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Hidradenitis suppurativa in a large cohort of Italian patients: evaluation of the burden of disease

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Short title: Burden of Hidradenitis Suppurativa in Italian patients

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Key Message: HS patient's burden and QoL improve in 9-month observation.

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1 **Abstract**

2 **Background:** Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, debilitating  
3 skin disease of the hair follicle that usually occurs after puberty with painful, deep-seated,  
4 inflamed nodules and sinus tracts in the apocrine gland-bearing areas of the body, most  
5 commonly the axillae, inguinal and anogenital regions, with a relevant impact on patients'  
6 quality of life (QoL).

7 **Objective:** To evaluate how the burden of HS disease impacts on patient well-being and  
8 working activities in a large Italian population over a period of 9 months

9 **Methods:** A multicenter, prospective, epidemiologic cohort study was conducted in adult  
10 Italian patients with HS. HS severity was assessed through Hurley stage and HS Physician's  
11 Global Assessment (HS-PGA); clinical improvement by HS Clinical Response (HiSCR) and  
12 Partial Response; and disease burden through QoL questionnaires (HIDRADisk, Skindex-16,  
13 Dermatology Life Quality Index [DLQI]), and Work Productivity and Activity Impairment–  
14 General Health (WPAI:GH).

15 **Results:** A total of 308 patients (56.2% women; mean age 35.2±12.9 years) were enrolled in  
16 27 dermatologic clinics. Men were older (37.4 years vs 33.5), more smoking addicted (74.1%  
17 vs 60.1%) and alcohol consumer (34.1% vs 13.9%), while women were more obese (34.10%  
18 vs 22.22%).

19 At baseline, most patients had a Hurley severity stage of 2 (43.9%), a moderate HS-PGA score  
20 (57.1%) and poor QoL (HIDRADisk: 65.7±23.3, Skindex-16: 60.3±26.9, and DLQI: 10.8±8.1).  
21 Patients with more severe disease showed worse QoL. Mean values for the variables related to  
22 HS severity decreased during the study period. The achievement of HiSCR and Partial  
23 Response increased during the study.

24 **Conclusion:** This study offers insight on the disease burden of HS in an Italian population. Our  
25 results underline the impact of QoL evaluation, also with the use of the HIDRADisk, in clinical  
26 routine as a support to validated severity clinical and instrumental indexes for a “360-degree”  
27 assessment of HS patient's burden of disease.

28

## 29 **Introduction**

30 Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, debilitating skin disease of  
31 the hair follicle that usually occurs after puberty with painful, deep-seated, inflamed nodules  
32 and sinus tracts in the apocrine gland-bearing areas of the body, most commonly the axillae,  
33 inguinal and anogenital regions [1]. HS, which has an estimated prevalence in Italy of 0.056%  
34 [2], shows a relevant impact on patients' QoL [1]. In fact, the chronic nature of HS deeply  
35 affects interpersonal relationships, self-esteem, perception of self and public image, and even  
36 work employment. Therefore, many patients with HS report depression [1, 3-5] and  
37 stigmatization [1, 6-7]. In addition, fever and fatigue often arise in severe cases and may prevent  
38 individuals from performing even common everyday tasks [1]. Incorporating an instrument to  
39 assess the burden of a disease in medical practice can provide a greater patient satisfaction and  
40 an improved clinical outcome [8]. However, the impact of chronic skin diseases on different  
41 aspects of QoL - such as psychosocial, occupational, and interpersonal - is often underestimated  
42 by healthcare systems for disease severity assessment, bringing to light room for improvement  
43 [8-9]. In the last years this need has become a focus for HS disease, leading to the development  
44 of specific QoL questionnaires such as HSIA&HSSA (10), HS Burden of Disease (11) and  
45 HIDRADisk [12]. In this scenario, the HIDRADisk questionnaire is the first Italian-validated  
46 visual instrument jointly completed by patient and dermatologist that measures HS burden in a  
47 large sample population [12-13]. It explores the impact of HS on 10 domains, such as the  
48 general state of health, pain, odour, symptom control, skin involvement, personality, social life,  
49 sexual life, work, and daily activities. The answers are graphically represented on a disk, giving  
50 as result the area of a polygon which shrinks when the burden of disease decreases [13]. Adding  
51 these new tools to the current generic QoL and working impact measurements should highlight  
52 how the burden of HS weights on patients' QoL leading healthcare systems to recognize this  
53 burden in the HS disease management.

54 This long-term observational study evaluated, adding the HIDRADisk to the current generic  
55 QoL and working impact tools, how the burden of HS disease impacts on patient well-being  
56 and working activities in a large Italian population over a period of 9 months.

## 57 **Materials and methods**

58 For further details, see the online supplementary material (see  
59 [www.karger.com/doi/10.1159/000 xxxxxx](http://www.karger.com/doi/10.1159/000 xxxxxx)) [1, 14-21] (shown in Fig. 1).

## 60 **Results**

61 A total of 308 patients (56.2% women; mean age 35.2±12.9 years) were enrolled in 27  
62 dermatologic clinics. Two hundred and ninety-one patients (94.5%) attended the 3-month visit

63 and 253 (82.1%) reached the 9-month visit. Forty-nine patients were lost to follow-up and 6  
64 withdrew consent. Patient demographics and baseline clinical characteristics are described in  
65 Table 1. The study population was mainly composed of smokers and overweight/obese patients.  
66 The most frequently reported concomitant medical condition was obesity (11.4%), but 70.5%  
67 of enrolled patients did not report any other major disease.  
68 Characteristics were similar between men (43.8% of the population) and women, but men were  
69 older (37.4 years vs 33.5,  $p=0.008$ ), more smoking addicted (74.1% vs 60.1%,  $p=0.001$ ), and  
70 more alcohol consumer (34.1% vs 13.9%,  $p<0.001$ ). Women were more obese, BMI  $\geq 30$   
71 (34.10% vs 22.22%,  $p=0.013$ ), than men.

### 72 Clinical presentation of HS

73 Characteristics of HS at baseline and during the study are summarized in Table 1 and 2. HS  
74 was frequently localized in the axilla (56.5%), in the groin region (54.6%), and in the genital  
75 (30.2%) and perineal area (26.6%). Men presented more frequently lesions in the gluteal region  
76 (60%,  $p<0.001$ ), perianal area (56.1%,  $p=0.009$ ) and trunk (56.1%,  $p=0.024$ ), while women in  
77 the breast area (85.7%,  $p<0.001$ ) and groin region (63.7,  $p=0.004$ ). At baseline, most patients  
78 had an average Hurley severity stage of 2 (43.9%) and a moderate HS-PGA score (57.1%)  
79 without difference between gender (Table 1). Mean values for the variables related to HS  
80 severity decreased during the study period. In fact, the percentage of patients with Hurley stage  
81 1 increased during the study (29.5% at baseline and 36.1% at 9 months), while those with  
82 Hurley stage 3 decreased (26.6% at baseline and 17.7% at 9 months). For those patients who  
83 completed the 9-month follow-up visit, the Hurley stage change during the study is detailed in  
84 Figure 2a. As well, patients assessed as mild HS-PGA increased at 3 (30.9%) and 9 months  
85 (34.0%) and those assessed as moderate HS-PGA decreased at 3 (48.5%) and 9 months (40.3%).  
86 The percentage of patients achieving the HiSCR and the Partial Response increased at the end  
87 of the study: at 9 months, 47.0% of the patients achieved HiSCR and 57.7% achieved Partial  
88 Response. The patients needing a professional caregiver (nurse) during the course of the study  
89 reduced: 19.8% at baseline, 16.5% at 3 months, and 12.3% at 9 months.

### 90 QoL and burden of disease

91 *Baseline.* Patients showed a poor QoL, as evaluated by HIDRADisk (65.7 $\pm$ 23.3), Skindex-16  
92 (60.3 $\pm$ 26.9), and DLQI (10.8 $\pm$ 8.1) (shown in Table 1). Women reported poorer QoL (higher  
93 HIDRADisk [ $p=0.019$ ], Skindex16 [ $p=0.020$ ], and DLQI [0.121] total scores). In general,  
94 patients with more severe disease (Hurley stage 3) showed worse QoL, as captured by  
95 HIDRADisk total scores (shown in Table 3). In particular, following HIDRADisk items, severity  
96 of disease weighted heavily especially on those dimensions related to signs and symptoms (skin

97 appearance, odour, and pain), but also on the items related to personality and symptoms  
98 management.

99 *Study period.* All QoL questionnaires scores decreased (shown in Table 4). The HIDRADisk,  
100 Skindex16, DLQI, WPAI:GH scores were higher among patients with Hurley severity stage 3  
101 and lower in Hurley severity stage 2 and 1, respectively. The improvement in QoL during 9  
102 months has been observed also by stratifying for Hurley stage (shown in Fig. 2b). Number of  
103 nodules, abscesses, and fistulas was correlated with QoL scores (p-value <0.0001) at each visit,  
104 although with a low coefficient (> 0.30; shown in Table S1). All QoL scores (HIDRADisk,  
105 DLQI and Skindex-16) correlated with clinical indexes (Hurley and HS-PGA scores, as well as  
106 HiSCR and Partial Response; Table S1). All correlations between QoL total score and working  
107 activity impairment (WPAI:GH question 6) were positive and statistically significant (p-value  
108 <.0001) at each visit; after 9 months, the correlation coefficients were >0.65 (shown in Table  
109 5).

110 HS burden, as per patients' perception of HS severity, measured using the Subject Satisfaction  
111 Questionnaire at baseline, 3 and 9 months, was "very high" (14.6%, 10.2%, 8.7%), "high"  
112 (40.3%, 29.83%, 25.2%), "fair" (29.2%, 39.3%, 42.6%), "mild" (11.4%, 15.8%, 16.9%), and  
113 "very mild" (4.9%, 4.9%, 6.6%), respectively. The two questions evaluating the influence of  
114 HIDRADisk use on patient-physician relationship obtained the highest satisfaction scores by  
115 the majority of patients through the study (>78% at baseline, >80% at 3 and 9 months) (shown  
116 in Fig. S1a-b).

### 117 HS clinical management

118 Due to the observational nature of the study, the different HS treatments used were not objective  
119 of the analysis. Here we report the data spontaneously collected by centers.

120 The mean number of general practitioner and other specialist visits, as well as the need of  
121 medications/dressings, continuously decreased during the 9-month study period (shown in  
122 Table 2).

123 *Pharmacologic treatment.* The most reported therapies for HS were systemic antibiotics (25%)  
124 at baseline and biologics (28.9%) after 9 months, shown in Figure 3.

125 *Surgical treatment.* Although 151 patients (49.0%) reported  $\geq 1$  surgical treatment since the  
126 onset of the disease and 57 subjects (18.5%) had  $\geq 1$  previous surgical treatment in the last 12  
127 months before entering the study, only 5.8% and 3.6% of patients reported  $\geq 1$  surgical treatment  
128 for HS at 3 and 9-month visits, respectively.

### 129 **Discussion**



130 This is the first Italian study on QoL of patients with HS, conducted in a large nationwide HS  
131 cohort (n=308), with a prospective follow-up of 9 months. Of note, two Italian HS registries of  
132 245 and 944 patients were recently published by Bettoli et al. [22-23], which show  
133 demographics data similar to our population, but do not report QoL information and working  
134 impact assessment [22-23]. Our study was conducted in a larger number of Italian  
135 dermatologic clinics in comparison to “IRHIS 2 Project” [23], despite we collected data on a  
136 smaller population. We used HIDRADisk, the first validated tool specific for the QoL of  
137 patients with HS, to evaluate and monitor QoL changes, in addition to DLQI and Skindex-16  
138 questionnaires. In line with previous research, our baseline data show that HS mostly affects  
139 women, smokers and overweight/obese patients [1, 22-28]. As for other real-life studies, the  
140 majority of our patients had moderate disease severity (Hurley stage 2) [22, 29], and lesions  
141 were localized more frequently in the gluteal region, trunk, and perianal area in men and in the  
142 breast and groin region in women [28, 30]. QoL resulted worse in patients affected by a more  
143 severe disease and those cases with more fistulas and abscesses; in addition, our data support  
144 evidence that QoL is worse in female patients, impacting more on skin, sexuality, and social  
145 life. This aspect should be further studied to be fully explained. Moreover, HS impacts on  
146 working impairment and globally on psychophysical wellbeing. A significant correlation  
147 between QoL scores and both HS severity and activity impairment was shown throughout the  
148 study period, highlighting that HS burden is perceived more intensely in patients with a more  
149 severe disease.

