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Evidence for a 'window of opportunity' in hidradenitis suppurativa treated with adalimumab: a retrospective, real-life multicentre cohort study*

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Summary

Background The anti-tumour necrosis factor (TNF)-α adalimumab is the only licenced biologic for moderate-to-severe hidradenitis suppurativa (HS). No predictors of response have been identified so far.

Objectives To identify clinical parameters predicting response to adalimumab and confirm its efficacy/safety.

Methods The data of 389 patients with HS treated with adalimumab in 21 Italian centres were reviewed. Sex, age at onset/diagnosis/baseline, body mass index, smoking, phenotype, previous treatments, concomitant antibiotics and 'therapeutic delay', defined as the time from HS onset to adalimumab initiation, were assessed. Response to adalimumab and its impact on quality of life (QoL) were evaluated using the Hidradenitis Suppurativa Clinical Response (HiSCR) and the Dermatology Life Quality Index (DLQI) or the Visual Analogue Scale for pain (VAS pain), respectively. Logistic regression analysis was performed.

Results The therapeutic delay correlated to lack of response to adalimumab at week 16 [odds ratio (OR) 1·92 for therapeutic delay > 10 years; 95% confidence interval (CI) 1·28–2·89; P = 0·0016). HiSCR was achieved in 43·7% and 53·9% patients at week 16 and 52, respectively. Significant reductions in both DLQI and VAS pain

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were found between week 16 vs. baseline ($P < 0{\cdot}0001$ for both) and week 52 vs. baseline ($P < 0{\cdot}0001$ for both). Previous immunosuppressants inversely correlated to HiSCR at week 52 (OR = 1·74, 95% CI 1·04–2·91, P = 0·0342).

Conclusions Inverse correlation between therapeutic delay and clinical response was found, supporting early adalimumab use and providing evidence for a 'window of opportunity' in HS treatment. Adalimumab efficacy and safety were confirmed, along with patients' QoL improvement. Immunosuppressants could negatively influence the response to adalimumab inducing a switch to non-TNF-α-driven pathways.

What is already known about this topic?

- Adalimumab is an effective and safe biologic licenced for the treatment of moderate-to-severe hidradenitis suppurativa (HS) after failure of conventional treatments.
- There are no reliable parameters that predict the clinical response to adalimumab in this disease.

What does this study add?

- The therapeutic delay, defined as the time from HS onset to adalimumab initiation, significantly correlated to lack of clinical response to this drug, particularly at week 16 of treatment.
- This study suggests that using adalimumab in the early phases of HS should be highly encouraged.

Hidradenitis suppurativa (HS) is a chronic, inflammatory systemic disease affecting the skin with nodules, abscesses and fistulas on the axillary, inguinal and breast folds and on the anogenital areas.[1,2] Disease severity ranges from mild HS presenting with localized lesions to severe HS manifesting as multiple areas of inflammation, nodules and abscesses possibly forming plaques and interconnected sinus tracts, leading to hypertrophic scars.[3] The prevalence of disease is around 1% in Western Europe,[1,4] and, of note, the average interval from the self-reported onset of symptoms to diagnosis is 7·2 years.[5] HS is a debilitating disease interfering with many activities of daily life. A recent study demonstrated that HS may have a greater impact on quality of life (QoL) than psoriasis and other chronic medical conditions.[6]

The HS pathogenesis is complex and not completely elucidated but an innate immunity dysfunction leading to autoinflammation has recently been reported to play a crucial role,[7,8] with overexpression of proinflammatory cytokines such as interleukin (IL)-1β and IL-17, and tumour necrosis factor (TNF)-α both in the lesional skin and in the serum of patients.[9–12] Adalimumab (Humira®), a fully human IgG monoclonal antibody against TNF-α, is currently the only approved drug to treat moderate-to-severe HS based on the 12-week, placebo-controlled periods of the two phase III PIONEER trials.[13] Adalimumab at a weekly dose of 40 mg is an effective and safe therapeutic option also for long-term control of moderate-to-severe HS.[14,15] We conducted a real-life multicentre study to assess the impact of different clinical parameters on clinical response to adalimumab in a large cohort of patients with moderate-to-severe HS at week 16 and week 52 after adalimumab initiation.

