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A centre-based ambulatory care concept for hidradenitis suppurativa improves disease activity, disease burden and patient satisfaction: results from the randomized controlled EsmAiL trial

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Abstract

Background Hidradenitis suppurativa (HS) is an inflammatory disease of the inverse skin regions that occurs in young women, in particular, and affects approximately 1% of the population. Outpatient care is often inadequate and usually cannot prevent progression.

Objectives To evaluate in the EsmAiL ('Evaluation eines strukturierten und leitlinienbasierten multmodalen Versorgungskonzepts für Menschen mit Akne inversa') trial whether an innovative care concept can decrease disease activity and burden, and improve patient satisfaction.

Methods EsmAiL was conducted as a two-arm, multicentre, prospective, randomized controlled trial that included 553 adults with HS. Inclusion criteria were a minimum of three inflammatory lesions and at least a moderate impact of the disease on quality of life. The control group (CG) remained under standard care, while patients in the intervention group (IG) were treated according to a trial-specific, multimodal concept. The primary endpoint was the absolute change in International Hidradenitis Suppurativa Severity Score System (IHS4).

Results In total, 274 patients were randomized to the IG and 279 to the CG. Altogether, 377 attended the final assessment after 12 months of intervention. Participants in the IG ($n=203$) achieved a mean improvement in IHS4 of 9.3 points, while the average decrease in IHS4 in patients in the CG ($n=174$) was 5.7 points ($P=0.003$). Patients treated under the new care concept also reported a statistically significantly higher decrease in pain, Dermatology Life Quality Index and Hospital Anxiety and Depression Scale scores compared with those in the CG ($P<0.001$). Patient satisfaction was also statistically significantly higher in the IG compared with the CG ($P<0.001$).

Conclusions The establishment of standardized treatment algorithms in so-called 'acne inversa centres' in the ambulatory setting has a substantial, positive impact on the course of HS and significantly improves patient satisfaction.

What is already known about this topic?

- Hidradenitis suppurativa (HS) is a debilitating, complex disease.
- The current structure of outpatient care for patients with HS is inadequate.
- Access to HS specialists is limited, and although therapeutic options exist, they do not always fit patients' needs.

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What does this study add?

- There is a need to improve outpatient care for patients with HS.
- A structured, interdisciplinary treatment provided in the EsmAiL trial significantly improved patient satisfaction.

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition with a considerable disease burden.[1] The current structure of HS care in Germany is associated with several challenges that lead to substantial dissatisfaction and suffering among affected individuals.[2]

On average, a diagnosis of HS takes 7 years,[3] mainly because the few HS experts available are primarily located in specialized clinics, to which patients often have limited access. Owing to an insufficient ambulatory care network, the central point of contact is most often the emergency department or general practitioner, who is usually unfamiliar with the condition.[4]

First-line medical treatments include topical and oral antibiotics.[5,6] For moderate-to-severe disease, continuous treatment with adalimumab is indicated after failed systemic antibiotic therapy.[6] Even when treated based on current guidelines, roughly half of patients are dissatisfied with the current treatment modalities.[2]

In the EsmAiL trial ('Evaluation eines strukturierten und leitlinienbasierten multmodalen Versorgungskonzepts für Menschen mit Akne inversa') outpatient offices and clinics of various speciality in Germany were qualified as 'acne inversa centres' (AiZs), where patients were treated according to a structured, interdisciplinary treatment plan, based on current European guidelines and innovative findings. AiZs served as key points of care, optimizing and organizing treatment, as well as educating patients on reducing risk factors and empowering them to manage their chronic disease.

The EsmAiL trial investigated whether 12 months of care in an AiZ is better than 12 months under standard care in patients with HS.

Materials and methods

Trial design

EsmAiL was designed as a multicentre randomized controlled trial (RCT) with blinded assessment.

For the blinded assessment, so-called 'screeners' were recruited from a pool of doctors of several specialties and trained in the use of the intended HS classifications and survey instruments. Their task was to inform patients about the study and evaluate clinical endpoints at the beginning and end of the intervention period. The 1 : 1 randomization (block randomization with permuted blocks and variable block length) was carried out with a tool programmed into the project-specific electronic study manager, blinded at screener level and stratified with respect to Hurley stage and AiZ. To participate, interested patients had to register with the study team and were then given an appointment with one of the 15 trained screeners.

No changes to endpoints or data collection methods were made during the trial.

Interventions

Patients in the control group (CG) remained under standard outpatient care with no restrictions on patients' choice of available treatments. The treatment of patients in the intervention group (IG) was designed according to a step-by-step algorithm proposed by Gulliver *et al*.,[6] based on the European guidelines for HS treatment (Figure S1; see Supporting Information). As IAight® therapy (Lenicura, Wiesbaden, Germany) is an approved physical therapy option for HS, the treatment algorithm was modified for this treatment and enhanced by a particularly strong focus on patient education, improved pain management and lesion care. Other crucial aspects of AiZ care included the standardized qualification of the therapeutic teams, the establishment of a coordinated therapy plan and the evaluation of treatment results based on defined success indicators. The study was supported by an electronic patient file, to record longitudinal disease development.

In Germany, HS patient education, HS lesion care and IAight therapy are not reimbursed under regular care. In this study, innovation grants from health insurance companies paid for these treatments in patients in the IG. Patients in the CG could only receive IAight therapy at their own expense, which was a considerable hurdle to overcome.

Participants, data collection and endpoints

Patients were eligible to participate in the study if they were diagnosed with HS of any Hurley stage,[7] were aged $\geq$ 18 years, were able to understand the patient information and follow the study procedure, and provided written informed consent. Moreover, participants had to have at least three inflammatory lesions at the time of inclusion and the disease had to have at least a moderate impact on the patients' quality of life, as measured by a Dermatology Life Quality Index (DLQI) score of >5.[8] Participation was voluntary and patients could withdraw from the study at any time.