150 Our study was designed to take a picture of an Italian HS population collecting data on  
151 demographics, disease severity, QoL, and working impairment, excluding analysis on clinical  
152 management. We observed that HIDRADisk, Skindex-16, DLQI and WPAI:GH scores  
153 decreased during the study period, reflecting an improvement in the general health status of  
154 patients for both QoL and in the related fatigue from working and other regular daily activities.  
155 The mean number of pharmaceutical treatments used to treat HS decreased as well during the  
156 study, with the most reported therapy changing from systemic antibiotics (at baseline) to  
157 biologics (at 9 months). Apart from the treatment used, the HS perception and symptoms in this  
158 study population improved globally. In fact, because of the observational nature of this study,  
159 no specific analysis on treatment outcomes could be performed since treatments were  
160 independent from study start and could be changed at any time during the study. During the  
161 observational period, minor changes in the number of patients treated with medical therapies  
162 do not justify the QoL improvement observed. On the other hand, patients’ perception of HS

163 severity, measured using the Subject Satisfaction Questionnaire, decreased from “very high”  
164 (baseline) to “very mild” (9 months); patients’ perception of disease improvement may be  
165 influenced by the way the HIDRADisk use could affect patient-physician relationship (shown  
166 in Fig. S1a-b). Other authors have already found as anger and negative thoughts caused by HS  
167 can trigger negative countertransference on the part of the clinician escalating the interpersonal  
168 discord and diminishing empathy and active listening, leading to reduced quality of care and  
169 treatment effectiveness [31]. We believe that the burden reduction observed in our study could  
170 also be explained by the positive effect of improved patients’ communication with their  
171 dermatologist that may have been triggered by HIDRADisk use. In fact, throughout the study,  
172 most patients conveyed that HIDRADisk was suitable and useful for the physician to better  
173 understand their perceived burden of the disease, confirming the strong appreciation of the tool  
174 as already showed in the validation paper [13]. In general, all QoL questionnaires have proven  
175 to be responsive to changes in disease severity over 9 months. Accordingly, the total QoL score  
176 changed from high to low figures among those patients achieving at least the Partial Response.

177 In addition, other studies have demonstrated the positive effect on the general patient outcomes  
178 with the “Hawthorne effect” [32], or “the observer effect”- a type of reactivity in which  
179 individuals improve an aspect of their behavior in response to their awareness of being observed  
180 - during the study period.

181 As limitation of our analysis, we recognize that the Subject Satisfaction Questionnaire, a  
182 questionnaire specifically created by the study team, is not a validated tool, but on the other  
183 hand, the use of this questionnaire has proven the need for this kind of evaluations. Encouraging  
184 the patient self-assessment and the patient-physician discussion should be the strategy for a new  
185 HS management, and in the future, further studies should be developed aimed at verifying the  
186 use of this approach to HS to improve the burden of this disease.

187 Our study supports the evidence that HS is one of the most severe dermatological disease,  
188 affecting all aspects of patient’s life. The use of a quick and responsive QoL tool in the routine  
189 clinical practice can measure any variation in patient’s perception of their disease, improving  
190 the patients-physician relationship as a fruitful advantage for HS management regardless of the  
191 medical intervention used. Likewise, in the view of upgrading the standard of care for patients  
192 with HS, the clinical management of these patients has been recently expanded to a more  
193 heterogenous team of specialists -an HS-Multidisciplinary Unit [33]- and to new diagnostic  
194 instruments such as ultrasonography and Power Doppler sonography [33-34]. At this stage,

195 patient-reported outcomes in addition to physician assessments should be taken into  
196 consideration because of the profound impact of HS on patients' QoL.

197 In order to provide a "360-degree" assessment of patient's burden of disease in this new HS  
198 management scenario, our current results underline the impact of QoL evaluation, also with the  
199 use of the HIDRADisk, in clinical routine as a support to validated severity clinical and  
200 instrumental indexes.

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203 **Statement of Ethics**

204 The study was conducted in accordance with the Declaration of Helsinki and with approval from  
205 the regional Ethics Committee of Brescia (registration No. 2016/742-31/1).

206 **Conflict of Interest Statement**

207 Claudia De Cupis, Giuliana Gualberti, and Valeria Saragaglia are AbbVie employees and may own  
208 AbbVie stocks/options.

209 Paolo Amerio has received honoraria as a speaker and advisory board member by Abbvie srl.

210 The other authors have no conflicts of interest to declare.

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213 interpretation of the data, review, and approval of the manuscript.

214 **Author Contributions**

215 Giuliana Gualberti and Valeria Saragaglia contributed substantially to the planning and design of  
216 the study, and the data analysis. Claudia De Cupis contributed substantially to the data analysis  
217 and the critical review of the manuscript.

218 All authors contributed substantially to data collection, interpretation of data, medical writing,  
219 critical review of the manuscript and approved the final version.

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Hidradenitis suppurativa in a large cohort of Italian patients: evaluation of the burden of disease  
(HIDRAdisk study)

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Short title: Burden of Hidradenitis Suppurativa in Italian patients

formaterede: Understregning

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Key Message: HS patient's burden and QoL  
improve in 9-month observation.

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Keywords: Hidradenitis Suppurativa, Quality of Life, Burden of Disease, HIDRADisk

1 **Abstract**

2 **Background:** Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, debilitating  
3 skin disease of the hair follicle that usually occurs after puberty with painful, deep-seated,  
4 inflamed nodules and sinus tracts in the apocrine gland-bearing areas of the body, most  
5 commonly the axillae, inguinal and anogenital regions  
6 , with a relevant impact on patients' quality of life (QoL).

7  
8 **Objective:**

9 To evaluate how the burden of HS disease impacts on patient well-being  
10 and working activities in a large Italian population over a period of 9 months.

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11 **Methods:** A multicenter, prospective, epidemiologic cohort study was conducted in adult  
12 Italian patients with HS. HS severity was assessed through Hurley stage and HS Physician's  
13 Global Assessment (HS-PGA); clinical improvement by HS Clinical Response (HiSCR) and  
14 Partial Response; and disease burden through QoL questionnaires (HIDRADisk, Skindex-16,  
15 Dermatology Life Quality Index [DLQI]), and Work Productivity and Activity Impairment-  
16 General Health (WPAI:GH).

17 **Results:** A total of 308 patients (56.2% women; mean age 35.2±12.9 years) were enrolled in  
18 27 dermatologic clinics.

19 Men were older (37.4 years vs 33.5), more smoking  
20 addicted (74.1% vs 60.1%) and alcohol consumer (34.1% vs 13.9%), while women were  
21 more obese (34.10% vs 22.22%).

Kommenterede [UdMO1]:

22 At baseline, most patients had a Hurley severity stage of 2 (43.9%), a moderate HS-PGA score  
23 At baseline, most patients had a Hurley severity stage of 2 (43.9%), a moderate HS-PGA score  
24 (57.1%) and poor QoL (HIDRADisk: 65.7±23.3, Skindex-16: 60.3±26.9, and DLQI: 10.8±8.1).  
25 Patients with more severe disease showed worse QoL. Mean values for the variables related to  
26 HS severity decreased during the study period. The achievement of HiSCR and Partial  
27 Response increased during the study.

28 **Conclusion:** This study offers insight on the disease burden of HS  
29 in an Italian population. Our results underline the impact of QoL evaluation, also with the use  
30 of the HIDRADisk, in clinical routine as a support to validated severity clinical and  
31 instrumental indexes for a "360-  
32 degree" assessment of HS patient's burden of disease.

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## 35 Introduction

36 Hidradenitis suppurativa/~~aene inversa~~ (HS/AI) is a chronic, inflammatory, recurrent,  
 37 debilitating skin disease of the hair follicle that usually occurs after puberty with painful, deep-  
 38 seated, inflamed nodules and sinus tracts in the apocrine gland-bearing areas of the body, most  
 39 commonly the axillae, inguinal and anogenital regions (~~Dessau definition, 1st International~~  
 40 ~~Conference on Hidradenitis suppurativa/Aene inversa, March 30 April 1, 2006, Dessau,~~  
 41 ~~Germany~~) [1].~~HS, which has itsan estimated~~ prevalence in Italy ~~is estimated to beof~~ 0.056%  
 42 [2].~~HS has~~shows a relevant impact on patients' QoL [1]. In fact, the chronic nature of HS  
 43 deeply affects interpersonal relationships, self-esteem, perception of self and public image, and  
 44 ~~even work~~ employment. Therefore, many patients with HS report depression [1, -3-5] and  
 45 stigmatization [1, 6-7]. In addition, fever and fatigue often arise in severe cases and may prevent  
 46 individuals from performing even common everyday tasks [1]. ~~Evidence has shown that~~  
 47 ~~incorporating an instrument to assess the impact-burden of a disease on patient QoL into~~  
 48 ~~routinein~~ medical practice can ~~lead-provide toa~~ greater patient satisfaction and an improved  
 49 clinical outcome [~~reference98~~]. However, the impact of chronic skin diseases on different  
 50 aspects of QoL - such as psychosocial, occupational, and interpersonal - is ~~often~~  
 51 ~~underestimatednot taken enough into account~~ by ~~the~~ healthcare systems ~~for disease severity~~  
 52 ~~assessment, bringing to light room for improvement~~ [8-9].~~In the last years this need has~~  
 53 ~~become a focus for HS disease, leading to the development of specific QoL questionnaires such~~  
 54 ~~as HSIA&HSSA (10), HS Burden of Disease (11) and HIDRADisk [12]. In this scenario, the~~  
 55 HIDRADisk ~~questionnaire~~ is the first Italian-validated visual instrument jointly completed by  
 56 patient and dermatologist that measures HS burden in a large sample population [102-113]. ~~The~~  
 57 ~~questionnaireIt~~ explores the impact of HS on 10 domains, such as the general state of health,  
 58 pain, odour, symptom control, skin involvement, personality, social life, sexual life, work, and  
 59 daily activities. The answers are graphically represented on a disk, giving as result the area of  
 60 a polygon which shrinks when the burden of disease decreases [113]. ~~Adding these new tools~~  
 61 ~~to the current generic QoL and working impact measurements should highlight how the burden~~

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62 of HS weights on patients' QoL leading healthcare systems to recognize this burden in the HS  
63 disease management.

64 This long-term observational study evaluated, adding the HIDRAdisk to the current generic  
65 QoL and working impact tools, how the burden of HS disease impacts on patient well-being  
66 and working activities in a large Italian population over a period of 9 months

67 .

68 .

69

70 **Materials and methods**

71 **Materials and methods**

72 **Materials and methods**

73 For further details, see the online supplementary material (see  
74 [www.karger.com/doi/10.1159/000 xxxxxx](http://www.karger.com/doi/10.1159/000 xxxxxx)) [1, 14-21] (shown in Fig. 1).

75 **Results**

76 A total of 308 patients (56.2% women; mean age 35.2±12.9 years) were enrolled in 27  
77 dermatologic clinics. Two hundred and ninety-one patients (94.5%) attended the 3-  
78 month visit and 253 (82.1%) reached the 9-month visit. Forty-nine patients were lost to follow-  
79 up and 6 withdrew consent. Patient demographics and baseline clinical characteristics are  
80 described in Table 1. The study population was mainly composed of  
81 smokers and overweight/obese patients. The most frequently reported concomitant medical  
82 condition was obesity (11.4%). but 70.5% of enrolled patients did  
83 not report any other major disease.

84 Characteristics were similar between men (43.8% of the population) and women, but men were  
85 older (37.4 years vs 33.5, p=0.008), more smoking addicted (74.1% vs 60.1%, p=0.001), and  
86 more alcohol consumer (34.1% vs 13.9%, p<0.001). Women were more obese, BMI  
87 ≥30 (34.10% vs 22.22%, p=0.013), than men.