Methods

Demographics

In this real-life retrospective multicentre study, 21 Italian dermatology units contributed to collect demographic and clinical data of patients with moderate-to-severe HS undergoing adalimumab treatment from January 2016 to December 2018. Data included sex, age at HS onset (≤ 30, > 30–50, > 50 years), age at diagnosis (≤ 29, > 29 years), age at adalimumab initiation (≤ 30, > 30–50, > 50 years), body mass index (BMI; ≤ 25, > 25–30, > 30 kg m^{-2}), smoking (never smokers, current smokers, ex-smokers), family history of HS, comorbidities, treatments prior to and concomitant with adalimumab, and HS phenotypes according to the van der Zee and Jemec classification.[16] The latter one distinguishes six different clinical presentations, namely the regular, frictional furuncle, scarring folliculitis, conglobata, syndromic and ectopic type.[16] 'Therapeutic delay' was assessed as the time, in years, from HS onset to adalimumab initiation.

To be part of this study, each centre was asked to provide data of patients aged ≥ 18 years, affected with moderate-to-severe HS defined as having at baseline either Hurley stage ≥ 2 or International Hidradenitis Suppurativa Severity Score System (IHS4)[17] ≥ 4.

According to the Italian Drug Agency (AIFA) recommendations, only patients resistant to standard first-line treatments, such as systemic antibiotics including tetracyclines (doxycycline and minocycline), clindamycin plus rifampicin and/or acitretin, can be treated with adalimumab. We also evaluated whether patients had been given previous off-label systemic treatments, including immunosuppressive (ciclosporin, corticosteroids) and immunomodulating (dapsone, zinc gluconate) agents or retinoids other than acitretin, namely isotretinoin.

Patients were treated with adalimumab 160 mg on day 1, 80 mg on day 15 and a single 40-mg injection from week 4 onwards. Patients were assessed for their clinical response at week 16 and at week 52 after initiation of adalimumab treatment. All patients agreed with the treatment regimen and signed a written consent form to use personal data for the present study. In view of the retrospective nature of the study, only a notification to the Ethical Committee of the principal investigator centre (IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy) was requested.

Disease severity, quality of life and clinical response to adalimumab

At baseline, the patients were stratified according to Hurley stage,[3] a classification system subdivided into stage 1 (single or multiple abscesses without sinus tract formation or scarring), stage 2 (recurrent abscesses with one or more sinus tracts and scarring widely separated by normal skin) and stage 3 (diffuse involvement with multiple sinus tracts and no intervening normal skin). Disease severity was determined using IHS4[17] at baseline, week 16 and week 52. It is a recently validated scoring system calculated by the number of nodules (multiplied by 1) plus the number of abscesses (multiplied by 2) plus the number of draining tunnels (multiplied by 4), with a total score of ≤ 3 defining mild, 4–10 defining moderate and ≥ 11 defining severe disease.

The Dermatology Life Quality Index (DLQI) questionnaire[18] and the Visual Analogue Scale for pain (VAS pain),[19] which are measurement instruments widely accepted to evaluate QoL in HS, were also collected at baseline, week 16 and week 52.

Response to adalimumab was measured at week 16 and at week 52 by means of the Hidradenitis Suppurativa Clinical Response (HiSCR).[20] Based on this efficacy variable, clinical response is defined as an at least 50% reduction in total inflammatory nodule and abscess count (AN count), with no increase in abscess and/or draining fistula count relative to baseline. No response is defined as less than 50% reduction in total AN count or increase in abscess or draining fistula count relative to baseline.

