Wound Dressing in Patients with Hidradenitis Suppurativa: A Pilot Study

STUDY PROTOCOL
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1) Objectives*

The primary purpose of this research is to determine how the types of wound dressings affect quality of life for people with Hidradenitis Suppurativa (HS). The secondary purpose is to evaluate the utility of a starter kit concept for wound care in people with HS.

1. Primary outcome: quality of life as measured by the DLQI instrument.
2. Secondary outcomes include:
    a. Average pain as measured on NRS
    b. Maximal pain as measured on NRS
    c. Sleep assessment as measured on 5-point likert scale
    d. Drainage assessment as measured on 4-point likert scale
    e. Odor assessment as measured on 4-point likert scale
    f. Patients' overall preference of dressings for HS as measured on a 5-point likert scale
    g. Which dressings work best for which parts of the body as measured by patient log
    h. Frequency of dressing changes required as measured by patient log
    i. HS-Physician's Global Assessment (HS-PGA)
    j.

Study Endpoints:

Primary endpoint	Change in DLQI from baseline to week 6
Secondary endpoint	Change in average pain NRS from baseline to week 6
Secondary endpoint	Change in maximal pain NRS from baseline to week 6
Secondary endpoint	Change in sleep rating from baseline to week 6
Secondary endpoint	Change in drainage rating from baseline to week 6
Secondary endpoint	Change in odor rating from baseline to week 6

Secondary endpoint	Overall dressing preference for HS as noted by subjects on patient log
Secondary endpoint	Dressing preference for body parts as noted by subjects on patient log
Secondary endpoint	Average frequency of dressing changes as noted by subjects on patient log
Secondary endpoint	Change in HS-PGA at 6 weeks after initial assessment

2) Background*

Hidradenitis suppurativa (HS) is a chronic, inflammatory, skin condition characterized by recurrent, painful, draining nodules and abscesses, with resultant skin tunneling and scar formation. HS most commonly affects intertriginous areas such as the axillae, groin, buttocks, and breasts or inframammary region.[1] In moderate to severe stages of disease, destruction of the normal skin's architecture leads to the formation of sinus tracts and fistulas with dermal and subcutaneous fibrosis.[1] It is estimated that 1-4% of the population is affected by HS.[1]

One of the many challenging aspects that HS patients are faced with on a daily basis is wound care. Many HS abscesses and draining nodules and tunnels require frequent dressing changes, up to multiple times daily, given their high exudative nature.[1] Wound care in HS is further complicated by the anatomical predilection of HS wounds. Many dressings on the market are designed to be placed over flat surfaces, and it is often difficult for HS patients to accommodate these flat dressings over the dynamic contours of intertriginous areas such as the axillae, groin, and buttocks.

It is well known that the need for frequent dressing changes due to the heavy exudate in some patients and its odor, significantly impacts patient's quality of life.[1] However, there currently is no standard wound care protocol in place for addressing the wide variety of lesions seen in HS.[2] Therefore, we have designed a study where we will provide HS patients with different types, sizes, and quantities of FDA-cleared dressings, and we will ask them to keep a log of which types of dressings they found most useful for their wounds. Average as well as maximal pain scores will be measured on a numeric scale (NRS). Patient satisfaction, ease of use of dressings, and dressing preferences will be measured with a 5-point likert scale. Patients

will also be asked to log their dressing changes in order to track how often dressing changes are needed in HS. HS-PGA, drainage, perceived odor, and quality of sleep will be assessed (Table 1).

We will additionally study how the usage of antimicrobial dressings will have an effect on the wound microbiome in order to see how this affects healing in the setting of HS. The presence of bacteria in the wound bed will be determined by analyzing the collected wound swab samples. Standard molecular techniques will be utilized for bacterial analysis. The purpose of collecting swab samples is purely qualitative in its intent to gather data on bio-bioburden and microbiome composition. Ulcer swab results are not indicated for therapeutic treatment nor diagnosis of infection. The results of sample swabs will not have an impact on the treatment plan for each participant.

3) Inclusion and Exclusion Criteria*

Inclusion criteria:

- Men and women ≥18 years of age
- Diagnosed with Hidradenitis Suppurativa (all stages of disease) by Dermatologist
- Presence of at least one lesion with active drainage
- Willing and able to provided informed consent

Exclusion criteria:

- Subjects younger than 18-years-old.
- Prisoners
- Pregnant or lactating women
- Adults unable to consent

4) Procedures Involved*

Study duration:

Each subject will have three visits total over a 6-week period.