88 Clinical presentation of HS

89 Characteristics of HS at baseline and during the study are summarized in Table 1  
90 and 2. HS was frequently localized  
91 in the axilla (56.5%), in the groin region (54.6%), and in the genital (30.2%) and perineal area  
92 ~~Disease severity at baseline, assessed with Hurley stage, was similar between sexes (shown in~~  
93 ~~Table 1). Most patients reported HS lesions at~~ in the axilla (56.5%), in the groin region (54.6%),  
94 and in the genital (30.2%) and perineal area (26.6%). Men ~~reported-presented~~ more frequently  
95 lesions in the gluteal region (60%, p<0.001), perianal area (56.1%, p=0.009) and trunk (56.1%,  
96 p=0.024), while women ~~reported more lesions~~ in the breast area (85.7%, p<0.001) and groin  
97 region (63.7, p=0.004). At baseline, most patients had an average Hurley severity stage of 2  
98 (43.9%) and a moderate HS-PGA score (57.1%) without difference between gender (Table 1).

99  
100 Mean values for the variables related to HS severity decreased during the study period. As at  
101 baseline In fact, most patients had a Hurley severity stage of 2 after 3 and 9 months (41.9% and  
102 46.2%, respectively). The percentage of patients with Hurley stage 1 increased during the study  
103 (29.5% at baseline and 36.1% at 9 months), while those with Hurley stage 3 decreased (26.6%

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104 at baseline and 17.7% at 9 months). ~~For those patients who completed the 9-month follow-up~~  
105 ~~visit, the Hurley stage change during the study is detailed in Figure 2a. As well, Most of the~~  
106 ~~patients showed assessed as mild HS-PGA increased or moderate value for HS-PGA both at 3~~  
107 ~~(30.9% and 48.5% respectively) and 9 months (34.0% and 40.3% respectively) and those~~  
108 ~~assessed as moderate HS-PGA decreased at 3 (48.5%) and 9 months (40.3%).~~

109 ~~For those patients who completed the 9 months follow up visit, the HS-PGA assessment change~~  
110 ~~during the study is detailed in Figure 2b. A reduction in the number of lesions (“improvement”)~~  
111 ~~was observed in 42.6% and 51.8% of patients at 3 and 9 months, respectively, while 34.7% and~~  
112 ~~34.0% had the same number of lesions (“stable disease”), and 22.7% and 14.2% had an increase~~  
113 ~~in the number of lesions (“worsening”). The most reported lesion locations during the study~~  
114 ~~observation period at 3 and 9 months did not vary with respect to baseline: axilla (54.6% and~~  
115 ~~53.8%), groin (50.9% and 48.6%), genital (30.2% and 24.1%), and perineal area (23.0% and~~  
116 ~~21.0%), respectively. The percentage of patients achieving the HiSCR and the Partial Response~~  
117 ~~increased at the end of the study: at 9 months, 47.0% of the patients achieved HiSCR and 57.7%~~  
118 ~~achieved Partial Response. A reduction in The patients needing a professional caregiver (nurse)~~  
119 ~~during the course of the study was observed reduced: 19.8% at baseline, 16.5% at 3 months,~~  
120 ~~and 12.3% at 9 months compared with baseline (19.8%).~~

#### 121 QoL and burden of disease

122 Baseline. Patients showed a poor QoL, as evaluated by HIDRADisk (65.7±23.3), Skindex-16  
123 (60.3±26.9), and DLQI (10.8±8.1) (shown in Table 1). Women reported poorer QoL (higher  
124 HIDRADisk [p=0.019], Skindex16 [p=0.020], and DLQI [0.121] total scores). In general,  
125 patients with more severe disease (Hurley stage 3) showed worse QoL, as captured by  
126 HIDRADisk total scores (shown in Table 3). In particular, following HIDRADisk items, severity  
127 of disease weighted heavily especially on those dimensions related to signs and symptoms (skin  
128 appearance, odour, and pain), but also on the items related to personality and symptoms  
129 management.

130 Women reported poorer QoL (higher HIDRADisk [p=0.019], Skindex16 [p=0.020], and DLQI  
131 [0.121] total scores). In general, patients with more severe disease (Hurley stage ~~of~~ 3) showed  
132 worse QoL, as captured by HIDRADisk ~~items and~~ total scores (shown in Table 3). In particular,  
133 following HIDRADisk items, ~~In these patients,~~ severity of disease weighted heavily especially  
134 on those dimensions related to signs and symptoms (skin appearance, odour, and pain), but also  
135 on the items related to personality and symptoms management.

136 ~~During the st~~Study period, ~~a~~All QoL questionnaires scores decreased (shown in Table 4). The HIDRADisk,  
137 Skindex16, DLQI, WPAI:GH scores were higher among patients with Hurley severity stage 3

138 and lower in Hurley severity stage 2 and 1, respectively. The improvement in QoL -during 9  
139 months was significantly higher in the HIDRADisk group compared to the control group (p-value <0.0001).  
140 nodules, abscesses, and fistulas was correlated with QoL scores (p-value <0.0001) at each visit,  
141 although with a low coefficient (> 0.30; shown in Table S1).  
142 DLQI and Skindex-16) ~~were found to correlated~~ with clinical indexes (Hurley and HS-PGA scores, as well as  
143 HiSCR and Partial Response; -Table S1). All correlations between QoL total score and working  
144 activity impairment (WPAI:GH question 6) were positive and statistically significant (p-value  
145 <.0001) at each visit; after 9 months, the correlation coefficients were >0.65 (shown in Table  
146 5).

147 Number of nodules, abscesses, and fistulas was correlated with QoL scores (p-value <0.0001)  
148 at each visit, although with a low coefficient (> 0.30; shown in Table S1).

149 All QoL scores (HIDRADisk, DLQI and Skindex-16) ~~were found to correlated~~ with clinical  
150 indexes (Hurley and HS-PGA scores, as well as HiSCR and Partial Response; -Table S1). All  
151 correlations between QoL total score and working activity impairment (WPAI:GH question 6)  
152 were positive and statistically significant (p-value <.0001) at each visit; after 9 months, the  
153 correlation coefficients were >0.65 (shown in Table 5).

154  
155 HS burden, as per patients' perception of HS severity, measured using the Subject Satisfaction  
156 Questionnaire at baseline, 3 and 9 months, was "very high" (14.6%, 10.2%, 8.7%), "high"  
157 (40.3%, 29.8.3%, 25.2%), "fair" (29.2%, 39.3%, 42.6%), "mild" (11.4%, 15.8%, 16.9%), and  
158 "very mild" (4.9%, 4.9%, 6.6%), respectively. The two questions evaluating the influence of  
159 HIDRADisk use on patient-physician relationship obtained the highest satisfaction scores by  
160 the majority of patients through the study (>78% at baseline, >80% at 3 and 9 months) (shown  
161 in Fig. S1a-b).

#### 162 HS clinical management

163 Due to the observational nature of the study, the different HS treatments used were  
164 not objective of the analysis. Here we report the data spontaneously collected by centers.

165 The mean number of general practitioner and other specialist visits, as well as the need of  
166 medications/dressings, continuously decreased during the 9-month study  
167 period (shown in Table 2).

168 *Pharmacologic treatment.* The most reported therapies for HS were systemic  
169 antibiotics (25%) at baseline and biologics (28.9%) after 9 months, shown  
170 in Figure 3.

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171 *Surgical treatment.* Although 151 patients (49.0%) reported  $\geq 1$  surgical treatment since the  
172 onset of the disease and 57 subjects (18.5%) had  $\geq 1$  previous surgical treatment in the last 12  
173 months before entering the study, only 5.8% and 3.6% of patients reported  $\geq 1$   
174 surgical treatment for HS at 3 and 9-month visits, respectively.

## 175 Discussion

176

177

## 178 Discussion

179 This is the first Italian study on QoL of patients with HS, conducted in a large  
180 nationwide HS cohort (n=308), with a prospective follow-up of 9 months. Of note, two Italian  
181 HS registries of 245 and 944 patients were recently published by Bettoli et al. [22-23],  
182 which show demographics data similar to our population, but do not report QoL information  
183 and working impact assessment [22-23]. Our study was conducted in a larger number of Italian  
184 dermatologic clinics in comparison to "IRHIS 2 Project" [23], despite we collected data on a  
185 smaller population.

186 We used HIDRADisk, the first validated tool specific for the QoL of patients with HS, to  
187 We used HIDRADisk, the first validated tool specific for the QoL of patients with HS, to  
188 We used HIDRADisk, the first validated tool specific for the QoL of patients with HS, to  
189 We used HIDRADisk, the first validated tool specific for the QoL of patients with HS, to  
190 We used

191 HIDRADisk, the first validated tool specific for the QoL of patients with HS, to evaluate and  
192 monitor QoL changes, in addition to DLQI and Skindex-16 questionnaires  
193 . In line with previous research, our  
194 baseline data show that HS mostly affects women, smokers and overweight/obese patients  
195 [1, 22-28].

196 As for other real-life ~~populations-studies~~, the majority of our patients had moderate disease  
197 severity (Hurley stage 2) [22, 29], and lesions were ~~observed-localized~~ more frequently in the  
198 gluteal region, trunk, and perianal area in men and in the breast and groin region in women [28,  
199 30], ~~those findings validate the population chosen for our observation. QoL resulted worse in~~  
200 ~~patients affected by a more severe disease and those cases with more fistulas and abscesses; in~~  
201 addition, our ~~findings-data~~ support evidence that QoL is worse in female patients ~~is worse~~,  
202 impacting more on skin, sexuality, and social life, ~~as well as in those affected by a more severe~~  
203 ~~disease and those cases with more fistulas and abscesses. This aspect should be further studied~~

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204 ~~to be fully explained.~~ Moreover, ~~the impact of HS is reflected in~~ impacts on working impairment and globally ~~in an~~  
205 ~~extremely impacted~~ psychophysical wellbeing. A significant correlation between QoL scores and both HS severity  
206 and activity impairment was shown throughout the ~~observation study~~ period, highlighting that HS burden  
207 is perceived more intensely in patients with a more severe disease.

208  
209 ~~HS average severity scores, including the number of abscesses, nodules, and fistulas, were~~  
210 ~~lower after 9 months of observation.~~ ~~Our study was designed to take a picture of an Italian HS~~  
211 ~~population collecting data on demographics, disease severity, QoL, and working impairment,~~  
212 ~~excluding analysis on clinical management. We observed that~~ HIDRADisk, Skindex-16, DLQI  
213 and WPAI:GH scores ~~also~~ decreased during the study period, reflecting ~~the an~~ improvement in  
214 the general health status of patients for both QoL and in the related fatigue from working and  
215 other regular daily activities. The mean number of pharmaceutical treatments used to treat HS  
216 decreased as well during the study, with the most reported therapy changing from systemic  
217 antibiotics (at baseline) to biologics (at 9 months). Apart from the treatment used, the HS  
218 perception and symptoms in this study population improved globally. In fact, because of the  
219 observational nature of this study, no specific analysis on treatment outcomes could be  
220 performed since treatments were independent from study start and could be changed at any time  
221 during the study. During the observational period, minor changes in the number of patients  
222 treated with medical therapies do not justify the QoL improvement observed. ~~On the other hand,~~  
223 ~~patients' perception of HS severity, measured using the Subject Satisfaction Questionnaire,~~  
224 ~~decreased from "very high" (baseline) to "very mild" (9 months); patients' perception of disease~~  
225 ~~improvement may be influenced by the way the HIDRADisk use could affect patient-physician~~  
226 ~~relationship (shown in Fig. S1a-b).~~ Other authors have already found as anger and negative  
227 thoughts caused by HS can trigger negative ~~counter-transference~~ ~~countertransference~~ on the part  
228 of the clinician escalating the interpersonal discord and diminishing empathy and active  
229 listening, leading to reduced quality of care and treatment effectiveness [31]. We believe that  
230 the burden reduction observed in our study could also be explained by the positive effect of  
231 improved patients' communication with their dermatologist that may have been triggered by  
232 HIDRADisk use. ~~In fact,~~ throughout the study, most patients conveyed that HIDRADisk was  
233 suitable and useful for the physician to better understand their perceived burden of the disease,  
234 confirming the strong appreciation of the tool as ~~already~~ showed in the validation paper [103].  
235 ~~A recent Italian RWE study comparing different HS systemic therapies' efficacy by using~~  
236 ~~clinical scores confirmed HIDRADisk as a tool to detect the burden of disease [32].~~ In general,

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237 all QoL questionnaires ~~were have proven shown~~ to be responsive to changes in disease severity over 9  
238 months. Accordingly, the total QoL score changed from high to low figures among those  
239 patients achieving at least the Partial Response.