Statistical analysis

Continuous variables are reported as mean ± SD or median (interquartile range, IQR), as appropriate. Categorical data are reported as counts (percentages). A logistic regression analysis was performed to assess some patients' characteristics as predictors of nonresponse. The two endpoints considered were response to adalimumab at week 16 and at week 52. The following predefined patient characteristics were included in the analyses as predictors: sex, BMI (≤ 25, > 25–30, > 30 kg m^{-2}), smoking (never smokers, current smokers, ex-smokers), age of HS onset (≤ 30, > 30–50, > 50 years), age at diagnosis (dichotomized using the median value: ≤ 29, > 29 years), age at baseline (≤ 30, > 30–50, > 50 years), therapeutic delay (dichotomized using the median value, i.e. ≤ 10 or > 10 years), HS phenotypes, previous systemic retinoid therapy, previous systemic immunosuppressive/immunomodulating agents, systemic antibiotics concomitant with adalimumab. Firstly, a univariate logistic regression analysis was performed. Subsequently, a multivariate model was fitted including only the variables significantly associated with the endpoint in the univariate analysis. The described univariate and multivariate regression approach were performed separately, considering the two above-mentioned endpoints. Estimated odds ratios (OR) with their 95% confidence intervals (CIs) were calculated from logistic regression parameters. Considering only patients with a complete follow-up (week 52), a paired analysis was performed to assess the change of DLQI and VAS pain scores from baseline to week 16 and to week 52. After having calculated variations of VAS pain and DLQI scores within each patient across the three time points, a Wilcoxon signed-rank test analysis was performed to assess the statistical significance of variations between baseline and week 16 and week 52. McNemar's test was used to compare the proportion of responders (HiSCR) at week 16 vs. week 52. For descriptive purposes, a box plot was created showing time to treatment for responders and nonresponders. P-values lower than 0·05, two-sided, were considered statistically significant. No correction for multiple testing was performed. All the statistical analyses were performed with the statistical software SAS (release 9·4, SAS Institute, Inc., Cary, NC, USA).

Results

Clinical features

Demographic and clinical features at baseline of the 389 patients are summarized in Table 1. Male patients were 50·6% (n = 197 of 389) and the median age at baseline was 34 years. The median therapeutic delay was 10 years. A family history of HS was recorded in 81 of 388 patients (20·9%). Obesity was found in 104 of 385 patients (27%). There were 246 of 387 (63·6%) patients who were current smokers, 36 of 387 (9·3%) were ex-smokers and 105 of 387 (27·1%) were never smokers. The main HS-related comorbidities included diabetes mellitus type II (n = 25 of 389; 6·4%), acne vulgaris (n = 20 of 389; 5·1%), psoriasis (n = 19 of 389; 4·9%) and inflammatory bowel diseases (16 of 389; 4·1%). Previous treatments included systemic antibiotics in 374 of 389 (96·1%) patients, systemic retinoids in 114 of 389 (29·3%) patients and immunosuppressive/immunomodulating agents (ciclosporin, systemic corticosteroids or dapsone) in

106 of 389 (27·3%) patients. Systemic antibiotics were administered in combination with adalimumab in 125 of 389 (32·1%) patients at different time points of the study to control disease flares. There were 278 of 389 (71·5%) patients who had a regular phenotype, 41 of 389 (10·5%) a conglobata phenotype, 33 of 389 (8·5%) a frictional furuncle phenotype, 21 of 389 (5·4%) a scarring folliculitis phenotype, 14 of 389 (3·6%) a syndromic phenotype and two of 389 (0·5%) an ectopic phenotype.

Response to adalimumab

All data about clinical response in terms of HiSCR at week 16 were available. HiSCR at week 52 was available for 308 of 389 (79·2%) patients, as 76 (19·5%) patients had not yet achieved this time point at the moment of data collection and data were missing in the remaining five (1·3%) patients. Clinical response to adalimumab assessed with HiSCR was achieved by 170 of 389 (43·7%) and 166 of 308 (53·9%) patients at week 16 and week 52, respectively. In 41 patients who had interrupted adalimumab before week 52 due to ineffectiveness (n = 35) or adverse events/side-effects (n = 6), HiSCR at week 52 was considered to be 'not achieved'. In fact, in the six patients who had experienced adverse events/side-effects, adalimumab was also ineffective.

