to-severe form of HS and not responded to or are intolerant to 3 months of oral antibiotic therapy [9].

Clinical trials demonstrated safety and effectiveness of adalimumab [10]. However, comprehensive long-term data from the common clinical practice of HS are still limited [11–13].

The aim of this observational, multicenter study was to describe the patient cohort of 299 patients from the Czech Republic treated for moderate-to-severe HS with adalimumab as well as data related to drug survival, effectiveness, and health-related quality using long-term data from the BIOREP registry.

2. Methods

In this retrospective multicenter study, data from the nationwide BIOREP registry (established in May 2005) were used. BIOREP is a web-based database of patients with psoriasis, hidradenitis suppurativa (2011), and atopic dermatitis (2018) treated with biologics or targeted therapy. In the Czech Republic, biological therapy is administered at 37 specialized centres, 35 of which are included in the BIOREP registry. Adalimumab for HS was administered in 18 centres at the time of the analysis.

The study was conducted in accordance with the Helsinki Declaration of 1964 and all subsequent amendments, and all patients provided a written informed consent. Patient-level data used for this analysis were deidentified, and Institutional Review Board approval was not required for this study. Permission to use data from the BIOREP registry was obtained. Patients with HS who received at least one dose of adalimumab were analyzed. The cut-off date for our analysis was 15th of November 2021. Patients were treated according to the standard treatment regimen of adalimumab: 160 mg at baseline and 80 mg at week 2, followed by 40 mg weekly from week 4 or 80 mg every other week in maintenance phase [14, 15].

Patients' demographic and baseline clinical characteristics were collected including age, the age at onset of HS, gender, weight, height and body mass index (BMI), occupation, smoking status, alcohol consumption, family history of HS, patients' comorbidities, duration and severity of the disease, previous treatment, standardized measures of health status; Dermatology Life Quality Index (DLQI), pain according to visual analogue scale (VAS), number of abscesses, inflammatory nodules and draining tunnels, and International Hidradenitis Suppurativa Severity Score System (IHS4). This validated scoring system was calculated by the number of nodules*1 + number of abscesses*2 + number of draining tunnels*4 with a total score: ≤3—mild, 4–10—moderate, and ≥11—severe [16] Level of white blood cell count and C-reactive protein (CRP) was analysed when available. In addition, the age at onset of adalimumab treatment was recorded.

2.1. Treatment Assessment. Disease severity was assessed using IHS4 at baseline, month 3, 6, and then every 6 months. The HS lesions were counted and included number of inflammatory nodules, abscesses, and draining fistulas.

The Dermatology Life Quality Index (DLQI) questionnaire and the Visual Analogue Scale for pain (VAS) which are instruments widely accepted to evaluate QoL in HS, were collected at baseline and month 3, 6, and then every 6 months.

2.2. Statistical Analysis. Collected parameters were summarized using descriptive statistics. Categorical outcomes were evaluated by the number and percentage in each category and continuous outcomes were assessed by mean and standard deviation (SD). The persistence on adalimumab was defined as the time from initiation of adalimumab treatment to the discontinuation, temporary termination, or switch of the treatment. Patients were censored in case they were lost to follow-up or in case no more follow-up visits were available. The persistence was assessed using Kaplan–Meier survival curves, which take into account right-censored data. Differences between survival curves were tested using the log-rank test at the significance level of 5.0%. Statistical analyses were performed using Stata software [17].

3. Results

3.1. Demographics and Clinical Characteristics. A total of 299 patients with moderate-to-severe HS were enrolled, 133 women (44.5%) and 166 men (55.5%) with a mean age of 44.9 years (SD 12.9). At baseline the HS status of patients was evaluated. Hurley stage I was shown in 1%, Hurley stage II in 37%, and Hurley stage III in 58%. The mean age at the time of diagnosis of HS was 33.6 years (SD 13.1), the mean age at the initiation of adalimumab treatment was 42.7 years (SD 12.7). The mean duration from diagnosis to the initiation of adalimumab was 9.1 years (SD 9.1). A total of 51 patients (17.1%) had a family history of HS. Almost 80% of patients were current smokers or ex-smokers with an average of 13.8 cigarettes smoked per day. More than half of the patients worked full-time, 22.4% were on disability pension, 6.7% were retired, 4.3% were studying, 4.3% worked half-time, 4.0% were unemployed, and 3.7% were on long-term incapacity for work (Tables 1 and 2).