240 In addition, other studies have demonstrated the positive effect on the general patient outcomes  
241 with the “Hawthorne effect” [32], or “the observer effect”- a type of reactivity in which  
242 individuals improve an aspect of their behavior in response to their awareness of being observed  
243 - during the study period.

244 ~~As limitation of our analysis, we recognize that the Subject Satisfaction Questionnaire, a~~  
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251 ~~As limitation of our analysis, we recognize that the Subject Satisfaction Questionnaire, a~~

252 ~~A possible limitation of our study is that it was performed in the referral HS management~~  
253 ~~clinical centers and this might not reflect specifically the HS populations followed in peripherie~~  
254 ~~centers of care.~~ As limitation of our analysis, we recognize that the Subject Satisfaction  
255 Questionnaire, a questionnaire specifically created by the study team, is not a validated tool,  
256 but on the other hand, the use of this questionnaire has proven the need for this kind of  
257 evaluations. Encouraging the patient self-assessment and the patient-physician discussion  
258 should be the strategy for a new HS management, and in the future, further studies should be  
259 developed aimed at verifying the use of this approach to HS to improve the burden of this  
260 disease.

261 Our study supports the evidence that HS is one of the most severe dermatological disease,  
262 affecting all aspects of patient’s life. The use of a quick and responsive QoL tool in the routine  
263 clinical practice can measure any variation in patient’s perception of their disease, improving  
264 the patients-physician relationship as a fruitful advantage for HS management regardless of the  
265 medical intervention used. Likewise, in the view of upgrading the standard of care for patients  
266 with HS, the clinical management of these patients has been recently expanded to a more  
267 heterogenous team of specialists -an HS-Multidisciplinary Unit [33]- and to new diagnostic  
268 instruments such as ultrasonography and Power Doppler sonography [33-34]. At this stage,

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269 patient-reported outcomes in addition to physician assessments should be taken into  
270 consideration because of the profound impact of HS on patients' QoL.

271 In order to provide a “360-degree” assessment of patient’s burden of disease in this new HS

272 In order to provide a “360-degree” assessment of patient’s burden of disease in this new HS

273 management scenario, our current results underline the impact of QoL evaluation, also with the

274 use of the HIDRADisk, in clinical practice-routine as a support to validated severity clinical and

275 instrumental indexes and emerging new ultrasound diagnostic ultrasonography tools.

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278 **Statement of Ethics**

279 The study was conducted in accordance with the Declaration of Helsinki and with approval from  
280 the regional Ethics Committee [of Brescia](#) (registration No. 2016/742-31/1).

281 **Conflict of Interest Statement**

282 Claudia De Cupis, Giuliana Gualberti, and Valeria Saragaglia are AbbVie employees and may own  
283 AbbVie stocks/options.

284 Paolo Amerio has received honoraria as a speaker and advisory board member by Abbvie srl.

285 The other authors have no conflicts of interest to declare.

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288 interpretation of the data, review, and approval of the manuscript.

289 **Author Contributions**

290 Giuliana Gualberti and Valeria Saragaglia contributed substantially to the planning and design of  
291 the study, and the data analysis. Claudia De Cupis contributed substantially to the data analysis  
292 and the critical review of the manuscript.

293 All authors contributed substantially to data collection, interpretation of data, medical writing,  
294 critical review of the manuscript and approved the final version.

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## **Materials and methods**Study

A multicenter, prospective, epidemiologic cohort study was conducted in Italian patients with diagnosis of HS enrolled between July 2016 and March 2017. Patients were visited according to local clinical practice and no additional diagnostic or monitoring procedures were applied because of the study participation. Study objective was to assess the impact of the HS burden on patient well-being and working activities in a large Italian HS population over a period of 9 months. At baseline, HS diagnosis was made according to current guidelines [1, 14] and its severity was assessed through Hurley stage [15] and HS Physician's Global Assessment (HS-PGA) [16]. Patients' own perception of HS severity and how the HIDRADisk could affect the relationship between patient and dermatologist were evaluated by the Subject Satisfaction Questionnaire [11], a questionnaire specifically created by the study team. Clinical improvement was assessed using the HS Clinical Response score [17] (HiSCR), defined as the reduction of  $\geq 50\%$  in total abscesses (A) and inflammatory nodules (N) count with no increase in abscesses and draining fistulas count compared with the baseline visit. For study purposes, we also assessed a Partial Response (PR) defined as a reduction of at least 25% of A and N compared with baseline. Patient disease burden was assessed using QoL questionnaires (HIDRADisk [11], Skindex-16 [18-19], Dermatology Life Quality Index [20] [DLQI]) and work activity/productivity with the Work Productivity and Activity Impairment–General Health [10-11] (WPAI:GH) questionnaire.

## Centers and subjects

The study was conducted in 27 Italian dermatologic centers on consecutive patients affected by HS. Inclusion criteria allowed men and women aged  $\geq 18$  years affected by HS of any grade, diagnosed  $\geq 6$  months before study entry by a dermatologist, and able to understand and complete study-related questionnaires. Exclusion criteria were the presence of current malignancies or any other relevant diseases (according to the physician's opinion) that could significantly affect QoL, relevant psychiatric comorbidities, and current participation in any HS clinical trial. Enrollment was unrestricted to any HS medical and surgical treatment. The study protocol was approved by each local ethics committee and all patients provided written informed consent for the use of their personal data. Each subject was evaluated at baseline and after about 3 and 9 months. In order to capture all clinical and QoL characteristics, the recruitment was designed to enroll both subjects on treatment with stable therapy and subjects planned to start a new medical/surgical treatment, in about a 1 to 1 ratio.

## Questionnaires

All questionnaires were completed electronically using a tablet device that did not allow unanswered questions. The HIDRADisk application used in the study was developed in accordance with the Food

and Drug Administration Patient-Reported Outcome Guidance for Industry [21]. All questionnaires were administered at each study visit.

#### Sample size

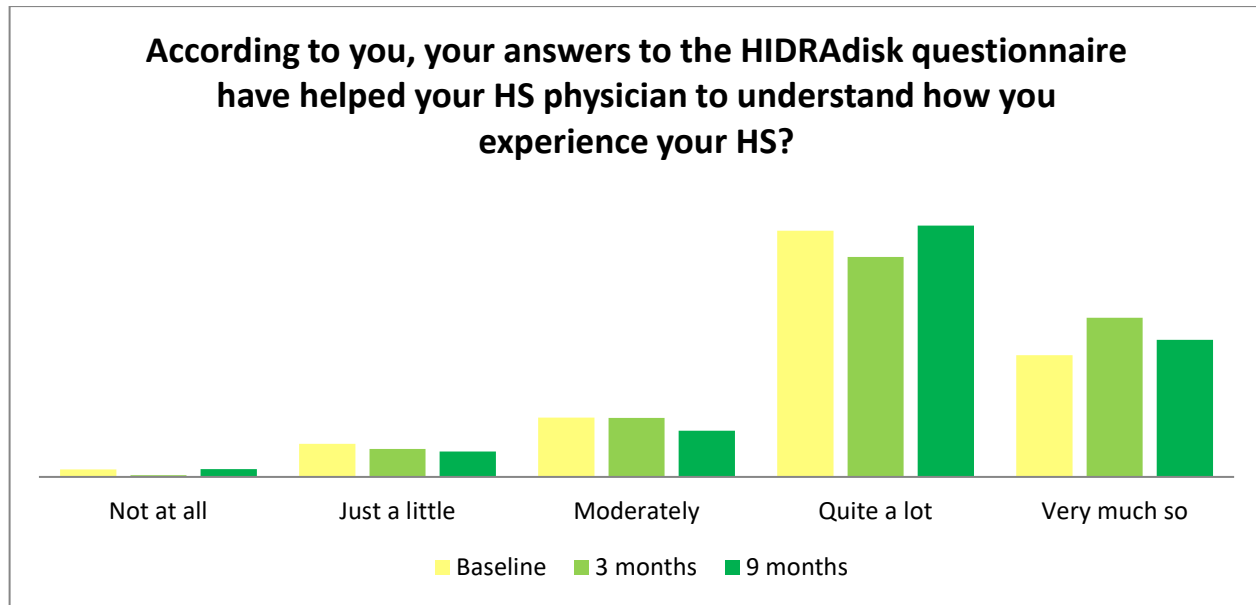
To estimate HS impact on patient QoL, a sample size of 300 patients was determined to allow an estimated 95% confidence interval of 1.32 points in the best-case scenario and of 2.54 in the worst-case scenario, calculated on the hypothesis of a mean DLQI score of 14 with different standard deviations and assuming that not all patients would complete the 9-month observation study.

#### Statistical analysis

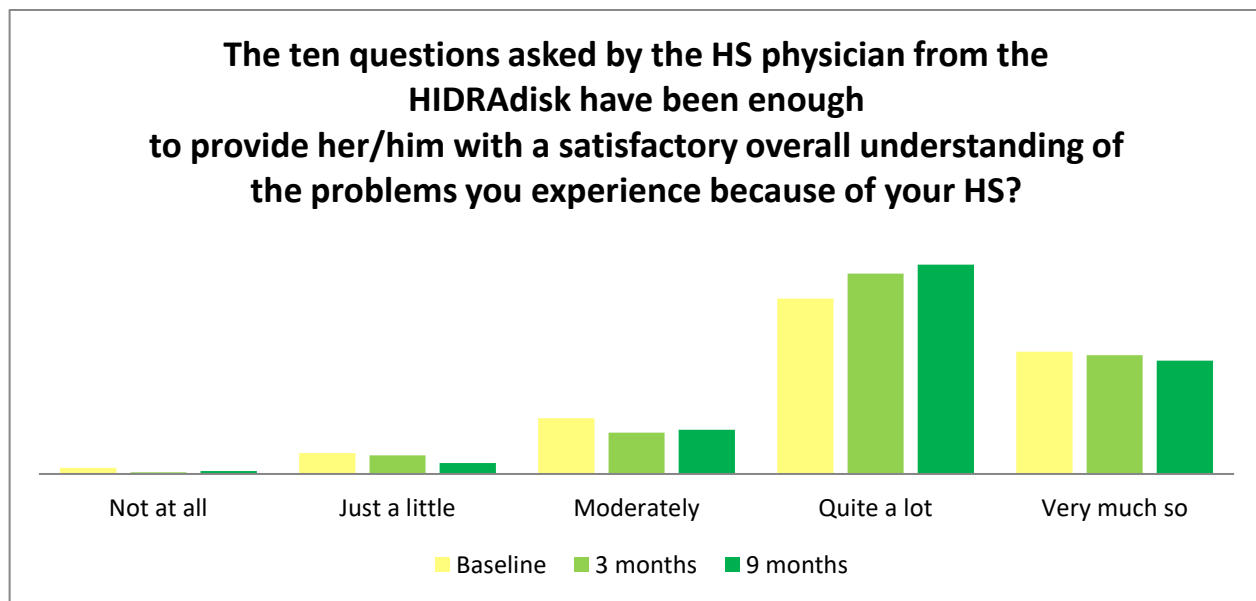
Patients' characteristics are summarized with descriptive statistics as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. Categorical data are compared by using the  $\chi^2$ , Fisher exact test, or T-test, as appropriate;  $P < 0.05$  was considered statistically significant. Correlations between activity/disease severity scores and QoL scores at 3 and 9 months were analyzed by Spearman's rank correlation for HiSCR variables (number of nodules, abscesses and draining fistulas) and the analysis of variance model for Hurley stage, HS-PGA, HiSCR, and partial response rates. Correlations between QoL scores and activity impairment (WPAI:GH question 6) at 3 and 9 months are provided in terms of Spearman's rank correlation. Results were based on non-missing data with no replacement of missing observations; data from patients with informed consent withdrawal were analyzed up to the measurement time point before the event.

