PROTOCOL

Hidradenitis suppurativa treated with follicular unit excision: A prospective controlled 24-week pilot study

Protocol Number: FUEHS001
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Author/s:
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Sponsor/s:

Statement of Compliance

This document is a protocol for a research project. This study will be conducted in compliance with all stipulation of this protocol, the conditions of the ethics committee approval, the NHMRC National Statement on ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95).

1. SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

I have read and approve this protocol. My signature confirms the agreement of both parties that the clinical study will be conducted with accordance with applicable ethnical review board (s) guidelines, the Declaration of Helsinki and IRB/EC procedures. I confirm that if I or any of my staff are members of the ethnical review board, we will abstain from voting on this protocol. Nothing in this document is intended to limit the authority of a physician to provide emergency medical care under applicable regulations.

Chief Investigator:			
Signature:	BEVIN BHOYRUL	Date:	16/8/2023
Name (please print):	BEVIN BHOYRUL		
Position:	CONSULTANT DERMATOLOGIST AND HAIR TRANSPLANT SURGEON		
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Table of Contents

2. STUDY SYNOPSIS

Provide brief information

Title:	Hidradenitis suppurativa treated with follicular unit excision: A prospective controlled pilot study
Short Title:	Hidradenitis suppurativa treated with follicular unit excision: A prospective controlled study
Design:	Open-label, interventional
Study Centres:	Sinclair Dermatology, Melbourne Australia
Hospital:	
Study Question:	How effective is follicular unit excision for the treatment of mild-moderate hidradenitis suppurativa?
Study Objectives:	
Primary Objectives:	The study's primary objective is to determine change in several hidradenitis suppurativa assessment scores score throughout follow-up visits in the first 24 weeks after follicular unit excision
Secondary Objectives	i) To compare the changes in Hidradenitis Suppurativa assessment scores between intervention and control groups up to 24 weeks and on the treated sites before and after follicular unit extraction ii) To compare the number of disease flares between the treated and control groups for 24 weeks after treatment iii) To determine if specimens contain hair follicles, sebaceous glands, apocrine glands and eccrine glands on histopathology
Key Inclusion Criteria:	i) Patients aged ≥18 years with hidradenitis suppurativa ii) Mild-moderate hidradenitis suppurativa defined by Hurley stage 1 up to 2A iii) Minimum diagnosis of 3 months prior to baseline iv) Active hidradenitis suppurativa present for ≥3 months from initial diagnosis
Key Exclusion Criteria:	i) Current treatment with systemic antibiotics, retinoids, immunosuppressants or biologic agents at discretion of the investigator ii) Extensive scarring iii) Absence of terminal hairs in target areas iv) Previous laser hair removal in target areas v) Pregnant or lactating women

Number of Planned Participants :	24
Investigational procedure:	Follicular unit excision using 0.8 mm Ertip® punch
Data analysis	The primary objective is to evaluate the efficacy of follicular unit excision in the treatment of adults with mild to moderate hidradenitis suppurativa. The primary analysis will be conducted to assess the primary and secondary endpoints once all participants have completed the Week 24 visit.
Safety considerations:	
Statistical Methods:	Paired *t* test to assess change in Hurley stage, Hidradenitis Suppurative-Physician's Global assessment score, numerical pain score, IHS4 score, HiSCR score.
Subgroups:	

3. GLOSSARY OF ABBREVIATIONS & TERMS

Abbreviation	Description (using lay language)
HS	Hidradenitis suppurativa
HF	Hair follicle
FUE	Follicular unit excision
IHS4	International Hidradenitis Suppurativa Severity Score System
Hi-SCR	Hidradenitis Suppurativa Clinical Response
HREC	Human Research Ethics Committee
HS-PGA	Hidradenitis Suppurativa Physician Global Assessment
ICH GCP	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice
Nd:YAG	Neodymium-doped yttrium aluminum garnet
SAE	Serious adverse event

4. STUDY SITES

4.1 STUDY LOCATION/S

Site	Address	Contact Person	Phone	Email
Sinclair Dermatology	2 Wellington Parade, East Melbourne	Bevin Bhoyrul	03 9654 2426	Bevin.bhoyrul@nhs.net

5. INTRODUCTION/BACKGROUND INFORMATION

5.1 LAY SUMMARY

This study is looking at follicular unit extraction to treat hidradenitis suppurativa, a condition that causes inflammation of hair follicles resulting in severe pain and scarring. Follicular unit extraction is a technique used in hair transplants to entirely remove hair follicles. We want to test whether or not by removing hair follicles using hair follicle extraction technique reduces inflammation and improve the quality of patients' life. We will do hair follicle extraction on both sides of either the armpit or groin and compare it with topical routine treatments to assess whether or not there is improvement. We will follow the participants until week 24 of the study.