To evaluate the primary endpoint, a clinical examination to assess disease severity was performed at baseline (t_0) and at the end of the study (t_4) by the screener. To prevent selection bias, screeners were blinded to inclusion criteria on the number of lesions and the DLQI score. To record patient-reported outcomes and demographic data, the corresponding questionnaires were handed to the patients by the screener immediately after they signed the consent form. Immediately following randomization, participants received another digital questionnaire with additional questions regarding their disease history, professional and personal situation, and the randomization result.

Validated instruments and variables were chosen based on the current literature. For categorization over the course of the disease, the Hurley staging system was used.[9]

The International Hidradenitis Suppurativa Severity Score System (IHS4; primary endpoint)[10] and pain level according to a numerical rating scale (NRS pain)[11] were used to record disease activity. To measure disease burden, DLQI[8] and Hospital Anxiety and Depression Scale (HADS) scores[12] and number of sick days at work were recorded. Socioeconomic variables considered were marital status, educational level and occupational status. Body mass index (BMI) and smoking status (including cigarettes smoked daily) served as risk factors. Patients were also asked about the treatments they had received in the 12 months prior to the study and during the intervention, as well as their satisfaction with the form of care received (details on endpoints and definition of response are provided in Table S1; see Supporting Information). Patients were asked to complete additional questionnaires every 3 months during the trial (t_0, t_1, t_2, t_3 and t_4).

Statistical analysis

Sample size calculation was based on an effect size of 0.25 (based on difference in mean IHS4 between patients in the IG and those in the CG). A power assumption of 80% and a significance level of 5% led to a required sample size of 247 patients per group. A buffer of 20% for dropouts led to a requirement of 592 patients; in total, 553 (93.4%) were recruited. Statistical analysis was carried out by the Martin Luther University Halle-Wittenberg, Germany, as an independent institution. To analyse the baseline characteristics, metric scaled variables were presented as mean (SD). Categorical variables were depicted by absolute/relative frequencies. Differences between study groups at baseline were tested using a χ^2-test or *t*-test, depending on whether they were based on categorical or metric values. The primary endpoint, as well as all continuous secondary endpoints, were analysed by linear regression. Differences between study groups were tested using *t*-tests for the corresponding regression coefficients. The secondary endpoint 'change in work status' was analysed in a logistic model. The difference between study groups was tested using a Wald test for the corresponding regression coefficient. All regressions were adjusted for group assignment, Hurley stage, time of assessment, baseline value of the endpoint and study centre. To analyse treatment satisfaction, which was solely recorded at t_4, the baseline value was not included as a random effect in the model. Differences in categorical endpoints between groups [e.g. 55% reduction in IHS4 (IHS4-55) and HiSCR; Table S1] were tested with a χ^2-test.

The analysis was carried out in the modified intention-to-treat population. Patients were included in the main statistical analysis if the second and final screener assessment at t_4 was available. To approximate full-sample analysis on all randomized patients, a multiple imputation by chained equations ($m=10$)[13] was applied for response after 1 year, using fully conditional specifications.[14] Hurley stage, study centre, respective endpoints in patient questionnaires for t_0, t_1, t_2, t_3 and t_4, as well as during AiZ assessments, were auxiliary variables.

The two-sided significance level was set at 5%. All analyses were performed with r, version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population

Patients were recruited throughout Germany from 29 September 2020 to 31 July 2021 by 15 trained screeners and allocated to either the CG ($n=279$) or the IG ($n=274$). Patients randomized to the CG received standard care, whereas patients in the IG were treated in one of 14 specialized AiZs (Table S2; see Supporting Information). After a 12-month intervention period, patients returned to the screeners for the final blinded assessment. The study ended on 31 July 2022. In total, 726 patients were screened at baseline, 553 of whom met the inclusion criteria; 377 patients (IG, $n=203$; CG, $n=174$) attended the final assessment (Figure 1).

Of the 377 participants evaluated at the end of the study, 46 (12.2%) were classified as having Hurley stage I HS, 236 (62.6%) as having Hurley stage II HS and 95 (25.2%) as having Hurley stage III HS at baseline (Table 1). Overall, patients had high disease activity and burden.

Effect on disease activity, disease burden and patient satisfaction

Statistical analysis showed that the impact of 12 months of care at an AiZ on IHS4, NRS pain, DLQI and HADS was statistically significantly higher compared with standard care (Figure 2, Table 2).

At the end of the intervention period, mean IHS4 score decreased by 9.3 points (50.2%) in the IG and by 5.7 points (30.9%) in the CG ($P=0.003$). The difference was also reflected in responder values for IHS4-55 [56.2% (IG) vs. 42.5% (CG); $P=0.011$], and in Hidradenitis Suppurativa Clinical Response (HiSCR) achievers [53.7% (IG) vs. 37.4% (CG); $P=0.002$]. Patients in the IG also reported a statistically significantly ($P<0.001$) higher decrease in pain (2.6 points, 38.2%) compared with those in the CG (1.5 points, 21.9%), which was also reflected in the proportion of pain responders [62.8% (IG) vs. 40.7% (CG); $P<0.001$].

The superiority of the effect of care in an AiZ over standard care was confirmed by the results of the patient-reported outcomes on disease burden. Mean DLQI decreased by 7.0 points (39.6%) in the IG and by 3.8 points (22.0%) in the CG ($P<0.001$). The proportion of patients reaching the minimal clinically important difference in DLQI score of 4 points was also statistically significantly different between groups [67.0% (IG) vs. 51.2% (CG); $P=0.002$].