The median IHS4, which was 17 at baseline, dropped to 10 at week 16 and to 8 at week 52 (Table 2). Time to treatment for responders and nonresponders is shown in Figure 1.

None of the following clinical parameters – sex, BMI, age at onset, age at diagnosis, age at baseline, HS phenotypes and smoking – correlated to response to adalimumab at week 16 or at week 52 (Table 3). Interestingly, the therapeutic delay was identified as a significant risk factor for nonresponse to adalimumab in terms of HiSCR both at week 16 (OR 1·92 for therapeutic delay > 10 years; 95% CI 1·28–2·89; P = 0·0016) and at week 52 (OR 1·60; 95% CI 1·01–2·53; P = 0·0435).

Previous immunosuppressive/immunomodulating agents such as ciclosporin, systemic corticosteroids and dapsone inversely correlated to the response to adalimumab in terms of HiSCR at week 52 (OR 1·78; 95% CI 1·08–2·95; P = 0·0250) but not at week 16 (OR 0·97; 95% CI 0·62–1·51; P = 0·8765). Considering the multivariate model including the two factors statistically significant at week 52 and adjusting for disease severity in terms of IHS4 at baseline, we found that only previous immunosuppressive/immunomodulating agents confirmed the statistical significance at multivariate analysis. The inverse correlation found at univariate analysis between therapeutic delay and HiSCR at week 52 was not confirmed on multivariate analysis (OR 1·59, 95% CI 0·99–2·55, P = 0·055) (Table 3).

When considering only the patients with complete follow-up (240 of 389 for DLQI and 253 of 389 for VAS pain), the median DLQI score, which was 20 at baseline, dropped to 10 at week 16 and to 7 at week 52. The median VAS pain score, which was 8 at baseline, dropped to 5 at week 16 and to 3 at week 52 (Table 2). We found a statistically significant reduction in DLQI scores between week 16 vs. baseline (P < 0·0001), week 52 vs. baseline (P < 0·0001) and week 52 vs.

Table 1 Patients' demographic and clinical features (n = 389)

Features	Values
Age at onset (years)[a]	20 (16–28)
Age at diagnosis (years)[a]	29 (21–37)
Age at baseline (years)[a]	34 (25–46)
Therapeutic delay (years)[a]	10 (5·8–20)
Males, n (%)	197 (50·6)
Body mass index, n (%)[b]	
≤ 25 kg m^{-2}	149 (38·7)
> 25–30 kg m^{-2}	132 (34·3)
> 30 kg m^{-2}	104 (27)
Current smokers, n (%)[c]	246 (63·6)
Family history of hidradenitis suppurativa, n (%)[d]	81 (20·9)
Previous systemic antibiotics, n (%)	374 (96·1)
Previous systemic retinoids, n (%)	114 (29·3)
Previous systemic immunosuppressive/ immunomodulating agents, n (%)	106 (27·3)
Systemic antibiotics concomitant with adalimumab, n (%)	125 (32·1)
Hidradenitis suppurativa phenotypes, n (%)	
Regular	278 (71·5)
Frictional furuncle	33 (8·5)
Scarring folliculitis	21 (5·4)
Conglobata	41 (10·5)
Syndromic	14 (3·6)
Ectopic	2 (0·5)

[a]Data are reported as median (interquartile range); [b]data on body mass index were missing for four patients; [c]data on smoking were missing for two patients; [d]data on family history of hidradenitis suppurativa were missing for one patient

Table 2 International Hidradenitis Suppurativa Severity Score System (IHS4), Dermatology Life Quality Index (DLQI), Visual Analogue Scale for pain (VAS pain) and Hidradenitis Suppurativa Clinical Response (HiSCR) scores at baseline, week 16 and week 52

	Scores		
	Baseline	Week 16	Week 52
IHS4[a] (n = 265)	17 (11–27)	10 (7–18)	8 (4–12)
DLQI[a] (n = 240)	20 (12–25)	10 (7–18)	7 (4–14)
VAS pain[a] (n = 253)	8 (6–9)	5 (3–6)	3 (2–5)
HiSCR[b]	NA	170 (43·7)	166 (53·9)