Table 1: Demographic and clinical patients' characteristics.

	N (percentage)/Mean (±SD)
Number of patients	299 (100.0%)
Men	166 (55.5%)
Age (years)	44.9 (±12.9)
Age at the time of diagnosis (years)	33.6 (±13.1)
Age at the time of initiation of adalimumab (years)	42.7 (±12.7)
Duration from diagnosis to the initiation of adalimumab (years)	9.1 (±9.1)
Previous surgery of HS	186 (62.2%)
Family history of HS	51 (17.1%)
Smokers + Ex-smokers	237 (79.3%)
Number of average cigarettes smoked per day	13.8 (±8.5)
Current job status—work absences	11 (3.7%)
Current job status—disability pension	67 (22.4%)
Comorbidities	176 (58.9%)
Arterial hypertension	79 (26.4%)
Diabetes mellitus type II	41 (13.7%)
Dyslipidemia	27 (9.0%)
Depression	16 (5.4%)
Anxiety disorder	8 (2.7%)
Crohn's disease	6 (2.0%)
Ulcerative colitis	1 (0.3%)
Baseline BMI (kg/m^2)	30.8 (±5.9)
Normal	56 (18.7%)
Overweight	79 (26.4%)
Obese	164 (54.8%)
Prior systemic antibiotic use	282 (94.3%)
Prior systemic retinoids use	75 (25.1%)
Prior autogenous vaccine therapy	21 (7.0%)
Prior systemic corticosteroid use	7 (2.3%)
Localization of disease	—
Axillae	220 (73.6%)
Inframammary folds + breasts	55 (18.4%)
Genitofemoral area	252 (84.3%)
Gluteal area	170 (56.9%)

HS, hidradenitis suppurativa; BMI, body mass index.

A total of 176 patients (58.9%) suffered from at least one comorbidity. The most common of them were arterial hypertension (26.4%) and diabetes mellitus type II (13.7%). A total of 9.0% had dyslipidemia, 5.4% depression, almost 3% anxiety disorder and 2.3% Crohn's disease or ulcerative colitis. Obesity was found in 164 patients (54.8%), 79 patients (26.4%) were found to be overweight (Table 1).

The previous therapy consisted of systemic antibiotic use (94.3% of patients), retinoids (25.1%), autogenous vaccine therapy (7.0%), and systemic corticosteroids (2.3%). The most affected region at the baseline was genitofemoral area (84.3% of patients) and axillary area (73.6% of patients) (Table 1).

3.2. Adalimumab Treatment. Out of 299 patients, a total of 216 patients (72.2%) completed 12 months of treatment, 137 patients (45.8%) completed 24 months, and 46 patients (15.4%) completed 48 months of adalimumab treatment. In total, 96.0% of analysed patients received Humira and 4.0% of patients were treated by biosimilars of adalimumab.

The mean VAS score was 5.2 (SD 2.7) at baseline. In terms of inflammatory serum markers, the mean baseline level of white blood cell count was 10.6×10^9 (SD 2.9), and a total CRP serum level was 20.3 mg/ml (SD 22.3) (Table 2).

During the adalimumab treatment, there was a substantial reduction in number of abscesses, nodules and draining fistulas, IHS4, and DLQI scores (Figure 1). At baseline, the HS status was assessed as severe in 249 patients (83.3%) based on IHS4 scoring and moderate or mild in 37 patients (12.4%) (Table 2). The proportion of patients with severe IHS4 score decreased from 83.3% to 39.6% after 3 months and to 30.1% patients after 12 months of adalimumab treatment and remained stable for the rest of follow-up (Figure 2).

The improvement in IHS4 correlated with the number of active HS lesions. The mean number of inflammatory nodules at baseline was 8.2, the mean number of draining fistulas was 5.0, and the mean number of abscesses was 3.0. The improvement was observed after only 3 months of treatment, mean values decreased to 3.5 of inflammatory nodules, 1.9 fistulas, and 1.1 abscesses. After 12 months of treatment the mean values were as follows: inflammatory nodules 2.8, draining fistulas 1.4, and abscesses 0.7. The number of active lesions was stable at low levels during the patients´ visits up to 48 months of treatment. A minor

Table 2: Baseline clinical characteristics, adalimumab treatment and adverse events.