With respect to the HADS, patients in the IG achieved a statistically significantly higher reduction in burden compared with those in the CG ($P<0.001$). HADS decreased by 3.7 points (22.3%) in patients in the IG vs. 0.4 points (2.4%) in the CG [HADS-Depression: –1.7 points (–22.7%) in the IG vs. 0.02 points (0.3%) in the CG ($P<0.001$); HADS-Anxiety: –2.0 points (–22.2%) in the IG vs. –0.4 points (–4.3%) in the CG ($P<0.001$)]. At baseline, 122 patients (60.1%) in the IG and 98 patients (56.3%) in the CG had critical values with regard to total HADS score. Of these patients, 44.3% in the IG returned to normal values vs. 26.0% in the CG ($P<0.001$).

Concerning patient satisfaction, participants in the IG reported statistically significantly higher values in all four domains of the adapted Treatment Satisfaction

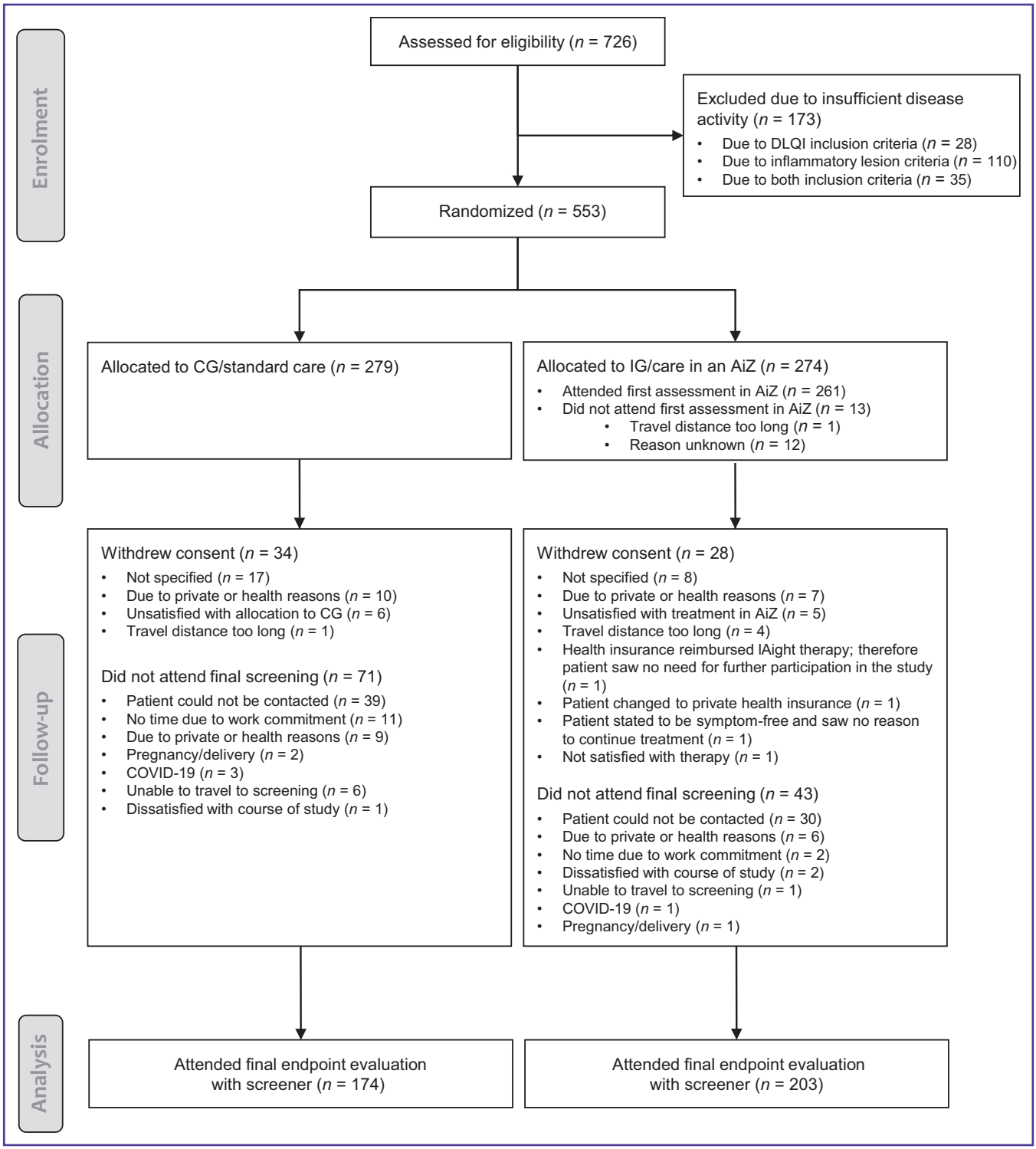

Figure 1 Consort flow diagram of patients recruited throughout Germany from 29 September 2020 to 31 July 2021 by 15 trained screeners and randomized to a control group (CG) that received standard care for hidradenitis suppurativa, or an intervention group (IG) treated at one of 14 specialized acne inversa centres (AiZs) in a study of an innovative care concept in HS (EsmAiL). DLQI, Dermatology Life Quality Index.

Questionnaire for Medication (Table 3): effectiveness [79.6 (IG) vs. 37.5 (CG); $P<0.001$]; side-effects [94.6 (IG) vs. 86.8 (CG); $P<0.001$]; convenience [69.1 (IG) vs. 55.5 (CG); $P<0.001$]; and global satisfaction [85.4 (IG) vs. 38.2 (CG); $P<0.001$].