5.2 INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic skin disease which predominantly affects the skin of intertriginous areas through an inflammatory process and results in recurrent nodules, abscesses, sinuses, fistulas, and scarring. Based on a limited number of smaller studies, the estimated lifetime risk is 1%, with 30% having moderate-to-severe disease[1]. HS develops at an average age of 22 years and persists for an average of 19 years. Genetic factors appear to play an important role in HS, given that up to 42% of patients report a family history of the condition[2]. HS has a severe emotional and psychosocial effect on sufferers, which includes a negative impact on their ability to function socially[1].

5.3 BACKGROUND INFORMATION

HS was once considered a disease of the apocrine gland, but newer evidence firmly implicates direct follicular involvement in disease pathogenesis. Over 95% of early lesions (< 3 days old) include

hyperkeratosis, occlusion of the follicular unit and an associated perifolliculitis. These are often accompanied by dilatation of the hair follicle (HF) and subsequent stasis in both the apocrine and eccrine glands. While apocrine stasis, hyperplasia and a periglandular inflammatory infiltrate are observed in and around the apocrine glands in 33–90% of cases of HS, they are universally accompanied by extensive inflammation of the HF, eccrine gland and cystic structures, and are thought to be a secondary phenomenon[3-8]. It has recently been observed that there is a thinning of the basement membrane zone around the junction between the HF and sebaceous gland in HS skin. This area of weakness may predispose to rupture of the hair follicle and spillage of its contents into the dermis and a subsequent inflammatory response[9]. Furthermore, the identification of free keratin filaments in the dermis supports that mechanism and is consistent with follicular rupture playing a key role in disease pathogenesis[10].

The management of HS is currently multifactorial. Lifestyle changes e.g., smoking cessation and weight loss can reduce the frequency of HS flares[3]. Other lifestyle modifications such as wearing loose clothing may reduce the severity of flares[11]. Systemic therapy includes antibiotics, hormonal therapy e.g. spironolactone, retinoids and immunosuppressants[3]. However, the disease often recurs following therapy interruption or discontinuation. The tumour necrosis factor-α inhibitor adalimumab is a relatively effective treatment, with 41.8-58.9% of adult patients achieving satisfactory clinical response[12]. In chronic refractory cases, surgery, including deroofing and incision and drainage or ablative lasers may be used[13]. Therefore, early intervention is critical to prevent progression of disease to a disfiguring recalcitrant stage.

Follicular unit excision (FUE) is a minimally invasive surgical technique used in hair transplantation surgery where hair grafts are extracted from the donor area and implanted in the recipient area under local anaesthesia[14]. Although grafts are usually harvested from the back and sides of the scalp, other donor sites include the beard, chest and other parts of the body. In FUE, the skin around a follicular unit is scored using a 0.8-1 mm circular punch mounted on a motorized hand device, and the graft is subsequently extracted[14]. The extraction leaves a wound which heals by secondary intention. Residual scars are pin-point dots which are virtually imperceptible to the naked eye.

Although FUE is mostly used in hair transplantation, it has been used for other dermatological indications. Notably, extraction of pigmented hair grafts and placement into depigmented skin in patients with stable with vitiligo resulted in skin re-pigmentation[15]. This is likely due to migration of follicular melanocytes to vitiliginous skin.

Laser hair removal has been shown to be effective in reducing flares and severity of HS[13,16]. In addition, deroofing with carbon dioxide laser with hair follicle removal using a neodymium-doped yttrium aluminum garnet (Nd:YAG) laser has been shown to reduce recurrence rates[13]. Even in mild HS, Nd:YAG laser hair depilation increased patient satisfaction and reduced mean HS severity score[17].

To our knowledge, FUE to treat HS has not been attempted. Apocrine and eccrine glands are known to reside next to HFs[18]. Given that HFs and/or apocrine glands are central to the pathophysiology of HS, and that laser hair removal laser has been shown to be an effective treatment, we propose that FUE can be an effective treatment modality for HS. In contrast to laser hair removal, FUE would also remove apocrine glands. In addition, hair removal using laser is often temporary, with hair regrowth occurring within a few months if laser treatment is not maintained. On the other hand, FUE would result in permanent removal of HFs and associated apocrine glands, thereby offering a more long-lasting solution.

6. STUDY OBJECTIVES

6.1 HYPOTHESIS

Participants receiving FUE will have lower scores for HiSCR, HS-PGA, IHS4, NRS30 compared to those receiving standard topical resorcinol/clindamycin.

6.2 STUDY AIMS

Purpose: This is a prospective, interventional study to evaluate the effectiveness of FUE in reducing severity score of mild to moderate HS.

Primary objective.

1. To evaluate the effectiveness of FUE in reducing severity score of mild to moderate HS.

Secondary objective.

2. Comparing scores of HS severity assessments between intervention and control group at week 6, 12 and 24 after follicular unit extraction.
3. Comparing scores of HS severity assessments before and after follicular unit extraction on the treated site at week 6, 12 and 24 after follicular unit extraction.
4. To compare the number of disease flares between intervention and control group over 24 weeks.
5. To determine if specimens contain HFs, sebaceous glands, apocrine glands and eccrine glands on histopathology.