**Fig. S1.** Subject's Satisfaction questionnaire responses

(a)



(b)



HS, hidradenitis suppurativa

**Table S1.** Correlation between QoL scores and number and kind of lesions (a) and clinical scores (b) at 9 months

(a)

|                       |             | Number of nodules    |         | Number of abscesses  |         | Number of fistulas   |         |
|-----------------------|-------------|----------------------|---------|----------------------|---------|----------------------|---------|
|                       |             | Spearman correlation | P value | Spearman correlation | P value | Spearman correlation | P value |
| Total HIDRADisk score |             | 0.3016               | <.0001  | 0.3482               | <.0001  | 0.3309               | <.0001  |
| DLQI total score      |             | 0.3470               | <.0001  | 0.3813               | <.0001  | 0.3325               | <.0001  |
| Skindex-16            | Total Score | 0.3652               | <.0001  | 0.3974               | <.0001  | 0.3646               | <.0001  |
|                       | Symptoms    | 0.3728               | <.0001  | 0.4061               | <.0001  | 0.3365               | <.0001  |
|                       | Emotions    | 0.3260               | <.0001  | 0.3379               | <.0001  | 0.3322               | <.0001  |
|                       | Functioning | 0.3251               | <.0001  | 0.3757               | <.0001  | 0.3734               | <.0001  |

DLQI, Dermatology Life Quality Index.

(b)

|                       |             | ANOVA on ranks P value |        |                   |                           |
|-----------------------|-------------|------------------------|--------|-------------------|---------------------------|
|                       |             | Hurley score           | HS-PGA | HiSCR achievement | Partial HiSCR achievement |
| Total HIDRADisk score |             | <.0001                 | <.0001 | <.0001            | <.0001                    |
| DLQI total score      |             | <.0001                 | <.0001 | <.0001            | <.0001                    |
| Skindex-16            | Total Score | <.0001                 | <.0001 | <.0001            | <.0001                    |
|                       | Symptoms    | <.0001                 | <.0001 | <.0001            | <.0001                    |
|                       | Emotions    | <.0001                 | <.0001 | <.0001            | <.0001                    |
|                       | Functioning | <.0001                 | <.0001 | 0.0001            | 0.0004                    |

DLQI, Dermatology Life Quality Index; HiSCR, Hidradenitis Suppurativa Clinical Response. HS-PGA, Hidradenitis Suppurativa Physician Global Assessment.

**Table 1. Patient demographics and clinical characteristics at baseline**

|  |                       | Total<br>n (%)           | Men<br>n (%)        | Women<br>n (%)       | P value** |
|--|-----------------------|--------------------------|---------------------|----------------------|-----------|
| Number of patients   |                       | 308                      | 135 (43.8)          | 173 (56.2)           |           |
| Age (years)  | Mean ± SD (range)     | 35.2±12.9 (18–70)        | 37.4±13.9 (18–70)   | 33.5±11.8 (18–62)    | 0.008     |
| Ethnicity  | White                 | 301 (97.7)               | 132 (97.8)          | 169 (97.7)           | 0.690     |
|  | Black                 | 2 (0.7)                  | 1 (0.7)             | 1 (0.6)              |           |
|  | Asian                 | 3 (0.9)                  | 2 (1.5)             | 1 (0.6)              |           |
|  | Other                 | 2 (0.7)                  | 0 (0)               | 2 (1.2)              |           |
| Civil status   | Single                | 186 (60.4)               | 81 (60.0)           | 105 (60.7)           | 0.394     |
|  | Married               | 106 (34.4)               | 50 (37.0)           | 56 (32.4)            |           |
|  | Divorced              | 14 (4.6)                 | 4 (3.0)             | 10 (5.8)             |           |
|  | Widower               | 2 (0.7)                  | 0 (0)               | 2 (1.2)              |           |
| Education level  | Primary school        | 7 (2.3)                  | 2 (1.5)             | 5 (2.9)              | 0.558     |
|  | Secondary school      | 82 (26.6)                | 41 (30.4)           | 41 (23.7)            |           |
|  | High school           | 152 (49.4)               | 64 (47.4)           | 88 (50.9)            |           |
|  | University            | 67 (21.8)                | 28 (20.7)           | 39 (22.5)            |           |
| Smoking habits   | Smoker                | 204 (66.2)               | 100 (74.1)          | 104 (60.1)           | 0.001     |
|  | Never smoked          | 79 (25.7)                | 21 (15.6)           | 58 (33.5)            |           |
|  | Ex-smoker (>6 months) | 25 (8.1)                 | 14 (10.4)           | 11 (6.4)             |           |
| Alcohol consumption  | Drinker               | 70 (22.7)                | 46 (34.1)           | 24 (13.9)            | <.001     |
|  | Non-drinker           | 233 (75.7)               | 85 (63.0)           | 148 (85.6)           |           |
|  | Ex-drinker (>1 month) | 5 (1.6)                  | 4 (3.0)             | 1 (0.6)              |           |
| BMI, kg/m <sup>2</sup>   | Mean ± SD (range)     | 27.5±5.6 (16-46)         | 27.1±5.0 (19-43)    | 27.7±6.0 (16-46)     | 0.383     |
|  | BMI <23               | 67 (21.8)                | 25 (18.5)           | 42 (24.3)            | 0.013     |
|  | 23 ≤ BMI <25          | 53 (17.2)                | 29 (21.5)           | 24 (13.9)            |           |
|  | 25 ≤ BMI < 30         | 99 (32.1)                | 51 (37.8)           | 48 (27.8)            |           |
|  | BMI ≥ 30              | 89 (28.9)                | 30 (22.2)           | 59 (34.1)            |           |
| Time from onset of HS symptoms to visit 1 (years) <sup>§</sup> | Mean ± SD (range)     | 11.4±10.1 (0.2-55.6)     | 11.3±9.7 (0.6-55.6) | 11.5±14.4 (0.2-46.5) | 0.861     |
| Time from HS diagnosis to visit 1 (years)*                     | Mean ± SD (range)     | 3.9±5.2 (0. 2-36.4)      | 4.2±6.0 (0.2-36.4)  | 3.7±4.4 (0.5-23.3)   | 0.424     |
| Duration of illness <sup>†</sup>                               | <5 years              | 235 (76.3)               | 102 (75.6)          | 133 (76.9)           | 0.956     |
|  | 5–14 years            | 54 (17.5)                | 24 (17.8)           | 30 (17.4)            |           |
|  | ≥14 years             | 19 (6.2)                 | 9 (6.7)             | 10 (5.8)             |           |
| Hurley stage at diagnosis                                      | 1                     | 92 (29.9)                | 34 (25.2)           | 58 (33.5)            | 0.094     |
|  | 2                     | 123 (39.9)               | 52 (38.5)           | 71 (41.0)            |           |
|  | 3                     | 73 (23.7)                | 36 (26.7)           | 37 (21.4)            |           |
|  | Missing               | 20 (6.5)                 | 13 (9.6)            | 7 (4.1)              |           |
| Patients with ≥1 previous pharmacologic treatment for HS       | No                    | 54 (17.5)                | 26 (19.3)           | 28 (16.2)            | 0.546     |
|  | Yes                   | 254 (82.5)               | 109 (80.7)          | 145 (83.8)           |           |
| Patients with ≥1 surgical treatment for HS since onset         |                       | 151 (49.0)               | 70 (51.8)           | 81 (46.8)            | 0.422     |
| Patients with ≥1 major concomitant pathology                   | No                    | 217 (70.5)               | 97 (71.8)           | 120 (69.4)           | 0.706     |
|  | Yes                   | 91 <sup>   </sup> (29.6) | 38 (28.2)           | 53 (30.6)            |           |
| HIDRADisk  | Mean ± SD (range)     | 65.7±23.3 (1–100)        | 63.0±22.3 (1–100)   | 67.8±23.9 (1–100)    | 0.019     |
| Skindex 16   | Mean ± SD (range)     | 60.3±26.9 (0–100)        | 56.8±25.7 (0–98)    | 63.0±27.5 (0–100)    | 0.020     |
| DLQI Total Score   | Mean ± SD (range)     | 10.8±8.1 (0-30)          | 9.9±7.8 (0-30)      | 11.4±8.3 (0-30)      | 0.121     |

BMI, body mass index; DLQI, Dermatology Life Quality Index; HS, Hidradenitis Suppurativa; IC, informed consent; QoL, quality of life; SD, standard deviation.

<sup>§</sup>Time from onset of HS symptoms to IC signature was calculated in years as the difference between date of IC signature and the date of onset of HS symptoms + 1 day.

\*Time from HS initial diagnosis to IC signature was calculated in years as the difference between date of IC signature and the date of HS diagnosis + 1 day.

In case of missing day of the date, 15 was imputed, and in case of missing day and month, July 1 was imputed. <sup>†</sup>Duration of illness was calculated, in years, as the difference between date of IC signature and the date of HS diagnosis + 1 day.

<sup>|||</sup>Patients could report >1 major other pathology; obesity was the most reported (11.4%).

\*\*Fischer exact test or T-test, as appropriated.

**Table 2.** HS characteristics and management through the study

| Parameters   |                          | Baseline                       |      | 3 months                        |      | 9 months                        |      |
|--|--------------------------|--------------------------------|------|---------------------------------|------|---------------------------------|------|
|  |                          | n = 308                        |      | n = 291                         |      | n = 253                         |      |
|  |                          | N                              | %    | N                               | %    | N                               | %    |
| Hurley stage   | 1                        | 90                             | 29.5 | 102                             | 36.6 | 86                              | 36.1 |
|  | 2                        | 134                            | 43.9 | 117                             | 41.9 | 110                             | 46.2 |
|  | 3                        | 81                             | 26.6 | 60                              | 21.5 | 42                              | 17.7 |
|  | Missing                  | 3                              | -    | 12                              | -    | 15                              | -    |
| Number of inflammatory nodules                             | Mean ± SD (range)        | 5.2±6.0 (0–50)                 |      | 3.4±4.0 (0–30)                  |      | 2.8±4.0 (0–28)                  |      |
| Number of abscesses  | Mean ± SD (range)        | 1.7±2.8 (0–30)                 |      | 1.3±2.4 (0–25)                  |      | 1.0±2.0 (0–21)                  |      |
| Number of fistulas   | Mean ± SD (range)        | 1.6±3.4 (0–40)                 |      | 1.3±2.9 (0–30)                  |      | 1.1±2.7 (0–340)                 |      |
| HS-PGA   | Clear*                   | 7                              | 2.3  | 17                              | 5.8  | 24                              | 9.5  |
|  | Minimal <sup>†</sup>     | 5                              | 1.6  | 14                              | 4.8  | 20                              | 7.9  |
|  | Mild <sup>‡</sup>        | 72                             | 23.4 | 90                              | 30.9 | 86                              | 34.0 |
|  | Moderate <sup>§</sup>    | 176                            | 57.1 | 141                             | 48.5 | 102                             | 40.3 |
|  | Severe <sup>  </sup>     | 21                             | 6.8  | 10                              | 3.4  | 8                               | 3.2  |
|  | Very severe <sup>¶</sup> | 27                             | 8.8  | 19                              | 6.5  | 13                              | 5.1  |
| HiSCR achievement <sup>+</sup>                             | Achieved                 | -                              | -    | 98                              | 33.7 | 119                             | 47.0 |
|  | Not achieved             | -                              | -    | 186                             | 63.9 | 128                             | 50.6 |
|  | Not evaluable            | -                              | -    | 7                               | 2.4  | 6                               | 2.4  |
| Partial response <sup>^</sup>                              | Achieved                 | -                              | -    | 144                             | 49.5 | 146                             | 57.7 |
|  | Not achieved             | -                              | -    | 140                             | 48.1 | 101                             | 39.9 |
|  | Not evaluable            | -                              | -    | 7                               | 2.4  | 6                               | 2.4  |
| Need of a professional caregiver (nurse)                   |                          | 61                             | 19.8 | 48                              | 16.5 | 31                              | 12.3 |
| Number of general practitioners + other specialists visits | Mean ± SD (IQR)          | 3.5±3.6 (1–4) <sup>¶¶</sup>    |      | 1.3±1.6 (0–2) <sup>¶¶¶¶</sup>   |      | 1.6±2.2 (0–2) <sup>¶¶¶¶</sup>   |      |
| Patients with ≥1 current pharmacologic treatment for HS    |                          | 212 <sup>#</sup>               | 68.8 | -                               |      | -                               |      |
| Patients with ≥1 surgical treatment for HS                 |                          | In the last year               |      | In the last 3 months            |      | In the last 6 months            |      |
|  |                          | 57                             | 18.5 | 18                              | 5.8  | 11                              | 3.6  |
| Number of flares   | Mean ± SD (IQR)          | 8.4±9.0 (3–12) <sup>‡‡</sup>   |      | 2.9±5.7 (1–3) <sup>§§</sup>     |      | 3.2±5.6 (1–3) <sup>§§§§</sup>   |      |
| Number of medications/dressing                             | Mean ± SD (IQR)          | 18.6±38.2 (1–12) <sup>¶¶</sup> |      | 12.2±26.8 (0–8) <sup>¶¶¶¶</sup> |      | 15.6±50.2 (0–8) <sup>¶¶¶¶</sup> |      |

IQR: inter quartile range

<sup>+</sup>HiSCR achievement is defined as at least a 50% reduction in the total abscesses and nodules count with no increase in abscess and no increase in draining fistula count relative to visit 1 and was automatically calculated by the System.