Regarding overall satisfaction with care structure, the proportion of patients who were very satisfied increased from 0.7% before treatment at an AiZ to 41%, while it remained at about 3% in the CG. Additionally, 35% of patients in the IG reported being 'rather satisfied' vs. 33% in the CG. A

Table 1 Baseline characteristics for 377 patients included in a study of an innovative care concept in hidradenitis suppurativa (EsmAiL)

	Intervention group ($n=203$)	Control group ($n=174$)
Age (years), mean (SD)	39.15 (9.88)	39.9 (11.59)
Sex		
Male	44 (21.7)	33 (19.0)
Female	159 (78.3)	141 (81.0)
Hurley stage		
I	26 (12.8)	20 (11.5)
II	125 (61.6)	111 (63.8)
III	52 (25.6)	43 (24.7)
IHS4, mean (SD)	18.53 (19.39)	18.47 (20.16)
NRS pain, mean (SD)	6.81 (2.17)	6.85 (2.08)
DLQI, mean (SD)	17.68 (6.36)	17.30 (6.62)
HADS, mean (SD)		
Total	16.57 (7.32)	16.93 (8.17)
Anxiety	9.07 (3.87)	9.30 (4.24)
Depression	7.50 (4.20)	7.63 (4.62)
Smoking behaviour		
Nonsmoker	40 (19.7)	34 (19.5)
Former smoker	41 (20.2)	24 (13.8)
Smoker	122 (60.1)	116 (66.7)
Cigarettes smoked daily ($n=226$), mean (SD)	14.01 (7.66)	14.27 (7.10)
BMI (kg m^{-2}), mean (SD)	32.47 (7.40)	31.85 (7.23)
Days unable to work ($n=264$),[a] mean (SD)	13.55 (25.44)	15.41 (33.00)
Work status		
Employed	152 (74.9)	112 (64.4)
Unemployed	51 (25.1)	62 (35.6)

Data are presented as n (%) unless otherwise stated. BMI, body mass index; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; IHS4, International Hidradenitis Suppurativa Severity Score System; NRS, numerical rating scale. aFor 12 months before inclusion in the trial.Data are presented as *n* (%) unless otherwise stated. BMI, body mass index; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; IHS4, International Hidradenitis Suppurativa Severity Score System; NRS, numerical rating scale. [a]For 12 months before inclusion in the trial.

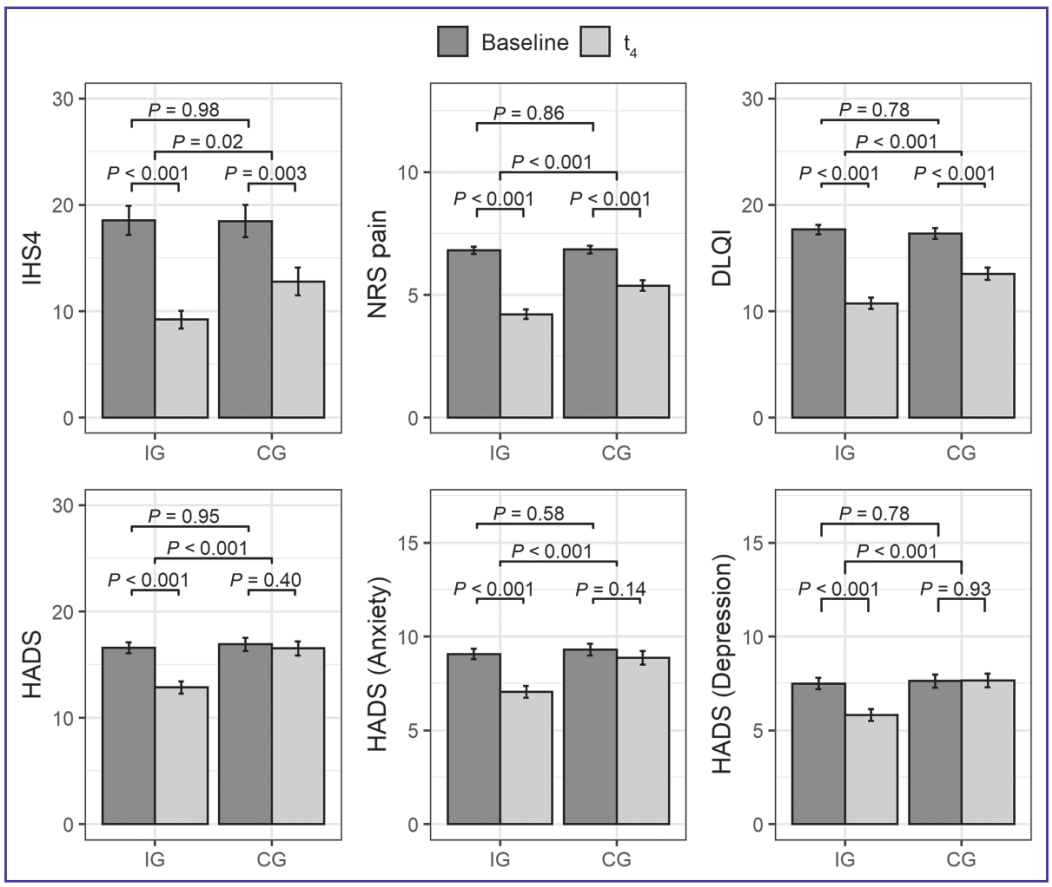

Figure 2 Mean baseline and t_4 (study end) International Hidradenitis Suppurativa Severity Score System (IHS4), numerical rating scale for pain (NRS pain), Dermatology Life Quality Index, total Hospital Anxiety and Depression Scale (HADS-total) and HADS subdomains (Anxiety and Depression) scores for the intervention group (IG) and control group (CG) in a study of an innovative care concept in hidradenitis suppurativa (EsmAiL).