[a]Data are reported as median (interquartile range). Only patients with complete follow-up data have been included in this analysis; [b]data are reported as number of patients (percentage) n, number of patients included in the analyses (exclusion reasons are ongoing therapy at the moment of data collection, drug interruption or missing data); NA, not applicable. For IHS4, DLQI and VAS-pain, all P-values for pairwise comparisons between t52 and t16 vs. baseline are < 0·0001; for HiSCR, P-value is 0·0004

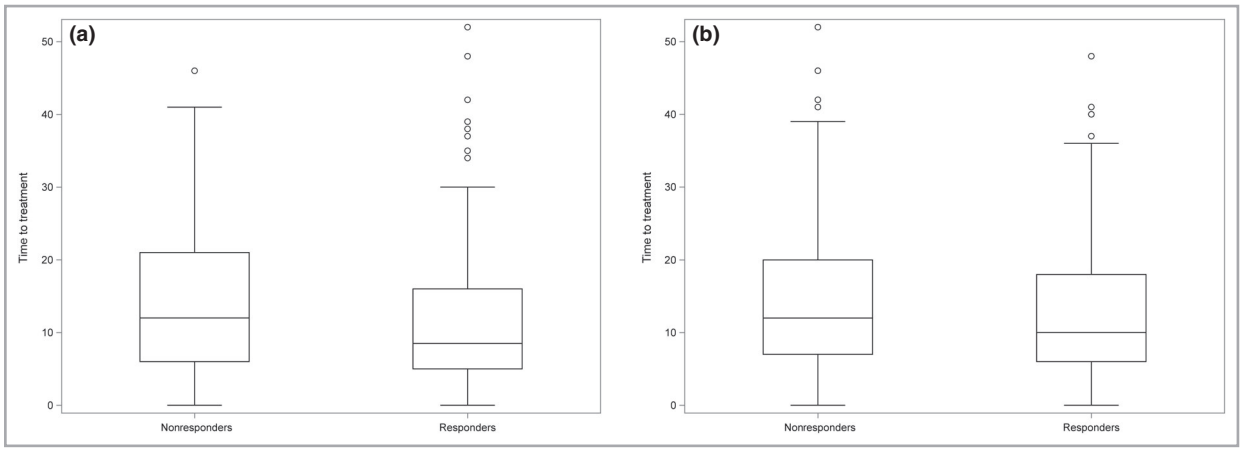

Figure 1 Box plot summarizing the distribution of time to treatment for responders and nonresponders (clinical response assessed using the Hidradenitis Suppurativa Clinical Response). (a) Response at week 16; (b) response at week 52. The horizontal line within the box represents the median value for time to treatment; the upper horizontal line of the box represents the 3rd quartile (Q3); the lower horizontal line of the box represents the 1st quartile (Q1). Upper fence is Q3 + 1·5 interquartile range; lower fence is the minimum observed value. Dots represent outliers.

week 16 ($P < 0·0001$). Likewise, we found a statistically significant reduction in VAS pain scores of week 16 vs. baseline ($P < 0·0001$), week 52 vs. baseline ($P < 0·0001$) and week 52 vs. week 16 ($P < 0·0001$).

Safety

The majority of adverse events were mild in severity and most frequently included asthenia, headache, arthralgia, upper respiratory tract infection, dizziness and nausea.

Five patients developed paradoxical skin reactions manifesting as psoriasis vulgaris (n = 3), pustular psoriasis (n = 1) and cutaneous vasculitis (n = 1). Another patient developed alopecia areata.

No events of active tuberculosis, lymphoma, nonmelanoma skin cancer, demyelinating disorder and no deaths were recorded. Three serious infections probably related to the treatment were reported in our cohort, including septicaemia (n = 2) and pneumonia sustained by *Aspergillus fumigatus* (n = 1). Acute myocardial infarction occurred in a 39-year-old male with multiple cardiovascular risk factors. Bladder cancer was diagnosed at week 40 after adalimumab initiation in a 52-year-old male patient.