	N (percentage)/Mean (±SD)
Baseline VAS	5.2 (±2.7)
Baseline DLQI	17.6 (±7.3)
Baseline white blood cell count $\times 10^9$	10.6 (±2.9)
Baseline CRP (mg/ml)	20.3 (±22.3)
Baseline IHS4 score	—
Severe (≥11)	249 (83.3%)
Moderate (4–10)	34 (11.4%)
Mild (≤3)	3 (1.0%)
Biologic adalimumab treatment	299 (100.0%)
Humira	287 (96.0%)
Biosimilars (hulio, hyrimoz, idacio)	12 (4.0%)
Adalimumab treatment	299 (100.0%)
Length of adalimumab treatment (years)	2.3 (±1.7)
Discontinuation/termination of treatment	66 (22.1%)
Adverse events	24 (8.0%)
Infection	14 (4.7%)
Malignity	3 (1.0%)
Skin disorders	4 (1.3%)
Cholangitis	1 (0.3%)
Cerebrovascular disease	1 (0.3%)
Latent tuberculosis	1 (0.3%)

VAS, visual analogue scale; DLQI, dermatology life quality index; CRP, C-reactive protein; IHS4 score, the international hidradenitis suppurativa severity score system.

increase in the number of draining tunnels (1.5 after 30 months and 1.6 after 48 months of treatment) could be observed (Figure 1).

Decreasing number of inflammatory lesions correlated to the improvement of patients' quality of life, reflected in the DLQI questionnaire. A mean DLQI score was 17.6 (SD 7.3) at baseline, dropped to 8.5 (SD 6.5) after 3 months and to 6.1 (SD 6.0) after 12 months of treatment and remained stable during observation period (Table 2, Figure 1).

Furthermore, we analysed the course of BMI level during the treatment, at baseline the mean BMI was 30.8 (SD 5.9), with a slightly decreasing trend to 30.2 (SD 5.0) at 24 months, 29.9 (SD 5.4) at 30 months, and 28.9 (SD 5.9) at 48 months.

3.3. Treatment Discontinuation. From all 299 analysed patients, 233 patients (77.9%) were still treated at the time of the data lock point. A total of 66 patients (22.1%) discontinued, temporarily terminated or switched the treatment; 17 due to lack of effectiveness (5.7%); 15 for adverse events (5.0%); 10 due to surgical procedure (3.3%); 7 for noncooperation (2.3%); 7 due to other reasons (2.3%); patient's choice in 5 (1.7%); 4 due to pregnancy (1.3%); and one patient committed suicide (0.3%) (Figure 3).

Ten of 66 patients (3.3% of all treated) temporarily interrupted the therapy due to adverse events (AEs), namely, COVID-19 infection ($n = 2$; 0.7%), and the following were observed in single patients: bronchopneumonia, upper respiratory tract infection, nonspecific influenza-like illness, nephritis, nonspecific urethritis, squamous cell carcinoma of the skin, latent tuberculosis infection, and neurological disorder.

Permanent discontinuation due to AEs was in 5 of 66 patients: squamous cell carcinoma of the skin ($n = 1$), lung carcinoma ($n = 1$), severe bronchopneumonia ($n = 1$), skin rash ($n = 1$), and not identified event ($n = 1$) (Table 2).

The mean duration of adalimumab treatment was 2.3 years (SD 1.7) for all analysed patients. In patients who discontinued the treatment, the mean duration was 1.7 years (SD 1.4). The mean duration of treatment in treated patients was 2.4 years (SD 1.8).

3.4. Drug Survival of Adalimumab. The persistence on adalimumab treatment was assessed using the Kaplan–Meier survival estimates. Adalimumab persistence rates were 92.5%, 80.5%, 71.0%, and 66.7% after 12, 24, 36, and 48 months of treatment, respectively (Figure 4(a)).

Survival estimates were also analysed according to the smoking status: patients, who never smoked and those, who were currently smoking or previously smoked. No statistically significant differences were observed between these two groups ($P = 0.330$) (Figure 4(b)). For nonsmokers the persistence rates were 91.2% after 12 months of treatment, 84.5% after 24 months, and 80.4% after 36 and 48 months of treatment. For smokers and ex-smokers, the persistence rates were 93.3%, 80.0%, 69.2%, and 64.0% after 12, 24, 36, and 48 months of treatment, respectively.