Table 2 Outcomes of 377 patients included in a study of an innovative care concept in hidradenitis suppurativa (EsmAiL) after 1 year

Outcomes	Δ Intervention group (IG) ($n=203$)	Δ Control group (CG) ($n=174$)	β for ΔIG vs. ΔCG[a]
IHS4	–9.30 (–11.42, –7.18)	–5.68 (–8.21, –3.15)	–2.56 (–5.88, –1.25)
NRS pain	–2.60 (–3.01, –2.19)	–1.47 (–1.86, 1.08)	–1.15 (–1.68, –0.63)
DLQI	–6.95 (–7.89, –6.00)	–3.79 (–4.73, –2.84)	–2.97 (–4.34, –1.61)
HADS total	–3.71 (–4.53, –2.89)	–0.40 (–1.34, 0.54)	–3.48 (–4.70, –2.27)
HADS-Anxiety	–2.02 (–2.47, –1.57)	–0.43 (–0.98, 0.12)	–1.69 (–2.39, –1.00)
HADS-Depression	–1.69 (–2.16, –1.22)	0.02 (–0.49, 0.53)	–1.80 (–2.45, –1.14)
BMI (kg m^{-2})	–0.65 (–1.20, –0.10)[b]	–0.01 (–0.87, 0.85)[c]	–0.64 (–1.62, 0.35)
Cigarettes smoked daily	–3.03 (–4.44, –1.62)[d]	–1.75 (–2.94, –0.55)[e]	–1.28 (–3.14, 0.58)
Employed participants	16 (7.9%; 3.5–19.0)	5 (2.9%; –16.9, 11.3)	1.44 (–0.11, 2.98)

Data are presented as mean changes and associated 95% confidence intervals (CIs; without adjustment for further covariates). BMI, body mass index; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; IHS4, International Hidradenitis Suppurativa Severity Score System; NRS, numerical rating scale. [a]Regression coefficients and associated 95% CIs in parentheses refer to the differences between ΔIG – ΔCG ($Mean_{IG}$ vs. $Mean_{CG}$) and were adjusted for Hurley stage, baseline value of the endpoint and study centre; [b]$n=122$; [c]$n=92$; [d]$n=115$; [e]$n=111$.

further 24% of patients in the IG were unsatisfied with the care structure (of whom 5% were very unsatisfied) vs. 64% of patients in the CG (of whom 33% were very unsatisfied) (Figure 3).

The results of the main analysis were found to be robust in the full sample analysis using multiple imputation for missing data (Table S3; see Supporting Information).

Effect on risk factors and work ability

The risk factors of smoking and obesity were relevant in both groups. About 60% of patients were smokers and participants had an average BMI of 32 kg m^{-2} at baseline. In the IG, smokers at t_0 smoked three fewer cigarettes daily than before ($P<0.001$; Table 2), while the reduction was 1.8 cigarettes in the CG ($P=0.004$). However, the difference between groups was not statistically significant ($P=0.18$).

For patients with an initial BMI > 30 kg m^{-2}, 12 months of care in an AiZ led to a statistically significant improvement in BMI of 0.7 kg m^{-2} ($P=0.023$), while patients in the CG did not experience a statistically significant effect [–0.0, $P=0.97$ (Table 2)].

At baseline, the average number of days absent from work due to HS in the 12 months prior to the study was 13.5 in the IG and 15.4 in the CG (Table 1). Moreover, 51 patients (25.1%) in the IG and 62 patients (35.6%) in the CG did not practise any profession. The number of people absent from work decreased by 5 (8.1%) in the CG ($P=0.38$) and by 16 (31.2%) in the IG ($P<0.002$). However, the difference between the IG an CG did not reach statistical significance within a logistic model ($P=0.07$). However, when analysing the change in the two study groups by multiple imputation in the full sample of 553 patients the differences between the IG and CG were also statistically significant for the number of patients employed.

Follow-up on treatment algorithm

The allocation of different treatment modalities in both groups is shown in Figure 4. In line with the treatment algorithm, patients in the IG received IAight therapy significantly more often than patients in the CG (96% vs. 26%; $P<0.001$). Although patients in the IG tended to receive fewer oral antibiotics than those in the CG (32% vs. 42%), as well as fewer biologics (11% vs. 16%), slightly more topical antibiotics were used by patients in the IG (17% vs. 14%). However, the differences were not statistically significant. Regarding surgical interventions, both groups had a similar proportion of patients who received an excision (15% in the IG vs. 14% in the CG), whereas significantly fewer patients in the IG needed an incision (17% vs. 30%; $P=0.007$).

Compliance with the proposed therapy plan at an AiZ, as well as with European guidelines in the CG,[5] was evaluated by a scenario analysis considering different levels of strictness for treatment recommendation (Table S4; see Supporting Information). The percentage of patients in the IG for whom the proposed and trained algorithm was applied correctly ranged from 75.4% to 96.1%. The guideline-recommended treatment was followed by 53.5 to 76.7% of patients in the CG.

Discussion

Current outpatient care for HS is often inadequate, which leads to considerable patient dissatisfaction (Figure 3).

Table 3 Adapted treatment satisfaction questionnaire for medication in a study of an innovative care concept in hidradenitis suppurativa (EsmAiL)

Domain	Intervention group (IG) ($n=203$)	Control group (CG) ($n=174$)	β for IG vs. CG[a]
Effectiveness	79.61 (76.02–83.19)[b]	37.50 (32.10–42.90)[c]	42.07 (35.83–48.32)
Side-effects	94.62 (92.22–97.01)[d]	86.77 (82.65–90.89)[e]	7.92 (3.30–12.54)
Convenience	69.08 (65.79–72.37)[b]	55.47 (50.75–60.19)[f]	13.78 (8.26–19.30)
Global satisfaction	85.39 (82.33–88.46)[b]	38.24 (32.85–43.63)[g]	47.25 (41.35–53.15)

Data are presented as mean (95% confidence interval; CI). [a]Regression coefficients and associated 95% CIs in parentheses refer to the differences between ΔIG – ΔCG ($Mean_{IG}$ vs. $Mean_{CG}$) and were adjusted for Hurley stage, baseline value of the endpoint and study centre; [b]$n=190$; [c]$n=149$; [d]$n=192$; [e]$n=163$; [f]$n=128$; [g]$n=152$.