Recruitment and procedures:

Participants recruited for this study will be patients at University of Miami Hospital (UMH) outpatient dermatology clinics and wound care centers, who present to UMH with a diagnosis of Hidradenitis Suppurativa (HS). During their office visit, patients will be invited to participate in a six-week study to determine which dressings are best suited for patients with HS.

Potential subjects will be informed of the study during their standard of care appointment and then asked if they would like to participate. After signing informed consent, a physical exam will be performed and information on the subjects' demographics, and medical history will be collected (visit 0). Quality of life will be assessed with DLQI instrument. Maximal and average pain will be assessed on a 5-

point likert scale. Quality of sleep, drainage, and odor will be assessed as well (Table 1). Photographs and measurements will be taken of wounds associated with HS. Any active wounds will receive standard of care, including cleaning and debridement to remove all nonviable soft tissue from the wound by scalpel, tissue nippers and/or curettes when appropriate. Wound swab samples will be collected from patients from one active wound at each visit. This site will be identified during the baseline visit. If debridement is indicated as part of standard care, prior to debridement of the wound, a wound swab sample will be collected from the wound bed. In circumstances where a layer of nonviable tissue is preventing swab collection, the swab sample should be collected during the course of the debridement process wherein the wound bed has been exposed. Subjects will be provided with a kit that will include 3 types of FDA-cleared dressings (1) Cutimed® Sorbact® Hydroactive B, 2) Cutimed® Siltec®, and, 3) Sorbion® Sana multi-star) that are available on the market and general wound care supplies (i.e. tape, gauze) that are also FDA-cleared and available on the market. Dressing instructions involve applying desired dressing daily to affected areas and securing with tape as needed. Participants may change dressings as needed. Instructions will be reviewed with participants upon enrollment. Participating subjects will also be given a 2-week log where they will be instructed to fill in which dressings they used on which wounds, and how often they changed the dressings.

Subjects will receive weekly phone calls in between follow ups (for a total of 4 phone calls) by the research team where they will be asked to answer questions on average and maximal pain, quality of sleep, drainage and odor. Subjects will be asked to follow up in 14 +/- 3 days from visit 0 (visit 1), at which point the physical exam will be performed. Maximal and average pain will again be assessed on a 5-point likert scale. Quality of sleep, drainage, and odor will be assessed as well (Table 1). Photographs and measurements of HS wounds will be taken and the dressing logs will be collected and evaluated. Wound swab samples will be collected from the wound that was pre-identified at baseline visit. Participants will share with study personnel which dressings were most useful to them, and this will dictate the dressing type that each subject receives for the remaining 4 weeks of the study period.

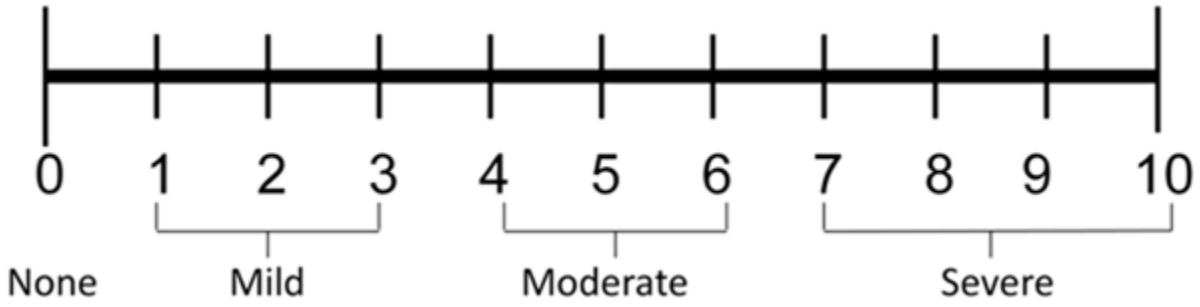
Visit 2 will take place 28 +/- 3 days after visit 1. Subjects will follow up for an end of treatment visit where they will have a physical exam. Maximal and average pain will again be assessed on a 5-point likert scale. Quality of sleep, drainage, and odor will be assessed as well (Table 1). Photographs and measurements of HS wounds will be taken. Wound swab samples will be collected from the wound that was pre-identified at baseline visit. Subjects' medical records will be reviewed to collect medical history, treatment plans and disease progress. Please see Table 1 below detailing the schedule of events.