<sup>^</sup>Partial response is defined as a reduction of at least 25% of abscesses and nodules count compared with baseline.

\*Clear = 0 abscesses, 0 draining fistulas, 0 inflammatory nodules, 0 non-inflammatory nodules.

<sup>†</sup>Minimal = 0 abscesses, 0 draining fistulas, 0 inflammatory nodules, presence of non-inflammatory nodules.

<sup>‡</sup>Mild = 0 abscesses, 0 draining fistulas, and 1 to 4 inflammatory nodules or 1 abscess or draining fistula and 0 inflammatory nodules.

<sup>§</sup>Moderate = 0 abscesses, 0 draining fistulas, and ≥5 inflammatory nodules or 1 abscess or draining fistula and ≥1 inflammatory nodules or 2 to 5 abscesses or draining fistulas and <10 inflammatory nodules.

<sup>||</sup>Severe = 2 to 5 abscesses or draining fistulas and ≥10 inflammatory nodules.

<sup>¶</sup>Very severe = ≥5 abscesses or draining fistulas.

#Patients could report >1 treatment: 22.9% reported anti-acne preparations, 20.7% reported antibacterials for systemic use, 16.4% reported immunosuppressants, and 12.9% reported antimycobacterials.

##Flares occurred in the 12 months before study start.

##Flares occurred in the previous 3 months.

###Flares occurred in the previous 6 months.

## Summarized considering the 6 months before the study start. Reported by 297 out of the 308 patients.

## Summarized considering the previous 3 months. Reported by the 291 patients who performed Visit 3.

## Summarized considering the previous 6 months. Reported by the 247 out of 253 patients who performed Visit 4.

HiSCR, hidradenitis suppurativa clinical response; HS, hidradenitis suppurativa; PGA, physician global assessment SD, standard deviation.



**Table 3.** The Relationship between HIDRADisk items and total score and Hurley stage/gender at baseline

|                      | <b>HIDRADisk Item Score</b><br>Mean $\pm$ SD (range: 0-10) |                  |                         |               |               |               |                  |               |                |               | <b>HIDRADisk Total Score</b><br>Mean $\pm$ SD<br>(range) |
|----------------------|--|------------------|-------------------------|---------------|---------------|---------------|------------------|---------------|----------------|---------------|--|
|                      | Skin   | Symptoms Control | Uneasiness/ Personality | Sexuality     | Social life   | Work          | Daily activities | Odour         | General Health | Pain          |  |
| <b>Hurley Stage</b>  |  |                  |                         |               |               |               |                  |               |                |               |  |
| Hurley I<br>n=90     | 6.5 $\pm$ 2.8  | 7.3 $\pm$ 2.8    | 5.7 $\pm$ 3.5           | 4.6 $\pm$ 3.7 | 3.5 $\pm$ 3.3 | 3.7 $\pm$ 3.6 | 5.1 $\pm$ 3.4    | 4.6 $\pm$ 3.7 | 5.3 $\pm$ 3.2  | 7.0 $\pm$ 3.1 | 53.3 $\pm$ 24.5 (0-98)                                   |
| Hurley II<br>n=134   | 7.9 $\pm$ 2.2  | 8.2 $\pm$ 2.1    | 7.1 $\pm$ 3.2           | 6.0 $\pm$ 3.7 | 4.6 $\pm$ 3.5 | 5.8 $\pm$ 3.5 | 6.2 $\pm$ 3.1    | 6.8 $\pm$ 3.3 | 6.5 $\pm$ 2.8  | 8.0 $\pm$ 2.3 | 67.1 $\pm$ 20.4 (0-100)                                  |
| Hurley III<br>n=81   | 8.8 $\pm$ 1.8  | 8.6 $\pm$ 2.1    | 8.2 $\pm$ 2.5           | 7.8 $\pm$ 3.0 | 5.6 $\pm$ 3.6 | 6.8 $\pm$ 3.4 | 7.4 $\pm$ 3.0    | 8.0 $\pm$ 2.6 | 7.6 $\pm$ 2.9  | 8.4 $\pm$ 2.3 | 77.1 $\pm$ 20.3 (27-100)                                 |
| <b>Gender</b>        |  |                  |                         |               |               |               |                  |               |                |               |  |
| Male                 | 7.5 $\pm$ 2.5  | 7.9 $\pm$ 2.4    | 6.7 $\pm$ 3.2           | 5.4 $\pm$ 3.7 | 4.1 $\pm$ 3.4 | 5.4 $\pm$ 3.7 | 6.1 $\pm$ 3.3    | 6.2 $\pm$ 3.4 | 6.3 $\pm$ 3.1  | 7.4 $\pm$ 2.8 | 63.0 $\pm$ 22.3 (0-100)                                  |
| Female               | 7.9 $\pm$ 2.4  | 8.1 $\pm$ 2.4    | 7.2 $\pm$ 3.3           | 6.6 $\pm$ 3.6 | 4.9 $\pm$ 3.6 | 5.5 $\pm$ 3.7 | 6.3 $\pm$ 3.3    | 6.7 $\pm$ 3.5 | 6.6 $\pm$ 3.1  | 8.1 $\pm$ 2.4 | 67.8 $\pm$ 23.9 (0-100)                                  |
| P value <sup>#</sup> | 0.062*   | 0.492            | 0.054                   | 0.003*        | 0.048*        | 0.982         | 0.627            | 0.121         | 0.231          | 0.022         | 0.019*   |

<sup>#</sup> Mann-Whitney test between gender

\* Statistically significant P value

**Table 4.** QoL and WPAI-GH Questionnaires total scores at baseline and end of study

| Questionnaire Total Score<br>Mean ± SD (range) |                           | Baseline Visit<br>n=308 | 3-month Visit<br>n=285 | 9month Visit<br>n=253 |
|--|---------------------------|-------------------------|------------------------|-----------------------|
| HIDRADisk total score                          |                           | 65.7±23.3 (1–100)       | 60.1±24.4 (1–100)      | 53.1±26.5 (0–100)     |
| DLQI total score                               |                           | 10.8±8.1 (0–30)         | 9.2±7.0 (0–30)         | 8.6±6.9 (0–29)        |
| Skindex-16 total score                         |                           | 60.3±26.9 (0–100)       | 51.1±27.9 (0–100)      | 46.2±27.1 (0–100)     |
| WPAI-GH  | Overall work impairment   | 36.0±33.7 (0–100)       | 32.3±30.4 (0–100)      | 28.4±28.8 (0–100)     |
|  | Total Activity impairment | 42.3±33.2 (0–100)       | 39.1±30.4 (0–100)      | 34.5±28.0 (0–100)     |

DLQI, Dermatology Life Quality Index; SD, standard deviation; WPAI-GH, Work Productivity and Activity Impairment–General Impairment.

**Table 5.** Correlation between QoL scores and working activity impairment

| Correlation between working activity impairment and |             | Baseline<br>N=308           |                | 3 months<br>N=291           |                | 9 months<br>N=253           |                |
|---|-------------|-----------------------------|----------------|-----------------------------|----------------|-----------------------------|----------------|
|   |             | <b>Spearman correlation</b> | <b>P value</b> | <b>Spearman correlation</b> | <b>P value</b> | <b>Spearman correlation</b> | <b>P value</b> |
| Total HIDRADisk score                               |             | 0.6048                      | <.0001         | 0.6505                      | <.0001         | 0.6682                      | <.0001         |
| DLQI total score                                    |             | 0.7494                      | <.0001         | 0.7313                      | <.0001         | 0.7604                      | <.0001         |
| Skindex-16  | Total Score | 0.7051                      | <.0001         | 0.6883                      | <.0001         | 0.7782                      | <.0001         |
|   | Symptoms    | 0.5975                      | <.0001         | 0.6658                      | <.0001         | 0.7388                      | <.0001         |
|   | Emotions    | 0.5883                      | <.0001         | 0.5634                      | <.0001         | 0.6877                      | <.0001         |
|   | Functioning | 0.6976                      | <.0001         | 0.6901                      | <.0001         | 0.7736                      | <.0001         |

DLQI, Dermatology Life Quality Index.

Fig. 1. Flow chart of Materials and Methods. A multicenter, prospective, epidemiologic cohort study in adult Italian patients with HS

## A multicenter, prospective, epidemiologic cohort study on adult patient with HS enrolled between July 2016 and March 2017 (N =308)



- Inclusion of all adult ( $\geq 18$  years) patients diagnosed with HS ( $\geq 6$  months and of any grade) before study entry and able to understand and complete study-related questionnaires
- Exclusion of patients with current malignancies or any other relevant diseases that could significantly affect QoL, have relevant psychiatric comorbidities, and current participation in any HS clinical trial

**V1 – Baseline**

**N=308**

**V2 – 3 months**

after Baseline  
**(N=291)**

**V3 – 9 months**

after Baseline  
**(N=253)**

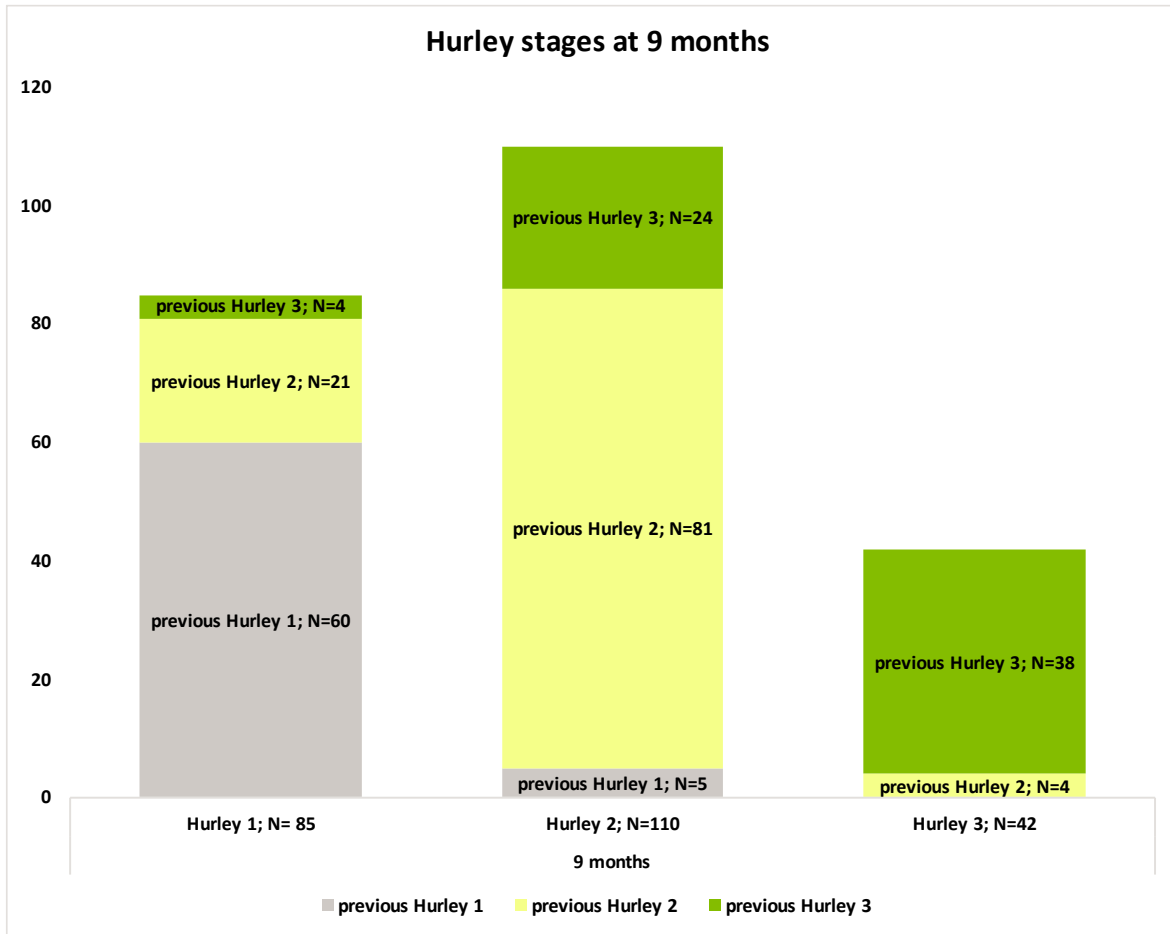


Visit date, Inclusion/exclusion criteria, Demographics, Lifestyle Habits, HS management, vital signs, Hidradenitis Suppurativa history, previous surgical treatments for HS, current HS severity scores, current location of HS lesions, previous pharmacological treatments for HS, questionnaires\*