Access to HS specialists is limited, and although therapeutic options exist, they do not always fit patient needs.[15] Recommendations on patient education and wound care are emphasized by experts, but guidelines for structured implementation are missing.[16]

EsmAiL is the first multicentre RCT with blinded assessment of the real-world care of people with HS, covering a 12-month period. The study population had substantial disease activity and a high disease burden; smoking and obesity were over-represented (Figure 1). The high burden of HS manifested in a low quality of life, a high level of depression and anxiety, and a decreased ability to work. About 70% of patients were employed, which is significantly lower than for the general age- and sex-adjusted German population.

The applied treatment algorithm was based on European guidelines, but included IAight therapy as a noninvasive, physical, first-line treatment option (Figure S1; see Supporting Information).[17–19] Moreover, a strong focus was placed on patient education and structured lesion care (Figure S2; see Supporting Information), as well as on an interdisciplinary approach. An AiZ serves as a central point of care that transfers patients to other disciplines such as psychiatrists and HS clinics, when needed.

Patients treated for 12 months in an AiZ experienced a significantly higher reduction in IHS4, NRS pain, DLQI and HADS scores compared with those under standard care. The results also translated to Hurley stage I–III patient subgroups, which all benefited significantly from the innovative care concept (Table S5; see Supporting Information), showing that the designed severity-dependent treatment plan can be successfully applied to the entire spectrum of HS disease.

HiSCR was achieved by 53.7% of participants of the IG vs. 37.4% in the CG. The results obtained in the IG with regard to moderate and severe disease are comparable to the effectiveness of adalimumab at week 12 in both PIONEER trials,[20] and better than the results obtained after 3 months of oral antibiotics (43% HiSCR-responders; Table S5).[21] There have been no other long-term studies regarding therapy options, except for adalimumab, which achieved a HiSCR of 54% in real-world settings after 1 year of observation.[20,22] However, it must be noted that the proportion of patients lost to follow-up (mainly due to a loss of efficacy) in the adalimumab open-label study was 68%,[20] a significantly larger dropout rate than in the EsmAiL trial (32%).

The primary treatment goal of patients with HS is a reduction in pain.[23] In EsmAiL, approximately 62% of patients in the IG attained a clinically meaningful difference in NRS pain and 67% achieved a meaningful improvement in DLQI. Both of these results were significantly different from those obtained in the CG (41% in NRS pain and 51% in DLQI).

At baseline, 60% of participants of the IG and 56% of those in the CG reported critical values in the HADS (Table 4). After 1 year of treatment at an AiZ, the proportion of patients in the IG with critical scores was reduced by 33%, whereas it remained constant in the CG. Disease-related factors such as pain can strongly influence HADS scores.[24] Therefore, better disease control leads to a reduction in disease-specific secondary disorders such as anxiety and depression. Other studies emphasize that, next to the allocation to effective therapies, patient education, as well as a positive and stable relationship with the therapist, plays a crucial role. A trusted, regular consultation leads to better treatment adherence and thus better control of disease symptoms.[12] This is also reflected in the fact that a significantly lower number of

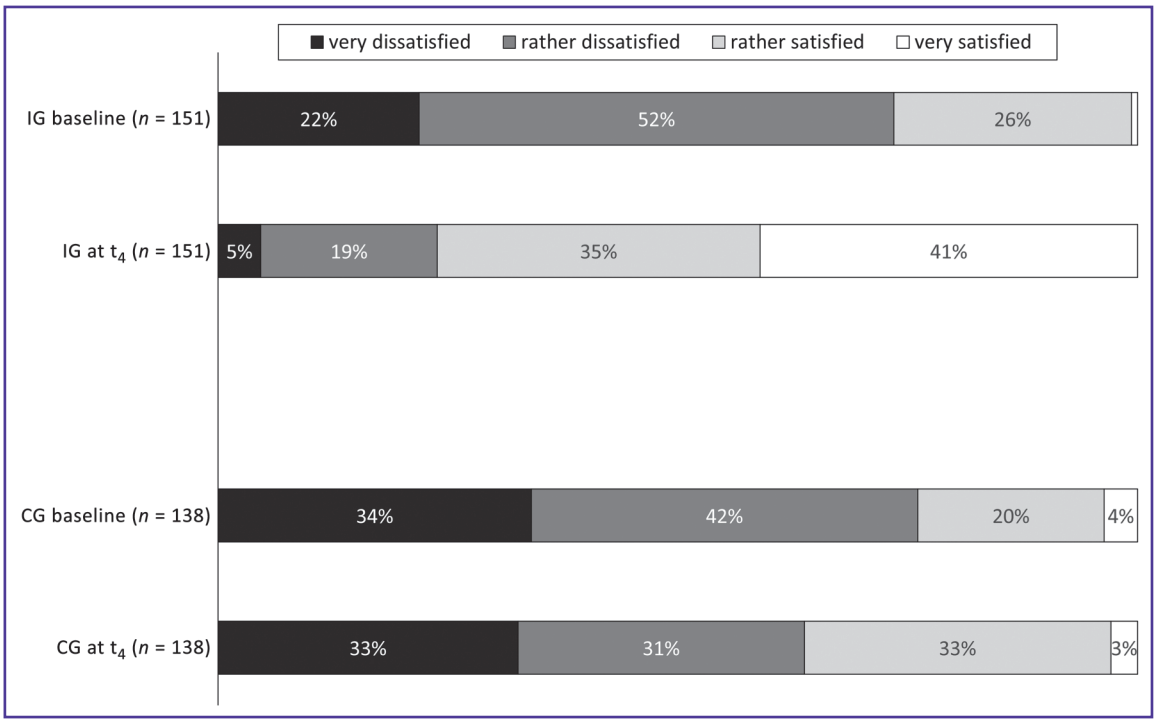

Figure 3 Satisfaction with care for patients in the intervention group (IG) and control group (CG) at baseline and t_4 (study end) in a study of an innovative care concept in hidradenitis suppurativa (EsmAiL).