The persistence on treatment was also analysed by the BMI category: patients with normal BMI (BMI ≤ 25) and patients with overweight or obese patients (BMI > 25). The persistence rates using the Kaplan–Meier method showed lower survival in overweight or obese patients, although the difference was not statistically significant ($P = 0.395$) (Figure 4(c)). The persistence rates were 95.9%, 85.7%, 75.0%, and 71.3% for patients with normal BMI after 12, 24, 36, and 48 months of treatment; and 91.8%, 79.4%, 70.2%, and 65.6% for patients with overweight or obese patients.

3.5. Adalimumab Safety Profile. A total of 24 (8.0%) adverse events were reported (Table 2). The most frequently recorded were infections (4.7%). Malignancies were reported in 1.0% and skin disorders in 1.3%. One percent of AEs was cholangitis (0.3%), cerebrovascular disease (0.3%), and latent tuberculosis (0.3%). Serious AEs included 3 of 14 reported infections (1.0%) and 1 of 3 reported malignancies (0.3%).

4. Discussion

The results of this multicenter retrospective study demonstrate the effectiveness and safety of adalimumab in the real-world setting.

The analysis of the demographic data showed higher percentage of male patients in our cohort (55%) similarly to other study confirming the fact, that men have increased disease severity [18].

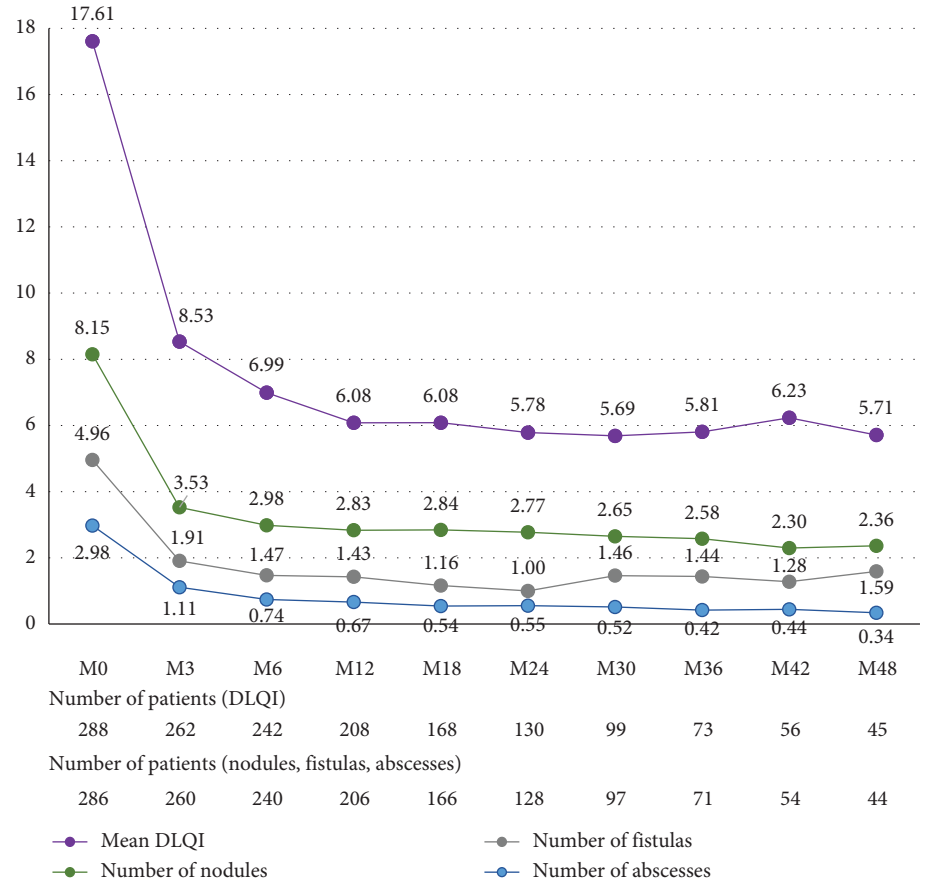

Figure 1: Number of abscesses, nodules, draining fistulas and DLQI during the adalimumab treatment.