Adalimumab discontinuation

Adalimumab discontinuation (both temporary and definitive) was reported in 58 of 389 (14·9%) patients. Definitive discontinuation was observed in 41 (10·5%) patients, in 35 of whom drug withdrawal was due to lack or loss of clinical efficacy and in six of whom was due to severe adverse events/side-effects [cancer, acute myocardial infarction, septicaemia (n = 2), pustular psoriasis and cutaneous vasculitis].

Temporary discontinuation was observed in 17 (4·4%) patients, nine of whom interrupted adalimumab to undergo surgical procedures on axillary, inguinal or gluteal areas and eight of whom spontaneously discontinued adalimumab on self-assessment of lack of effectiveness (n = 4) or pregnancy (n = 4). Two of 389 (0·05%) patients were lost to follow-up.

Discussion

Efficacy of adalimumab in the treatment of patients with moderate-to-severe HS refractory to conventional therapies has been widely demonstrated in two 12-week controlled clinical trials.[13] Recently, two extension studies pointed out adalimumab 40-mg weekly as a reasonable approach also for medium-to-long-term control of moderate-to-severe HS.[14,15]

Notably, Bettoli *et al.* showed that HS duration and diagnostic delay negatively impact on disease severity[21] and, according to the 'window of opportunity' hypothesis, it has been suggested that early treatment with adalimumab positively affects clinical response to the drug.[22] Likewise, early adalimumab treatment has been reported to be associated with better outcomes in both inflammatory bowel diseases and ankylosing spondylitis, reducing the risk of developing bowel strictures requiring intestinal surgery and irreversible bone damage leading to new bone formation, respectively.[23,24]

In HS, adalimumab should be started in a phase of the disease characterized by reversible lesions such as inflammatory nodules and abscesses before the development of lesions that cannot be reverted such as fistulas, sinus tracts and scarring sequelae.[22]

The main finding of our real-life study, conducted with a cohort of 389 patients with moderate-to-severe HS treated with adalimumab, is the significant inverse correlation between therapeutic delay and clinical response to the drug at week 16 of treatment. This may support early use of adalimumab in HS and provides evidence for a 'window of opportunity' in this disease. Of note, the inverse correlation

Table 3 Odds ratios (OR) and 95% confidence intervals (CI) for nonresponse to adalimumab according to baseline clinical parameters in patients with moderate-to-severe hidradenitis suppurativa at week 16 and week 52

	Week 16 (n = 389)			Week 52[c] (n = 308)		
Clinical parameters	OR	95% CI	P-value	OR	95% CI	P-value
Sex						
Females	1[a]		0·9849	1[a]		0·5860
Males	1	0·67–1·5		0·88	0·56–1·38	
Age (years) at hidradenitis suppurativa onset						
> 50	1[a]		0·8997	1[a]		0·7608
> 30–50	1·39	0·32–6·05		1·39	0·28–6·95	
≤ 30	1·28	0·31–5·20		1·11	0·24–5·04	
Age (years) at diagnosis						
≤ 29	1[a]		0·181	1[a]		0·8861
> 29	1·32	0·88–1·97		0·97	0·62–1·52	
Age (years) at baseline						
> 50	1[a]		0·1338	1[a]		0·3284
> 30–50	0·63	0·34–1·15		0·71	0·37–1·33	
≤ 30	0·53	0·28–0·99		0·61	0·32–1·17	
Body mass index						
≤ 25	1[a]		0·9080	1[a]		0·4293
> 25–30	1·08	0·67–1·72		1·39	0·82–2·36	
> 30	1·11	0·67–1·85		1·32	0·75–2·33	
Smoking						
Never smokers	1[a]		0·4763	1[a]		0·4897
Current smokers	1·18	0·75–1·87		0·77	0·46–1·29	
Ex-smokers	1·61	0·74–3·51		1·07	0·47–2·43	
Therapeutic delay, years[b]						
≤ 10	1[a]		0·0016	1[a]		0·0435
> 10	1·92	1·28–2·89		1·60	1·01–2·53	
Hidradenitis suppurativa phenotypes						
Regular	1[a]		0·5630	1[a]		0·8484
Frictional furuncle and scarring folliculitis	1·38	0·76–2·53		1·11	0·57–2·15	
Conglobata and ectopic	1·05	0·59–1·86		0·86	0·44–1·69	
Previous systemic retinoids						
No	1[a]		0·6245	1[a]		0·8987
Yes	0·90	0·58–1·39		1·03	0·63–1·69	
Previous systemic immunosuppressive/immunomodulating agents						
No	1[a]		0·8765	1[a]		0·0250
Yes	0·97	0·62–1·51		1·78	1·08–2·95	
Systemic antibiotics concomitant with adalimumab						
No	1[a]		0·0597	1[a]		0·7266
Yes	1·52	0·98–2·35		1·09	0·68–1·75	