Finally, in order to correlate the above outcomes with independent disease progression, HS-PGA score will be calculated at visits 0, 1 and 2. The HS-PGA instrument is a 6-point scale used to assess overall disease severity. HS-PGA will

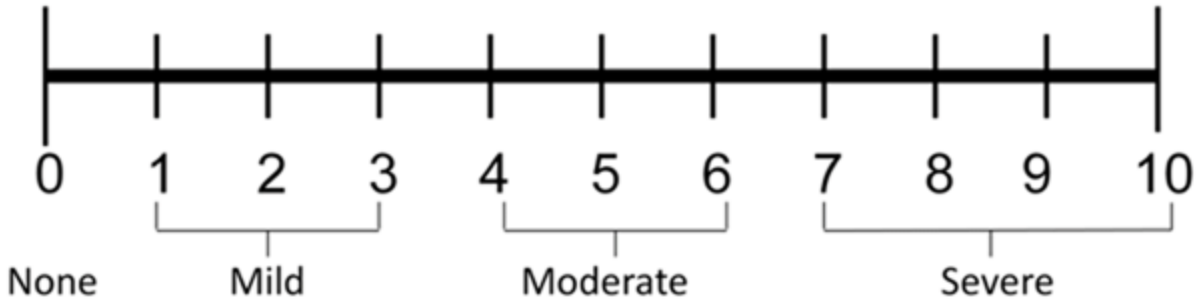
be completed at baseline and follow up visits (Table 1). HS affected areas will be evaluated and given a numerical score based on presence of abscesses, draining fistulas, inflammatory nodules, and non-inflammatory nodules. Then the points are added to create one global score. A 2 point reduction and above is considered a meaningful clinical response.

Assessments:

1. Maximal NRS:
   Please rate your pain **at its worse** over the last 24 hours on the scale below.



2. Average NRS:
   Please rate your pain **on average** over the last 24 hours on the scale below.



3. Drainage assessment:
   How much did your lesion(s) drain during the past 24 hours?

No draining	A little draining	Moderate draining	A lot of draining
1	2	3	4

4. Sleep assessment:
   How much was your sleep disturbed by HS last night?

Not at all	A little bit	Moderately	A great deal	Unable to sleep
1	2	3	4	5

5. Odor assessment:
   How would you rate the odor caused by the draining of your lesion(s) during the past 24 hours?

No odor	A little odor	Moderate odor	A lot of odor
1	2	3	4

6. Dressing's ease of use assessment:
How easy to use are your current dressings?

Very Difficult	Difficult	Neutral	Easy	Very Easy
1	2	3	4	5

7. Dressing satisfaction:
How satisfied are you with your current dressings?

Strongly Dissatisfied	Dissatisfied	Neutral	Satisfied	Strongly Satisfied
1	2	3	4	5

8. HS-PGA:

Appendix Table 1. **Hidradenitis Suppurativa Physician's Global Assessment Scale**

Rating	Description
Clear	0 abscesses, 0 draining fistulas, 0 inflammatory nodules, and 0 noninflammatory nodules
Minimal	0 abscesses, 0 draining fistulas, 0 inflammatory nodules, and presence of noninflammatory nodules
Mild	0 abscesses, 0 draining fistulas, and 1–4 inflammatory nodules or 1 abscess or draining fistula and 0 inflammatory nodules
Moderate	0 abscesses, 0 draining fistulas, and ≥5 inflammatory nodules or 1 abscess or draining fistula and ≥1 inflammatory nodule or 2–5 abscesses or draining fistulas and <10 inflammatory nodules
Severe	2–5 abscesses or draining fistulas and ≥10 inflammatory nodules
Very severe	>5 abscesses or draining fistulas

Table 1: Schedule of Events

	Baseline Visit Day 0	**Phone call 1** Day 7	**Follow-Up Visit** Day 14	**Phone call 2** Day 21	**Phone call 3** Day 28	**Phone call 4** Day 35	**End of Treatment Visit** Up to Day 42 after Baseline Visit
Visit Window		7 +/- 3 Days from Baseline Visit	14 +/- 3 Days from Baseline Visit	7+/- 3 Days from Follow-Up Visit	14+/- 3 Days from Follow-Up Visit	21+/- 3 Days from Follow-Up Visit	28+/- 3 Days from Follow-Up Visit
Visit #	**0**		**1**				**2**
Informed Consent/PHI authorization	X						
Demographics	X						
Medical History[A]	X						
Concomitant Medications & Procedures Assessment	X		X				X
Physical Exam[B]	X		X				X
Inclusion/Exclusion Determination	X						
Wound(s) Photograph	X		X				X
Dermatology Life Quality Index (DLQI)	X						X
Average 24 hours pain Score (NRS)	X	X	X	X	X	X	X
Maximal 24 hours pain Score (NRS)	X	X	X	X	X	X	X
Review Dressing Logs			X				X
Sleep assessment	X	X	X	X	X	X	X
Drainage assessment	X	X	X	X	X	X	X