Table 4 Responder data for the intervention and control groups in a study of an innovative care concept in hidradenitis suppurativa (EsmAiL) after 1 year

Responder	Intervention group ($n=203$)	Control group ($n=174$)	*P*-value (χ^2-test for difference)
IHS4 55%	114 (56.2)	74 (42.5)	0.011
IHS4 75%	80 (39.4)	47 (27.0)	0.015
IHS4 100%	34 (16.8)	21 (12.1)	0.199
HiScore 50	109 (53.7)	65 (37.4)	0.002
HiScore 75	79 (38.9)	42 (24.1)	< 0.001
HiScore 100	37 (18.2)	29 (16.7)	0.794
MCID Pain	123 (62.7)[a]	68 (40.7)[b]	< 0.001
MCID DLQI	136 (67.0)	89 (51.1)	0.002
HADS total	54 (44.3)[c]	19 (19.4)[d]	< 0.001
HADS-Anxiety	51 (38.3)[e]	28 (24.8)[f]	0.023
HADS-Depression	44 (45.8)[g]	14 (17.1)[h]	< 0.001

Data are presented as *n* (%). DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; IH4S, International Hidradenitis Suppurativa Severity Score System; MCID, minimal clinically important difference. [a]$n=196$; [b]$n=167$; [c]$n=122$; [d]$n=98$; [e]$n=133$; [f]$n=113$; [g]$n=96$; [h]$n=82$.

incisions had to be performed in patients in the IG compared with patients in the CG (Figure 4). Incisions are considered to be unplanned interventions to alleviate pain quickly and are therefore required less often when treatment plans are successful.

IHS4 is significantly associated with BMI and smoking status in patients with HS. The literature shows that adjuvant therapies for weight loss and nicotine abstinence in patients with HS can reduce disease activity.[25] Twelve months of treatment in an AiZ significantly reduced the BMI of and number of cigarettes smoked daily by patients in the IG [–3.03 cigarettes ($P<0.001$); –0.7 kg m^{-2} in BMI ($P=0.02$)], whereas the changes in the CG were significant for cigarettes smoked daily (–1.8; $P=0.004$) but not for BMI (–0.0 kg m^{-2}; $P=0.97$).

Pain and psychological impairment due to HS often lead to unemployment.[26]

One year of treatment at an AiZ resulted in 16 more patients returning to employment, which was statistically significantly more than at the beginning of the intervention ($P=0.002$). This effect was not achieved in the CG (five patients; $P=0.38$), reinforcing the assumption that HS leads to unemployment due to its progressive character and that the economic situation of patients is a result of the disease and not vice versa.

Remarkably, and unexpectedly, patients in the CG also reported a significant decrease in IHS4, NRS pain and DLQI (Figure 2). Scenario analysis showed that most patients in the CG were treated according to guidelines and were likely to have been motivated to seek care due to their

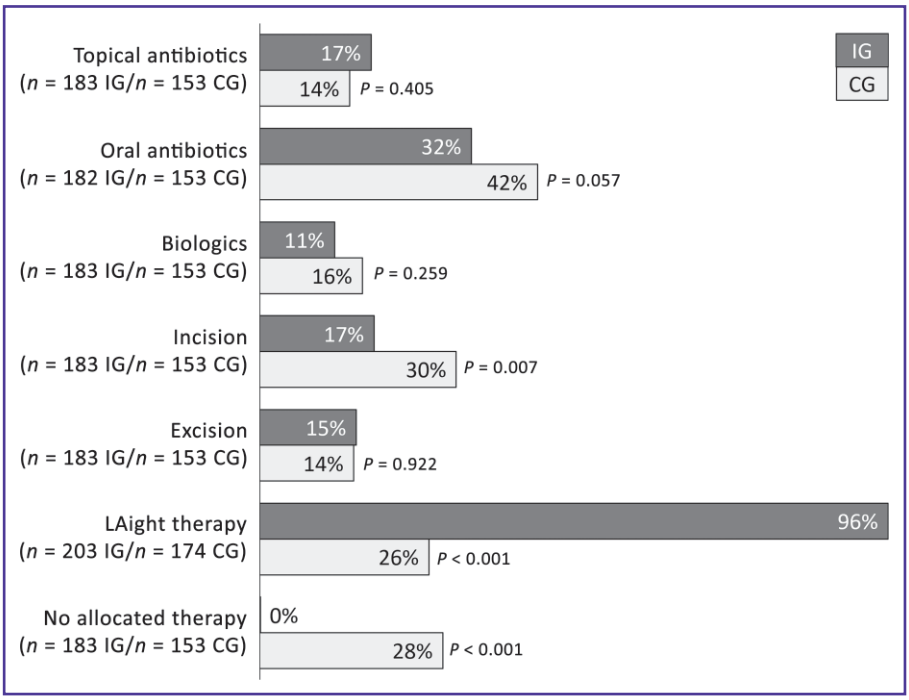

Figure 4 Therapy allocation for patients in the intervention group (IG) and control group (CG) over 12 months of care in a study of an innovative care concept in hidradenitis suppurativa (EsmAiL).

participation in the study (Table S4). However, this effect did not translate into a decrease in depression and anxiety, and did not improve satisfaction with care.

A potential selection bias resulted from the fact that patients learned about the study through various channels, including social media. Thus, our cohort represented a well-informed patient population. It was expected that these patients would be more severely affected than the average HS population and more likely to be unsatisfied with the therapy options currently offered in standard care. Dropouts and patients lost to follow-up did not deviate from the analysed 377 patients with respect to demographics and the primary endpoint (Table S6; see Supporting Information). Only HADS-Depression (IG) and DLQI (CG) showed slight deviations. This was accounted for in the full sample analysis and did not alter the results of the main analysis.