[a]Reference category; [b]effect of therapeutic delay at week 16 in regression analysis adjusted for disease severity in terms of IHS4 at baseline: OR 1·81, 95% CI 1·20–2·74, P = 0·0046; [c]at multivariate analysis, including 'Therapeutic delay' and 'Previous systemic immunosuppressive/immunomodulating agents' and adjusted for disease severity in terms of IHS4 at baseline, the following results were obtained: Therapeutic delay (≤ 10 vs. > 10 years): OR = 1·59, 95% CI 0·99–2·55, P = 0·055; and Previous systemic immunosuppressive/immunomodulating agents (Yes vs. No): OR = 1·74, 95% CI 1·04–2·91, P = 0·0342 IHS4, International Hidradenitis Suppurativa Severity Score System

between therapeutic delay and clinical response was evident also at week 52 with univariate analysis but was not confirmed with multivariate analysis, although it was close to reaching statistical significance.

In our study, previous immunosuppressive/immunomodulating agents, such as ciclosporin, systemic corticosteroids and dapsone, showed a statistically significant inverse correlation to the response to adalimumab at week 52, an intriguing, albeit hard to explain, finding that also fits in well with the early use of adalimumab. Theoretically, these agents could have influenced the immunological profile of our patients, inducing a switch to other non-TNF-driven inflammatory pathways, such as IL-17 and IL-23-related ones,[11,25,26] and consequently interfering with the clinical behaviour of the disease and response to adalimumab.

Clinical response to adalimumab assessed through HiSCR at week 16 and week 52 was achieved in 44% and 62% of patients, respectively, a result that is in line with previously

reported controlled clinical trials.[13–15] Interestingly, baseline DLQI and VAS pain scores showed a marked reduction at week 16, which progressed up to week 52, suggesting that improvement in patients' QoL paralleled the clinical response, particularly in terms of IHS4.

On the other hand, it is of note that patients with great improvement in QoL have shown a less evident clinical response in terms of HiSCR. This may be due to a decrease in the inflammatory component and volume of nodules/abscesses, along with a decrease in purulent discharge from abscesses/fistulae, despite lack of reduction in the number of lesions.

On the other hand, sex, BMI, age at onset/diagnosis/baseline, HS phenotypes and smoking were not associated with the clinical response to adalimumab. The lack of correlation between parameters such as BMI and smoking and clinical response to adalimumab is unexpected, considering that these factors seem to play a pathogenetic role and negatively impact on disease severity.[27,28] Actually, to the best of our knowledge there are no data in the literature supporting that an increased BMI and/or smoking might impair the clinical response to adalimumab.

The safety profile of adalimumab in our cohort of patients was excellent, with only mild reported adverse events, including transient asthenia, headache and nausea. Adalimumab discontinuation occurred in 14·9% of patients, mainly due to lack/loss of efficacy.

A limitation of this study is its retrospective and observational nature and the fact that the study population was limited to patients with moderate-to-severe HS resistant to standard first-line treatments according to the AIFA recommendations.

In summary, our findings indicate that adalimumab yields significant improvement in HS with a good safety profile, encouraging early use of this drug to better control disease progression.

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