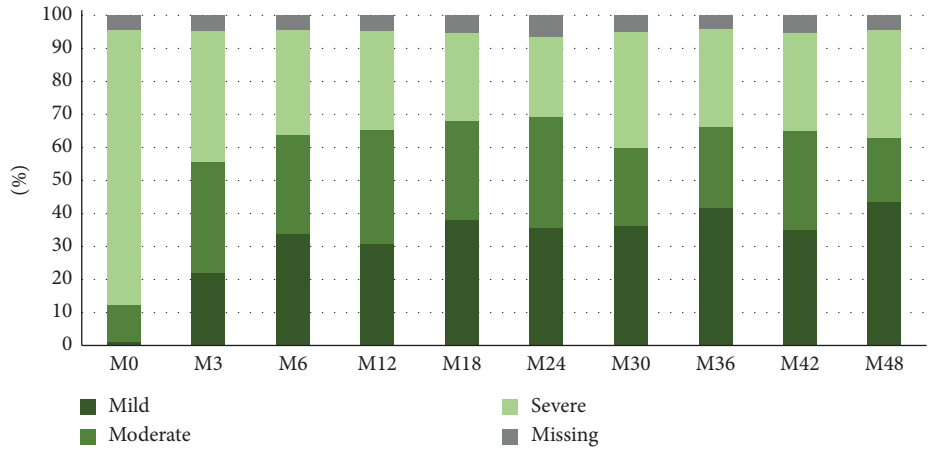

Figure 2: Score of severity according to IHS4 during the adalimumab treatment.

The long duration of disease before initiation of biologic therapy (9.1 years) pose a problem in HS likewise to other chronic inflammatory skin diseases, including psoriasis, moreover a common feature is diagnostic delay in HS and the average interval from self-reported onset of symptoms to diagnosis is 7.2 years [19].

In our cohort, approximately 80% of the patients were active smokers or ex-smokers, which is in accordance to the meta-analysis [20] reporting that patients with HS are about 4 times (OR, 4.26) more likely to be smokers. However, our cohort shows even higher percentage of smokers when compared to the other HS registries [21]. This has proven to be unsurprising, as it correlates with the fact that the Czech Republic is among the 7 countries in the world with the highest amounts of cigarettes smoked per person [22].

The IHS4 severity score is recognized as simple and practical validation system which was adapted for daily practice and has been used in several clinical trials

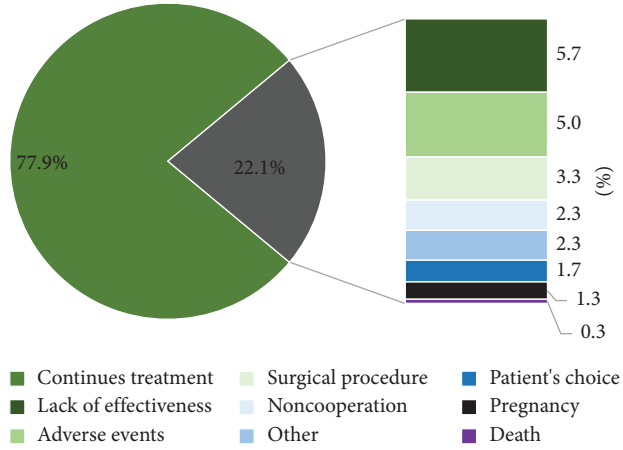

Figure 3: Reasons for discontinuation of treatment.