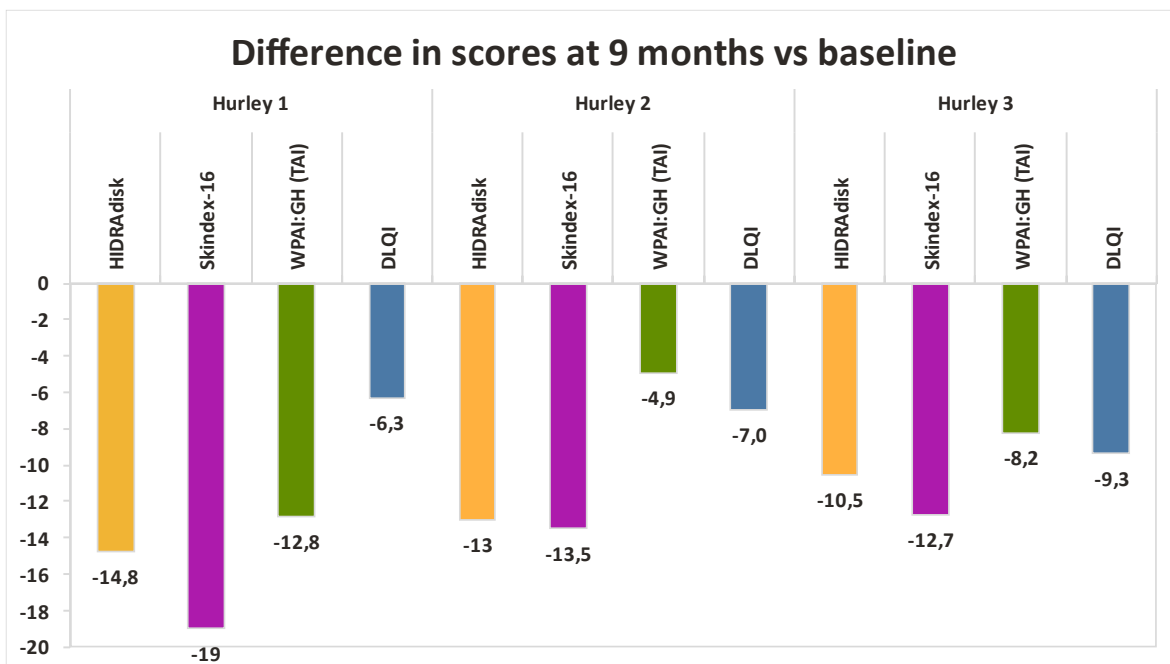
Visit date, HS management, vital signs, surgical treatments for HS, current HS severity scores, current location of HS lesions, questionnaires\*

\* HIDRADisk, Skindex-16, WPAI:GH, DLQI, Subject Satisfaction Questionnaire

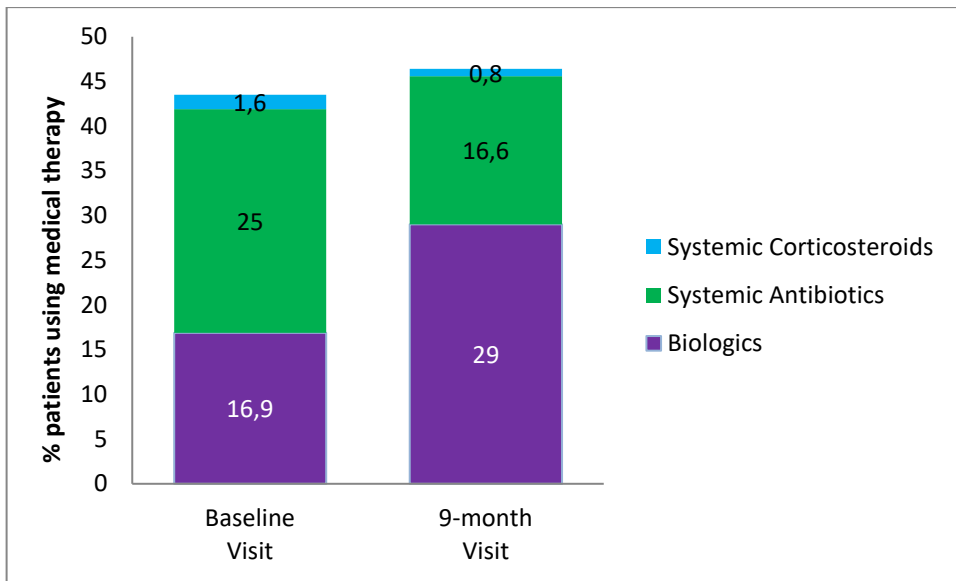
**Fig. 2. (a)** Hurley stage change at 9 months with respect to baseline



**(b)** Change in PROs scores at 9 months vs baseline stratified by Hurley score



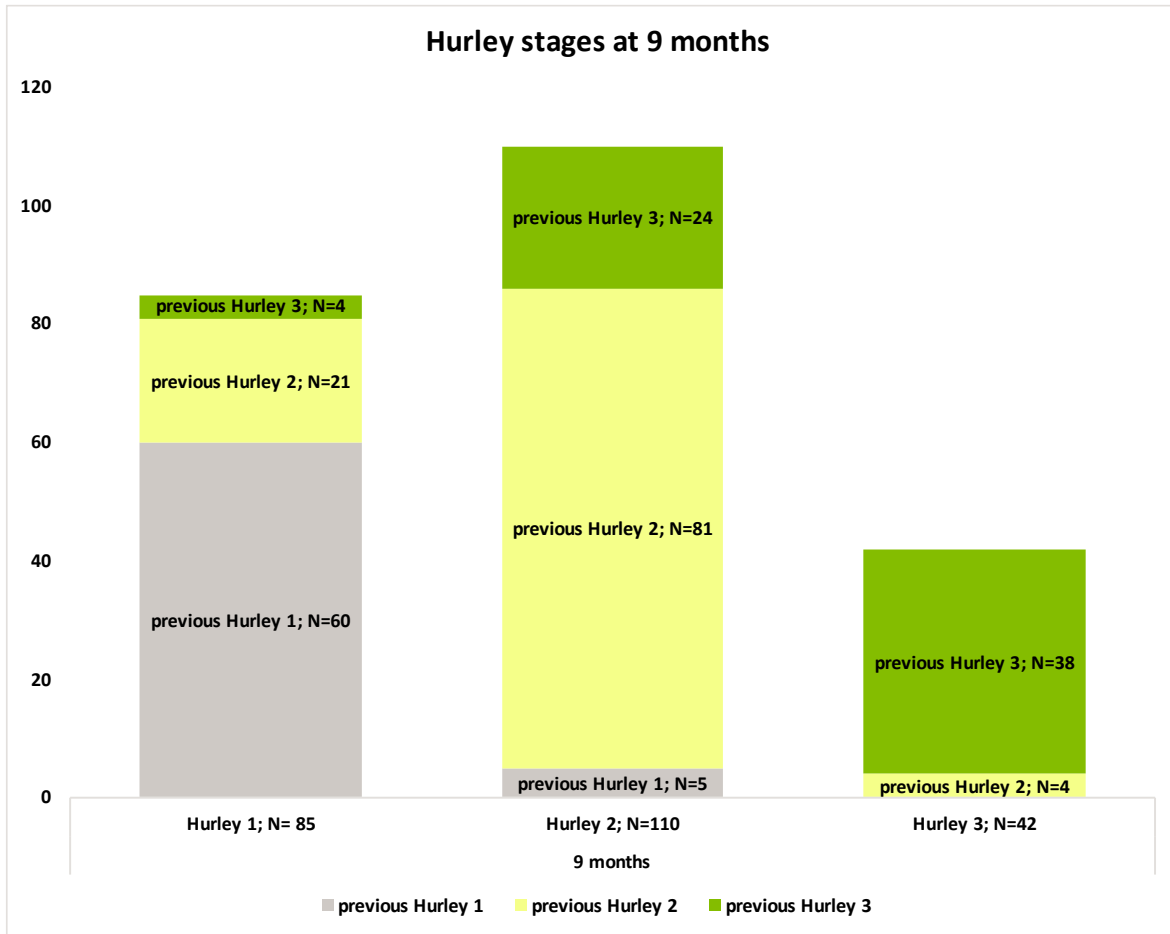
**Fig. 3.** Medical therapy through the study



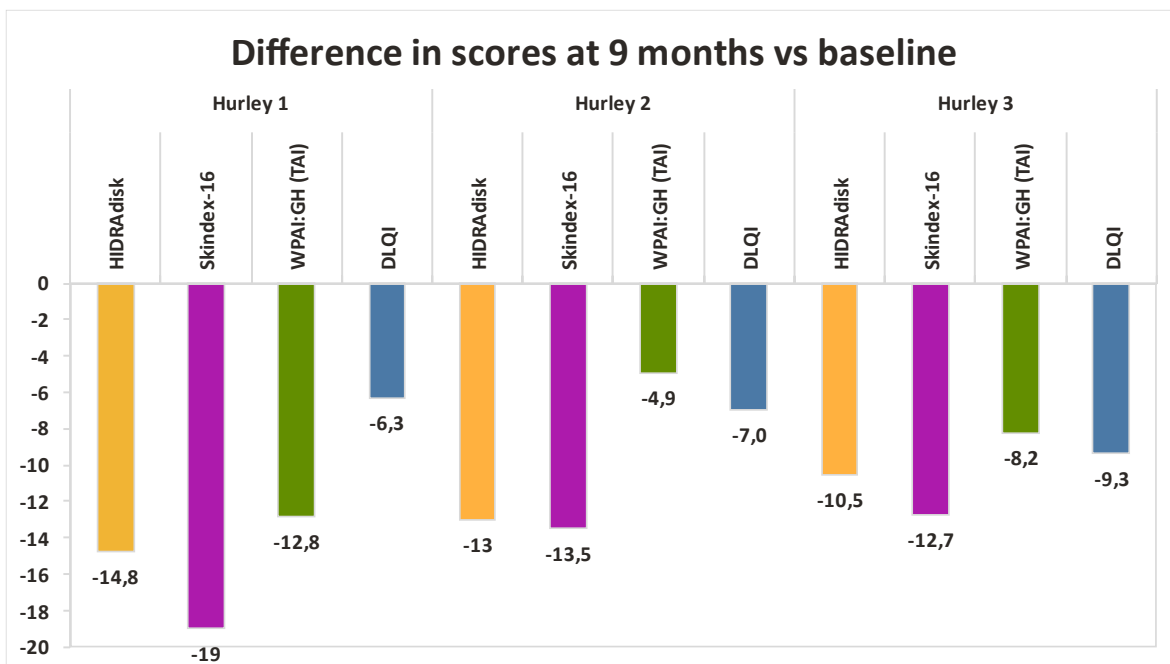
At baseline 52 patients were treated with biologics, 77 with systemic antibiotics and 5 with systemic corticosteroids (out of 308 patients)