Dressing Satisfaction	X		X				X
Dressings' Ease of Use	X		X				X
Odor assessment	X	X	X	X	X	X	X
HS-PGA	X		X				X
Wound Swab Sample Collection	X		X				X
Adverse Events Assessment			X				X

A: Detailed HS history will be gathered, including current wound care regime (types and number of dressings utilized per week, including an estimate of anticipated dressings needed per week), exacerbating and alleviating factors; B: Hurley staging will be assessed, as well as types (inflammatory, sinus tracts, ulcerations), number, and location of lesions

5) Data and Specimen Banking*

6.1 Collection and Analysis of Wound Swabs

The following study procedures for wound swabs will be performed at the pre-designated wound sites only. Wound swab samples will be collected at the Baseline Visit 0, Follow-Up Visit 1, and Follow-Up Visit 2.

Wound swabs will be collected from all study wounds. If debridement is indicated as part of standard care, wound swabs will be performed prior to the debridement Wound swab sample will be collected from the wound bed using the Levine technique. In circumstances where a layer of nonviable tissue is preventing swab collection, the swab sample should be collected during the course of the debridement process wherein the wound bed has been exposed. Wound swab samples from enrolled subjects will be collected and sent out for further processing and analysis to Dr. Irena Pastar's laboratory. The labels of the tubes will be coded to protect the identity of the subjects. Samples will be stored in a -80°C freezer prior to shipment to the processing laboratory. Samples will be shipped on dry ice.

6.2 Dressing Logs and Photographs

The dressing logs and photographs collected from each patient will be de-identified and stored in a computer located in the Dermatology Research office. The computer

is located in a locked room in the University of Miami Hospital West Building, Room 506, 1321 NW 14th St, Miami, Fl, 333125.

Statistical analysis will be performed using software already available in the lab. This information will be protected in a locked office (see Confidentiality section below) and will only be able to be accessed by the primary investigator and the co-investigators. The photographs will then be downloaded as encrypted, de-identified JPEG/TIFF files and stored in the PI computers protected by login and password (see section 16).

6) Data Management*

The investigator (or research staff) will record the data collected in a manner that does not include any direct identifiers of the subject. The investigator will assign a code to each subject and link the code to the subject's identity. The link to the subject's identity will be maintained on a document separate from the research data. Both documents will be stored on password-protected media on a University of Miami encrypted device. The data will be stored for at least 3 years after the study has concluded and will be destroyed at the earliest opportunity in accordance with University of Miami's policies thereafter. Data will only be accessed by designated study team members.

Statistical analysis of collected data will be performed using IBM SPSS Statistics for Windows (IBM Corporation, Armonk, NY, USA). Mean and range will be calculated for continuous variables. Pearson's chi-squared test will be used to test for independence between categorical variables; for expected values less than 5, Fisher's exact test of independence will be used.

Adverse Events

7) Adverse Events*

8.1 Definition of Adverse events

An adverse event (AE) is any untoward medical occurrence (e.g., any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a subject or clinical investigation subject after providing written informed consent for participation in the study. Therefore, an AE may or may not be temporally or causally associated with the use of a medicinal (investigational) product. In addition, all reports of intentional misuse and abuse of the product are also considered an adverse event irrespective if a clinical event has occurred. The investigator has the responsibility for managing the safety of individual subject and identifying adverse events. Qualified study personnel will be readily available to advise on trial related medical questions or problems. The occurrence of adverse

events must be sought by non-directive questioning of the subject at each visit during the study. Adverse events also may be detected when they are volunteered by the subject during or between visits or through physical examination findings, laboratory test findings, or other assessments. Adverse events must be recorded in the Adverse Events eCRF under the signs, symptoms or diagnosis associated with them, accompanied by the following information (as far as possible) (if the event is serious refer to Section 8.2):