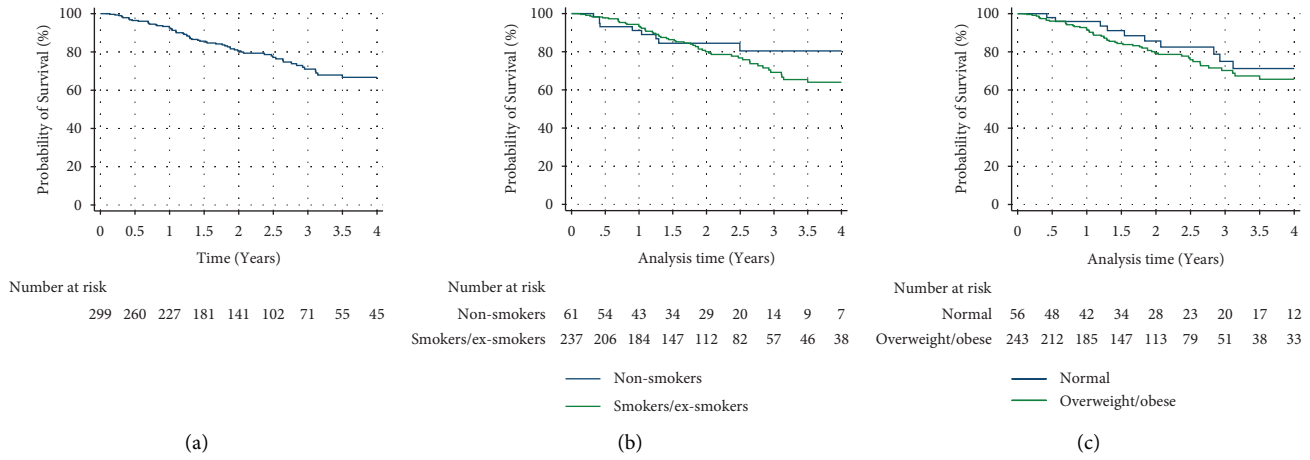

Figure 4: Persistence on adalimumab treatment (a) all population, (b) non-smokers, smokers/ex-smokers, (c) normal and overweight/obese patients.

[16, 23, 24]. We used this scoring system to assess therapeutical response in our cohort.

During the adalimumab treatment, there was a substantial reduction in number of abscesses, nodules and draining fistulas, IHS4 and DLQI scores. The proportion of patients with severe IHS4 dropped from 249 (83.3%) at initial baseline to 65 (30.1%) after 12 months; this trend was maintained up to the 48th month. The results are comparable to the response observed in the SOLACE and OLE study, which also collected real-world data [12, 25]. To our knowledge, our study offers real-world data with the longest mean duration of treatment of 2.3 years, and a maximum treatment period of 48 months. In most of patient cases, the clinical response to adalimumab has been sustained. The long-term response in our cohort may be also explained by the slightly improvement of patients BMI levels during the treatment. It has been proven that elevated BMI in HS is associated with decreased response to adalimumab therapy [26].

Adalimumab persistence rates in our cohort were 92.5%, 80.5%, 71.0%, and 66.7% after 12, 24, 36, and 48 months of treatment, respectively, which was higher than in other one-center study with a median survival probability of 74.1% after one year [27].

Survival estimates were also analysed according to the smoking status and BMI. Although no statistically significant differences were observed, there was observable better treatment persistence in patients who never smoked contrast to those who were smokers or ex-smokers. The difference was also observed between obese and nonobese patients.

Adalimumab discontinuation occurred in 22.1% of patients, with the main reason being loss of treatment efficacy.

The safety profile of adalimumab in the analysed group of patients was good and in accordance with other real-world data [28]. A total of 8.0% AEs were reported. The most frequent mild AEs were infections (4.7%) and skin disorders (1.3%); the serious AEs included severe infections (1%) and malignancies (0.3%).

The limitations of our study include its retrospective design and the absence of a control group, which is typical in studies that use realworld data. Under discussion could also be the evaluation of efficacy with IHS4 only. IHS4 was recognized as validated and simple to use scoring system for clinical research and daily practice (14). In addition, the

correlation between IHS4 and Hidradenitis Suppurativa Clinical Response (HiSCR) was described by Caposiena and Gulliver (12, 27). Notwithstanding these limitations, our study is the long follow-up period with a large number of patients in a real-world and provide evidence that adalimumab achieves IHS4 and DLQI improvement with some sustainability of response.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

AS, EM, and DS declare, that they have nothing to disclose. MK has served as consultants, speakers, or investigators for Abbvie, Amgen, Eli-Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, and UCB. PA has served as consultant, speaker, or investigator for Abbvie, Amgen, BMS, Eli Lilly, Janssen, Leo Pharma, L´Oréal, MSD, Novartis, Pfizer, Pierre Fabre, Sanofi and UCB. JF has served as consultants, speakers, or investigators for Abbvie, Amgen, Eli-Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, and UCB. MA received honoraria from Abbvie, MSD, BMS, Novartis, L´Oréal, and Pierre Fabre.