At end of study 73 patients were treated with biologics, 51 with systemic antibiotics and 2 with systemic corticosteroids (out of 253 patients)

**Fig. 2. (a)** Hurley stage change at 9 months with respect to baseline



**(b)** Change in PROs scores at 9 months vs baseline stratified by Hurley score



**Table 2.** HS characteristics and management through the study

| Parameters   |                          | Baseline                       |      | 3 months                       |      | 9 months                        |      |
|--|--------------------------|--------------------------------|------|--------------------------------|------|---------------------------------|------|
|  |                          | <i>n</i> = 308                 |      | <i>n</i> = 291                 |      | <i>n</i> = 253                  |      |
|  |                          | N                              | %    | N                              | %    | N                               | %    |
| Hurley stage   | 1                        | 90                             | 29.5 | 102                            | 36.6 | 86                              | 36.1 |
|  | 2                        | 134                            | 43.9 | 117                            | 41.9 | 110                             | 46.2 |
|  | 3                        | 81                             | 26.6 | 60                             | 21.5 | 42                              | 17.7 |
|  | Missing                  | 3                              | -    | 12                             | -    | 15                              | -    |
| Number of inflammatory nodules                             | Mean ± SD (range)        | 5.2±6.0 (0–50)                 |      | 3.4±4.0 (0–30)                 |      | 2.8±4.0 (0–28)                  |      |
| Number of abscesses  | Mean ± SD (range)        | 1.7±2.8 (0–30)                 |      | 1.3±2.4 (0–25)                 |      | 1.0±2.0 (0–21)                  |      |
| Number of fistulas   | Mean ± SD (range)        | 1.6±3.4 (0–40)                 |      | 1.3±2.9 (0–30)                 |      | 1.1±2.7 (0–340)                 |      |
| HS-PGA   | Clear*                   | 7                              | 2.3  | 17                             | 5.8  | 24                              | 9.5  |
|  | Minimal <sup>†</sup>     | 5                              | 1.6  | 14                             | 4.8  | 20                              | 7.9  |
|  | Mild <sup>‡</sup>        | 72                             | 23.4 | 90                             | 30.9 | 86                              | 34.0 |
|  | Moderate <sup>§</sup>    | 176                            | 57.1 | 141                            | 48.5 | 102                             | 40.3 |
|  | Severe <sup>  </sup>     | 21                             | 6.8  | 10                             | 3.4  | 8                               | 3.2  |
|  | Very severe <sup>¶</sup> | 27                             | 8.8  | 19                             | 6.5  | 13                              | 5.1  |
| HiSCR achievement <sup>+</sup>                             | Achieved                 | -                              | -    | 98                             | 33.7 | 119                             | 47.0 |
|  | Not achieved             | -                              | -    | 186                            | 63.9 | 128                             | 50.6 |
|  | Not evaluable            | -                              | -    | 7                              | 2.4  | 6                               | 2.4  |
| Partial response <sup>^</sup>                              | Achieved                 | -                              | -    | 144                            | 49.5 | 146                             | 57.7 |
|  | Not achieved             | -                              | -    | 140                            | 48.1 | 101                             | 39.9 |
|  | Not evaluable            | -                              | -    | 7                              | 2.4  | 6                               | 2.4  |
| Need of a professional caregiver (nurse)                   |                          | 61                             | 19.8 | 48                             | 16.5 | 31                              | 12.3 |
| Number of general practitioners + other specialists visits | Mean ± SD (IQR)          | 3.5±3.6 (1–4) <sup>¶¶</sup>    |      | 1.3±1.6 (0–2) <sup>¶¶¶¶</sup>  |      | 1.6±2.2 (0–2) <sup>¶¶¶¶</sup>   |      |
| Patients with ≥1 current pharmacologic treatment for HS    |                          | 212 <sup>#</sup>               | 68.8 | -                              |      | -                               |      |
| Patients with ≥1 surgical treatment for HS                 |                          | In the last year               |      | In the last 3 months           |      | In the last 6 months            |      |
|  |                          | 57                             | 18.5 | 18                             | 5.8  | 11                              | 3.6  |
| Number of flares   | Mean ± SD (IQR)          | 8.4±9.0 (3–12) <sup>‡‡</sup>   |      | 2.9±5.7 (1–3) <sup>§§</sup>    |      | 3.2±5.6 (1–3) <sup>§§§§</sup>   |      |
| Number of medications/ <u>dressing</u>                     | Mean ± SD (IQR)          | 18.6±38.2 (1–12) <sup>¶¶</sup> |      | 12.2±26.8 (0–8) <sup>¶¶¶</sup> |      | 15.6±50.2 (0–8) <sup>¶¶¶¶</sup> |      |

IQR: inter quartile range

<sup>+</sup>HiSCR achievement is defined as at least a 50% reduction in the total abscesses and nodules count with no increase in abscess and no increase in draining fistula count relative to visit 1 and was automatically calculated by the System.

<sup>^</sup>Partial response is defined as a reduction of at least 25% of abscesses and nodules count compared with baseline.

\*Clear = 0 abscesses, 0 draining fistulas, 0 inflammatory nodules, 0 non-inflammatory nodules.

<sup>†</sup>Minimal = 0 abscesses, 0 draining fistulas, 0 inflammatory nodules, presence of non-inflammatory nodules.

<sup>‡</sup>Mild = 0 abscesses, 0 draining fistulas, and 1 to 4 inflammatory nodules or 1 abscess or draining fistula and 0 inflammatory nodules.

<sup>§</sup>Moderate = 0 abscesses, 0 draining fistulas, and ≥5 inflammatory nodules or 1 abscess or draining fistula and ≥1 inflammatory nodules or 2 to 5 abscesses or draining fistulas and <10 inflammatory nodules.

<sup>||</sup>Severe = 2 to 5 abscesses or draining fistulas and ≥10 inflammatory nodules.

<sup>¶</sup>Very severe = ≥5 abscesses or draining fistulas.



#Patients could report >1 treatment: 22.9% reported anti-acne preparations, 20.7% reported antibacterials for systemic use, 16.4% reported immunosuppressants, and 12.9% reported antimycobacterials.

##Flares occurred in the 12 months before study start.

##Flares occurred in the previous 3 months.

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## Summarized considering the 6 months before the study start. Reported by 297 out of the 308 patients.

## Summarized considering the previous 3 months. Reported by the 291 patients who performed Visit 3.

## Summarized considering the previous 6 months. Reported by the 247 out of 253 patients who performed Visit 4.

HiSCR, hidradenitis suppurativa clinical response; HS, hidradenitis suppurativa; PGA, physician global assessment SD, standard deviation.

**Table 3.** The Relationship between HIDRADisk items and total score and Hurley stage/gender at baseline

|                      | HIDRADisk Item Score<br>Mean ± SD (range: 0-10) |                     |                            |           |                |         |                     |         |                   |         | HIDRADisk<br>Total Score<br>Mean ± SD<br>(range) |
|----------------------|---|---------------------|----------------------------|-----------|----------------|---------|---------------------|---------|-------------------|---------|--|
|                      | Skin  | Symptoms<br>Control | Uneasiness/<br>Personality | Sexuality | Social<br>life | Work    | Daily<br>activities | Odour   | General<br>Health | Pain    |  |
| <u>Hurley Stage</u>  |   |                     |                            |           |                |         |                     |         |                   |         |  |
| Hurley I<br>n=90     | 6.5±2.8   | 7.3±2.8             | 5.7±3.5                    | 4.6±3.7   | 3.5±3.3        | 3.7±3.6 | 5.1±3.4             | 4.6±3.7 | 5.3±3.2           | 7.0±3.1 | 53.3±24.5 (0-98)                                 |
| Hurley II<br>n=134   | 7.9±2.2   | 8.2±2.1             | 7.1±3.2                    | 6.0±3.7   | 4.6±3.5        | 5.8±3.5 | 6.2±3.1             | 6.8±3.3 | 6.5±2.8           | 8.0±2.3 | 67.1±20.4 (0-100)                                |
| Hurley III<br>n=81   | 8.8±1.8   | 8.6±2.1             | 8.2±2.5                    | 7.8±3.0   | 5.6±3.6        | 6.8±3.4 | 7.4±3.0             | 8.0±2.6 | 7.6±2.9           | 8.4±2.3 | 77.1±20.3 (27-100)                               |
| <u>Gender</u>        |   |                     |                            |           |                |         |                     |         |                   |         |  |
| Male                 | 7.5±2.5   | 7.9±2.4             | 6.7±3.2                    | 5.4±3.7   | 4.1±3.4        | 5.4±3.7 | 6.1±3.3             | 6.2±3.4 | 6.3±3.1           | 7.4±2.8 | 63.0±22.3 (0-100)                                |
| Female               | 7.9±2.4   | 8.1±2.4             | 7.2±3.3                    | 6.6±3.6   | 4.9±3.6        | 5.5±3.7 | 6.3±3.3             | 6.7±3.5 | 6.6±3.1           | 8.1±2.4 | 67.8±23.9 (0-100)                                |
| P value <sup>‡</sup> | 0.062*  | 0.492               | 0.054                      | 0.003*    | 0.048*         | 0.982   | 0.627               | 0.121   | 0.231             | 0.022   | 0.019*   |

<sup>‡</sup> Mann-Whitney test between gender

\* Statistically significant P value

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Manuscript DRM-2020-9-4: Resubmission

Dear Editorial Board,

We are now resubmitting our manuscript (DRM-2020-9-4) which was improved addressing all the comments received by the reviewers.

We hope the manuscript in its present form will be considered acceptable for publication in "Dermatology".

Best regards

Dott Luca Stingeni

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Responses to reviewers:

Editor-in-Chief comments:

Reviewer no 2 is an experienced 'HS-ologist' and reviewer. So, a stronger and clearer structure in your otherwise very interesting paper is advisable.

**Response:** *We thank the Editor in Chief for giving us this opportunity. We have now restructured the manuscript and provided a more straightforward interpretation of the results. We hope to have addressed all the concerns.*

Reviewer 1 report:

Very nice works - the authors present a broad study of a large cohort of patients with HS and with a broad number of patient-reported instruments and clinical outcomes.

**Response:** *We thank the reviewer for the positive comment*

Reviewer 2 report:

DRM-2020-9-4

Hidradenitis suppurativa in a large cohort of Italian patients: management and burden of disease (HIDRAdisk study) by Fabbrocini et al.

The purpose of the study is to address HS disease burden in 308 Italian patient group over a 9-month period. Overall, it show that the patients with a severe disease have a lower QoL. It show a decrease over time during different medical treatments

After reading the paper I still haven't understood if the authors want to show that the HIDRAdisk questionnaire is useful (fig 3), the impact of HS on the QoL during treatment (unspecified treatment and unspecified HS severity, fig. 2), or the change of medical treatment in a cohort over time (fig. 4).

**Response:** We thank Reviewer 2 for the detailed comment that gave us the possibility to improve our work. We have better clarified all the points he/she raised, redefining the title, and reshaping the paper. The new title reads “Hidradenitis suppurativa in a large cohort of Italian patients: evaluation of the burden of disease”, which we feel is addressing more precisely the content of the manuscript. In detail, the aim of the manuscript is to describe the burden of the disease on patient well-being and working activities in a large cohort of Italian patients, managed in real world clinical practice.

We have therefore thoroughly reviewed the paper to better clarify all the results. We have substituted the previous Figure 2 with a more detailed and dynamic figure showing in panel (a) the Hurley stage change at 9 months with respect to baseline and in panel (b) the Change in PROs scores at 9 months vs baseline stratified by Hurley score. The new figure should better describe the change in clinical condition and relate it to the change in burden of disease, as captured by the different PROs used in the study.

We have also added in Table 3 the Relationship between HIDRADisk items and total score and gender in order to address the different disease burden perceived by women, as also described in the text.

We feel these changes have now strengthened our work and we hope this would be considered acceptable for publication