1. The severity grade.
- mild: usually transient in nature and generally not interfering with normal activities
- moderate: sufficiently discomforting to interfere with normal activities
- severe: prevents normal activities

2. its relationship to the study treatment (suspected: Yes/No). If the event is due to lack of efficacy or progression of underlying illness (i.e. progression of the study indication), the assessment of causality will usually be 'Not suspected'. The rationale for this guidance is that the symptoms of a lack of efficacy or progression of underlying illness are not caused by the trial drug, they happen in spite of its administration and/or both lack of efficacy and progression of underlying disease can only be evaluated meaningfully by an analysis of cohorts, not on a single subject.
3. its duration (start and end dates) or if the event is ongoing, an outcome of not recovered/not resolved must be reported.
4. whether it constitutes a serious adverse event (SAE - see Section 8.2 for definition of SAE) and which seriousness criteria have been met.
5. action taken regarding with study intervention.

All adverse events must be treated appropriately. Treatment may include one or more of the following:
- study dressing regime not changed
- study dressing regime interrupted/dressings withdrawn

Conditions that were already present at the time of informed consent should be recorded in medical history of the subject. Adverse events (including lab abnormalities that constitute AEs) should be described using a diagnosis whenever possible, rather than individual underlying signs and symptoms. Adverse event monitoring should be continued for at least 10 weeks following the last date of study dressing usage. Once an adverse event is detected, it must be followed until its resolution or until it is judged to be permanent (e.g. Continuing at the end of the study), and assessment must be made at each visit (or more frequently, if necessary) of any changes in severity, the suspected relationship to the interventions required to treat it, and the outcome.

8.2 Serious adverse events

An SAE is defined as any adverse event [appearance of (or worsening of any pre-existing)], undesirable sign(s), symptom(s) or medical conditions(s) which meets any one of the following criteria:

- fatal
- life-threatening. Life-threatening in the context of a SAE refers to a reaction in which the subject was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if it were more severe
- results in persistent or significant disability/incapacity
- constitutes a congenital anomaly/birth defect
- requires inpatient hospitalization or prolongation of existing hospitalization, unless hospitalization is for:
    - routine treatment or monitoring of the studied indication, not associated with any deterioration in condition
    - elective or pre-planned treatment for a pre-existing condition that is unrelated to the indication under study and has not worsened since signing the informed consent
    - social reasons and respite care in the absence of any deterioration in the subject's general condition
    - treatment on an emergency outpatient basis for an event not fulfilling any of the definitions of a SAE given above and not resulting in hospital admission
- is medically significant, e.g. defined as an event that jeopardizes the subject or may require medical or surgical intervention to prevent one of the outcomes listed above

Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious reactions, such as important medical events that might not be immediately life threatening or result in death or hospitalization but might jeopardize the subject or might require intervention to prevent one of the other outcomes listed above. Such events should be considered as "medically significant". Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization or development of dependency or abuse (please refer to the ICHE2D Guidelines).

8.3 SAE reporting

To ensure subject safety, every SAE, regardless of causality, occurring after the subject has provided informed consent and until 10 weeks following the last administration of study dressings must be reported within 24 hours of learning of its occurrence.

All follow-up information for the SAE including information on complications, progression of the initial SAE and recurrent episodes must be reported as follow-up to the original episode within 24 hours of the investigator receiving the follow-up information. An SAE occurring at a different time interval or otherwise considered

completely unrelated to a previously reported one must be reported separately as a new event.

If the SAE is not previously documented (new occurrence) and is thought to be related to the study treatment, a CMO & PS Department associate may urgently require further information from the investigator for health authority reporting.

Suspected Unexpected Serious Adverse Reactions (SUSARs) will be collected and reported to the competent authorities and relevant ethics committees in accordance with EU Guidance 2011/C 172/01 or as per national regulatory requirements in participating countries. Any SAEs experienced after the 10 week period following the last administration of study treatment should only be reported if the investigator suspects a causal relationship to study treatment. Any SAEs reported up to the subject's last visit will be reported in the AE eCRF. SAEs beyond that date will only be recorded in the Safety database.

Risks to subjects in this study include contact dermatitis in the skin areas exposed to the dressings provided in this study. However, we will be utilizing FDA-cleared dressings that are available on the market and therefore pose a risk that is no higher than the current risk subjects are undertaking while utilizing other dressings over the same skin areas.