Acknowledgments

The authors wish to thank all of the dermatologists and collaborators who participated in the creation of BIOREP for their efforts and dedication to the project. The authors would also like to thank BIOREP Group Members: Zdenek Antal, Petr Arenberger, Jirina Bartonova, Linda Blahova, Petra Brodska, Petra Cetkovska, Martin Cetkovsky, Dominika Diamantova, Olga Filipovska, Petra Gkalpakioti, Spyridon Gkalpakiotis, Martina Grycova, Jiri Horazdovsky, Katerina Hrazdirova, Eduard Hrncir, Hana Janatova, Jaromira Janku, Renata Kopova, Dora Kovandova, Iva Lomicova, Alena Machovcova, Hana Malikova, Miroslav Necas, Helena Nemcova, Jitka Osmerova, Zuzana Plzakova, Marie Policarova, Tomas Pospisil, Miloslav Salavec, Ivana Strouhalova, David Stuchlik, Alena Stumpfova, Jaroslav Sevcik, Jan Sternbersky, Jiri Stork, Katerina Svarcova, Katerina Tepla, Martin Tichy, Yvetta Vantuchova, and Ivana Vejrova. This work was supported by the Cooperatio 39-Oncology and hematology, Charles University grant.

References

[1] J. R. Ingram, "The epidemiology of hidradenitis suppurativa," *British Journal of Dermatology*, vol. 183, no. 6, pp. 990–998, 2020.

[2] V. A. Zouboulis, K. C. Zouboulis, and C. C. Zouboulis, "Hidradenitis suppurativa and comorbid disorder biomarkers, druggable genes, new drugs and drug repurposing—a molecular meta-analysis," *Pharmaceutics*, vol. 14, no. 1, p. 44, 2021.

[3] T. Tzellos, C. C. Zouboulis, W. Gulliver, A. Cohen, P. Wolkenstein, and G. Jemec, "Cardiovascular disease risk factors in patients with hidradenitis suppurativa: a systematic review and meta-analysis of observational studies," *British Journal of Dermatology*, vol. 173, no. 5, pp. 1142–1155, 2015.

[4] E. Shavit, J. Dreiher, T. Freud, S. Halevy, S. Vinker, and A. Cohen, "Psychiatric comorbidities in 3207 patients with hidradenitis suppurativa," *Journal of the European Academy of Dermatology and Venereology*, vol. 29, no. 2, pp. 371–376, 2015.

[5] T. V. Nguyen, G. Damiani, L. a. V. Orenstein, I. Hamzavi, and G. Jemec, "Hidradenitis suppurativa: an update on epidemiology, phenotypes, diagnosis, pathogenesis, comorbidities and quality of life," *Journal of the European Academy of Dermatology and Venereology*, vol. 35, no. 1, pp. 50–61, 2021.

[6] H. Killasli, K. Sartorius, L. Emtestam, and Å Svensson, "Hidradenitis suppurativa in Sweden: a registry-based cross-sectional study of 13,538 patients," *Dermatology*, vol. 236, no. 4, pp. 281–288, 2020.

[7] G. Kokolakis, K. Wolk, S. Schneider-Burrus et al., "Delayed diagnosis of hidradenitis suppurativa and its effect on patients and healthcare system," *Dermatology*, vol. 236, no. 5, pp. 421–430, 2020.

[8] A. v. Marzano, G. Genovese, G. Casazza et al., "Evidence for a "window of opportunity" in hidradenitis suppurativa treated with adalimumab: a retrospective, real-life multicentre cohort study," *British Journal of Dermatology*, vol. 184, no. 1, pp. 133–140, 2021.

[9] State Institute for Drug Control, 2022, https://www.sukl.eu/modules/medication/search.php?lang=2.

[10] A. B. Kimball, M. M. Okun, D. A. Williams et al., "Two phase 3 trials of adalimumab for hidradenitis suppurativa," *New England Journal of Medicine*, vol. 375, no. 5, pp. 422–434, 2016.

[11] V. Bettoli, M. Manfredini, G. Calamo et al., "Long-term adalimumab treatment of hidradenitis suppurativa: results and practical insights from a real-life experience," *Dermatologic Therapy*, vol. 31, no. 6, Article ID e12737,, 2018.

[12] W. Gulliver, A. Alavi, M. c. Wiseman et al., "Real-world effectiveness of adalimumab in patients with moderate-to-severe hidradenitis suppurativa: the 1-year SOLACE study," *Journal of the European Academy of Dermatology and Venereology*, vol. 35, no. 12, pp. 2431–2439, 2021.

[13] L. m. Prens, K. Bouwman, P. Aarts et al., "Adalimumab and infliximab survival in patients with hidradenitis suppurativa: a daily practice cohort study," *British Journal of Dermatology*, vol. 185, no. 1, pp. 177–184, 2021.