Another bias was that IAight therapy is an entirely new form of treatment that is neither a drug nor a surgical intervention, so patients are more open to testing it. These biases were reinforced by the inclusion criteria as they only selected patients with a certain level of disease activity and burden. In the literature, the expected distribution is reported to be 45.5% for Hurley stage I, 41.5% for Hurley stage II and 13% for Hurley stage III HS,[5,27,28] confirming a shift in the EsmAiL sample towards higher HS severity grades (especially Hurley stage II).

Moreover, patients in both groups were regularly contacted by the study team if they did not complete the questionnaires in a timely manner. This might have increased the response rate of patients in the CG who therefore received additional attention and, most likely, were also motivated to seek care.

Treatment in an AiZ is superior to the current standard care and significantly improves patient satisfaction. Owing to the standardized curriculum and structured training, our treatment plan was followed for most patients (Table S4). The results also showed that the AiZs were successful in providing a thorough and detailed explanation of the currently indicated treatment strategies, which resulted in many patients undergoing treatment that they had initially declined (Figure S3; see Supporting Information). Fewer oral antibiotics and biologics were used than recommended in the European guidelines for level of disease activity at baseline,[5,6] reducing costs and preventing the formation of antibiotic resistance and side-effects. Moreover, the treatment of patients in an AiZ improves their ability to work and results in a significantly lower socioeconomic burden.

Currently, IAight therapy is not widely available outside Germany, which may limit the implementation of the new care concept in other countries.

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Conflicts of interest

M.S. reports auditor activity on the implementation of the contract 'AOK-Priomed Acne inversa' for LENICURA; the receipt of honoraria for lectures from AbbVie; and the funding of travel, congress and hotel fees from AbbVie and Pfizer. P.S. has received grants or contracts from Novartis and Almirall; consulting fees from AbbVie, Allergika, Almirall-Hermal, Amgen, Beiersdorf, Biocryst, BMS, Boehringer Ingelheim, Celgene, CSL Behring, Eli Lilly, Falk, Galderma, Hexal, Janssen, Klinge, Klosterfrau, LEO Pharma, LETI Pharma, L'Oréal, Novartis, Octapharma, Pfizer, Pflüger, Pharming, Regeneron, Shire, Takeda, Sanofi–Genzyme and UCB Pharma; and has had a leadership or fiduciary role for the Society of dermopharmazie, unrelated to work presented here. G.N. reports consulting fees from Dessau Medical Center, which received a consulting fee from Mölnlycke Health Care GmbH, for which he served as a consulting physician; has received speaker fees for attending the European Academy of Dermatology and Venerology (EADV) hidradenitis suppurativa course held on 28–30 November 2022 in Porto, Portugal; and has received an Eli Lilly scholarship for attending the EADV Congress 2021. F.B. has received consulting fees from AbbVie, Incyte, AbbVie Deutschland, MoonLake, Novartis Pharma, Janssen Cilag and UCB Pharma; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events for AbbVie, Incyte, AbbVie Deutschland, Novartis Pharma, Janssen Cilag and UCB Pharma; support for attending meetings and/or travel from AbbVie, Incyte, AbbVie Deutschland, Novartis Pharma, Janssen Cilag and UCB Pharma; and has participated on a data protection monitoring board or advisory board for AbbVie, Incyte, AbbVie Deutschland, Novartis Pharma, Janssen Cilag, UCB Pharma and Boehringer Ingelheim Pharma. U.K. has received consulting fees from Novartis; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Novartis; has participated on a data protection monitoring board or advisory board for Novartis, EsmAiL and EpiCAi; and has had a leadership or fiduciary role for Deutsche Gesellschaft für Wundheilung und Wundbehandlung. K.H. has patents planned, issued or pending (DE102015000150B4); and has stocks or stock options in LENICURA (CEO and stockholder of the company). M.G. has received grants or contracts for clinical studies on hidradenitis suppurativa as deputy Principal Investigator (PI) sponsored by Novartis, Janssen and UCB, and for clinical studies on pemphigus vulgaris and bullous pemphigoid as PI sponsored by Argenx, and for a clinical study on prurigo nodularis as PI sponsored by Galderma (institutional contract; no personal payment); consulting fees from Almirall (personal payment) and Argenx (payment to institution); payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from GSK, Eli Lilly and Janssen (personal payment); support for attending meetings and/or travel from UCB (travel support); has participated in data protection monitoring or advisory boards for UCB, GSK and LEO (personal payment); and is a member of the Board of Directors and Treasurer of the German Society of Dermatology ('Deutsche Dermatologische Gesellschaft'), Section Editor of the *Journal der Dt. Dermatologischen Gesellschaft* and a member of the Board of Directors of the

University Hospital Würzburg (all unpaid). S.G. reports grants or contracts from Novartis and Pierre Fabre; consulting fees from AbbVie, BMS, MSD, Genzyme, Klinge Pharma, Sun Pharma, Kyowa-Kirin, Novartis and Pierre Fabre; has participated on a data safety monitoring or advisory board for Alcedis; and is a member of DeCOG (German dermatological cooperative oncology group), unrelated to the work presented herein.

Data availability

The data underlying this article were provided by the GB-A under licence/by permission. Data will be shared on request to the corresponding author with permission of the GB-A.

Ethics statement

The research complied with the guidelines for human studies and was conducted according to the ethical principles of the Declaration of Helsinki and the principles of Good Clinical Practice (ICH Good Clinical Practice), and was registered with the German Clinical Trials Registry (DRKS00022135) before the first patient was recruited. The study protocol was approved by independent ethics committees and informed consent was obtained from each patient before any study-specific procedures were carried out.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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