8) Potential Benefits to Subjects*

Direct benefits to subjects include complimentary access to various high quality dressings that they might otherwise not have had access to as they may not be covered by insurance for HS.

9) Vulnerable Populations*

Pregnant women, prisoners, and children younger than 18 years old are excluded.

10) Setting

Patients will be recruited from outpatient dermatology clinics and wound centers at the University of Miami Clinics and Hospital at 1295 NW 14th St, Suite K/L/M, Miami, FL 33125. Subjects will be offered follow up at outpatient dermatology research offices located at the University of Miami Hospital West Building, 1321 NW 14th St., Suite 506, Miami, FL, 33125. All of the necessary procedures for the study will take place at this location.

11) Resources Available

Hadar Lev-Tov, M.D., is a dermatologist with expertise in wound healing disorders including Hidradenitis Suppurativa; he will be the primary investigator on this study. All subjects will be recruited from outpatient dermatology clinics and wound centers and he can perform detailed wound and skin evaluations.

All associated study personnel are CITI certified and have extensive data analysis training.

12) Prior Approvals

None.

13) Recruitment Methods

Thirty subjects (30) with a diagnosis of Hidradenitis Suppurativa will be recruited by the Investigator and study staff. Subjects will be recruited from outpatient dermatology clinics and the Wound Care Center at the University of Miami. During their standard visit, subjects will be offered the opportunity to enroll in the study. If subjects agree to take part in this study, study staff will guide subjects through the informed consent process. Subjects will be asked to sign the informed consent form and the photo consent form before the study procedures begin. Subjects will be given ample time to consider the study and all questions will be answered by study staff. Subjects will be enrolled from the date of protocol approval for a 12 months period.

14) Local Number of Subjects

This is a pilot study for which we intend to reach 20 subjects. We anticipate a high drop-out rate, and therefore intend to recruit and enroll a total of 30 subjects locally.

15) Confidentiality

The camera will be stored in a locked office in 1321 NW 14th St. University of Miami Hospital West Building, Suite 506, Miami FL 33125 until the end of the recruitment. The collected coded and encrypted images will be stored in the computers found at the research office protected by a password. The collected coded dressing logs will be stored at the research office in a locked cabinet. Both the encrypted images and the dressing logs will be securely stored for at least 3 years after the research project has concluded. Please see section 7 (‘*Data*

Management') for more details on data coding and storage. Only the primary investigator and co-investigators will have access to the images, camera, and subject information.

16) Provisions to Protect the Privacy Interests of Subjects

All study records will be stored a password-protected computer, in a locked room. A separate datasheet will be created that will tabulate patients' names, MRN, date of birth and assign a subject ID. This subject ID will act as a code during the 6 weeks the subject is actively participating in the study. A second datasheet will contain only the subject ID and study relevant data. This will effectively create a de-identified database that will be used for analysis at the end of the study.

17) Consent Process

Consent will be obtained by a member of the study team in writing and will take place in outpatient dermatology clinics and wound centers after the subject completed their clinic visit. In the clinic, study staff will guide the subjects through the consent process. Study staff will describe the study and the procedures involved to the subject and review the potential risks and benefits. The subject will be given ample time to consider the study. Once the subject agrees to participate, an Informed Consent Form will be signed.

18) Process to Document Consent in Writing

Attached.

NOTE: IT IS UNCLEAR WHETHER YOU WILL NEED A PARTIAL WAIVER OF HIPAA FOR RECRUITMENT PURPOSES. IF YOU NEED IT, YOU NEED TO ADD THE FOLLOWING:

19) Authorization for Use and Disclosure of Protected Health Information (HIPAA)

If the research team will access patient medical records or other identifiable health information for this research, you must obtain a waiver of the requirement for written authorization from the patients to access their medical records.

Confirm that you will destroy or de-identify the information you collect at the earliest opportunity. ☒ ***I confirm***

Confirm that the information you collect will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other research for which the use or disclosure of PHI is permissible.
☒ ***I confirm***

References

1. Falola RA, DeFazio MV, Anghel EL, Mitnick CD, Attinger CE, Evans KK. What Heals Hidradenitis Suppurativa: Surgery, Immunosuppression, or Both? *Plast Reconstr Surg.* 2016;138(3 Suppl):219S-229S.
2. Alavi A, Kirsner RS. Local wound care and topical management of hidradenitis suppurativa. *J Am Acad Dermatol.* 2015;73(5 Suppl 1):S55-61.