[14] F. Martora, C. Marasca, G. Fabbrocini, and A. Ruggiero, "Strategies adopted in a southern Italian referral centre to reduce adalimumab discontinuation: comment on 'Can we increase the drug survival time of biologic therapies in hidradenitis suppurativa?" *Clinical and Experimental Dermatology*, vol. 47, no. 10, pp. 1864-1865, 2022.

[15] J. Askling, R. F. van Vollenhoven, F. Granath et al., "Cancer risk in patients with rheumatoid arthritis treated with anti-tumor necrosis factor alpha therapies: does the risk change with the time since start of treatment?" *Arthritis & Rheumatism*, vol. 60, no. 11, pp. 3180–3189, 2009.

[16] C. C. Zouboulis, T. Tzellos, A. Kyrgidis et al., "Development and validation of the International Hidradenitis Suppurativa Severity Score System (IHS4), a novel dynamic scoring system to assess HS severity," *British Journal of Dermatology*, vol. 177, no. 5, pp. 1401–1409, 2017.

[17] *StataCorp. Stata Statistical Software: Release 15*, StataCorp LLC, College Station, TX, USA, 2017.

[18] T. Shih, J. R. Seivright, S. A. McKenzie et al., "Gender differences in hidradenitis suppurativa characteristics:

a retrospective cohort analysis," *International Journal of Women's Dermatology*, vol. 7, no. 5, pp. 672–674, 2021.

[19] D. m. Saunte, J. Boer, A. Stratigos et al., "Diagnostic delay in hidradenitis suppurativa is a global problem," *British Journal of Dermatology*, vol. 173, no. 6, pp. 1546–1549, 2015.

[20] P. Acharya and M. Mathur, "Hidradenitis suppurativa and smoking: a systematic review and meta-analysis," *Journal of the American Academy of Dermatology*, vol. 82, no. 4, pp. 1006–1011, 2020.

[21] V. Bettoli, L. Naldi, S. Cazzaniga et al., "Overweight, diabetes and disease duration influence clinical severity in hidradenitis suppurativa-acne inversa: evidence from the national Italian registry," *British Journal of Dermatology*, vol. 174, no. 1, pp. 195–197, 2016.

[22] Oecd, *Health at a Glance 2013: OECD Indicators*, OECD, Paris, France, 2013.

[23] J. W. Frew, C. S. Jiang, N. Singh et al., "Clinical response rates, placebo response rates, and significantly associated covariates are dependent on choice of outcome measure in hidradenitis suppurativa: a post hoc analysis of PIONEER 1 and 2 individual patient data," *Journal of the American Academy of Dermatology*, vol. 82, no. 5, pp. 1150–1157, 2020.

[24] A. Chiricozzi, G. Giovanardi, S. Garcovich et al., "Clinical and ultrasonographic profile of adalimumab-treated hidradenitis suppurativa patients: a real-life monocentric experience," *Acta Dermato-Venereologica*, vol. 100, no. 13, Article ID adv00172, 2020.

[25] C. C. Zouboulis, M. M. Okun, E. P. Prens et al., "Long-term adalimumab efficacy in patients with moderate-to-severe hidradenitis suppurativa/acne inversa: 3-year results of a phase 3 open-label extension study," *Journal of the American Academy of Dermatology*, vol. 80, no. 1, pp. 60–69.e2, 2019.

[26] J. W. Frew, N. Singh, C. S. Jiang, R. Vaughan, and J. G. Krueger, "The impact of body mass index upon the efficacy of adalimumab in hidradenitis suppurativa," *Frontiers of Medicine*, vol. 8, Article ID 603281, 2021.

[27] H. Khosravi, A. M. Anderson, C. Kettering, A. Mizes, and T. Patton, "Real-world experience of adalimumab in the treatment of hidradenitis suppurativa," *Journal of the American Academy of Dermatology*, vol. 84, no. 5, pp. 1406–1409, 2021.

[28] A. Hafner, P. D. Ghislain, R. Kovács et al., "Improvement in Hidradenitis Suppurativa and quality of life in patients treated with adalimumab: real-world results from the HARMONY Study," *Journal of the European Academy of Dermatology and Venereology*, vol. 35, no. 11, pp. 2277–2284, 2021.