6.3 OUTCOME MEASURES

1. Hidradenitis suppurativa clinical response score (HiSCR)
2. Hidradenitis suppurativa – Physician's global assessment (HS-PGA)
3. International Hidradentitis Suppurativa Severity Score System (IHS4)
4. Pain score (NRS30)
5. Number of abscesses and nodule counts at each visit
6. Number of flare ups as well as location of flare ups

6.4 STUDY TYPE & DESIGN & SCHEDULE

6.4.1 STUDY ASSESSMENTS

6.4.1.1 SUBJECT DEMOGRAPHICS

Demographic and baseline characteristics to be collected on participants include: Date of birth, gender, ethnicity and child-bearing potential (for females only).

20 participants will be recruited and divided into intervention and controlled group in a 1:1 ratio.

6.4.1.2 MEDICAL HISTORY

Medical history and current medical conditions will be collected. Only data up to 6 months prior to signing of the informed consent and until the start of study treatment is required. Whenever possible, diagnoses and not symptoms will be recorded.

6.4.1.3 CONCOMITANT TREATMENT

All treatments administered during the 6 months prior to start of study treatment (including any treatment started during the screening period) will be collected.

6.4.1.4 PHYSICAL EXAMINATION

A physical examination, including general appearance, will be performed. If indicated, based on medical history and/or symptoms, additional exams will be performed at the discretion of the investigator.

Information for all physical examinations must be included in the source documentation at the study site. Significant findings that are present prior to the informed consent by the subject must be included in the Medical History. Significant findings made after the signing of the informed consent that meet the definition of an adverse event will be recorded.

6.4.1.5 PHENOTYPE BASELINE

The HS of the participants will be documented in the screening visit to identify its phenotype as follicular vs inflammatory (See Appendix 1).

6.4.1.6 MANAGEMENT OF FLAREUPS

Participants may be given medications to prevent flares to stabilize the condition prior to follicular unit extraction. This may be resorcinol 15% cream and/or oral antibiotics such as doxycycline 100mg. Often, flareups may need surgical management or intralesional corticosteroids. These are given as part of standard routine care to minimize flare-ups for the hidradenitis suppurativa and alleviate symptoms for patients and is part of management guidelines.

Participants may be given a sheet to document their flareups (Appendix 3). Participants may take photos of the flareups on their phone to show to the investigator but this is optional only. Investigators will not be collecting photos taken by participants.

Participants are divided into the intervention group and control group. The control group will be managed with topical clindamycin. A staff member of Sinclair Dermatology not involved in this study will randomise participants into the intervention and controlled group using the program from www.randomizer.org in a 1:1 stratification ratio. The treatment group will be treated with follicular unit extraction. Due to the study design (the intervention being surgical and the controlled group being a topical application), investigators and participants are unable to be blinded as to which participants will be in the treatment or control group. As there will be 24 participants in this study, numbers 1-24 will be randomly allocated to either control or treatment group using randomizer.org prior to recruitment of the study. Participants will then be allocated a number in the order in which they are recruited in the study and subsequently will be placed in the group that the number has been randomised into.

6.4.1.7 FOLLICULAR UNIT EXTRACTION AND HISTOPATHOLOGY

Participants will be taken to the procedure room. Local anaesthesia will be injected into diseased hair-bearing area on both sides of either the axillae or groin. FUE will be performed by the investigator (who is experienced in FUE) using 0.8/0.9/1.0 mm Ertip® punch. The extracted hair follicular unit samples will have histopathological analysis to confirm complete removal of hair follicles, sebaceous glands, aporcrine glands and eccrine glands. These samples are not kept for future studies and will be discarded once complete removal of the pilosebaceous units are confirmed. Participants will not be charged for samples being analysed to confirm complete removal of the pilosebaceous units.

6.4.1.8 HIDRADENITIS SUPPURATIVA SEVERITY ASSESSMENT

As part of standard routine care, participants will have the Hurley Stage of their HS, nodule count and abscess count documented at baseline. This is part of standard routine care to assess whether treatment is effective, and it will also allow us to calculate the hidradenitis suppurativa clinical response (HiSCR). HiSCR is defined as a ≥50% reduction in inflammatory lesion count (abscesses and inflammatory nodules), and no increase in abscesses or draining fistulas when compared with baseline[19,20]. Participants will also have their hidradenitis suppurativa-physician's global

assessment (HS-PGA) and International Hidradenitis Suppurative Severity Score System (IHS4) score documented in follow-up visits. Pain will be assessed using the numerical scale 30 (NRS30) pain score (See Appendix 1)[19,21,22].

These assessments will be done at week 0, week 6, week 12 and week 24.

6.4.1.9 STUDY COMPLETION

This prospective interventional study is expected to be completed within 12 months. Participants who are recruited will only be involved up to 24 weeks of duration, but the prospective interventional study overall will be completed within 12 months when the final participant has had their final visit. Data analysis and submission of the primary manuscript will occur within 6 months of study closure. Participants involved in the study will receive ongoing care as per standard practice.

6.4.2 STUDY SCHEDULE

A table of the visits schedule and study procedures is in Appendix 2.

Randomisation will occur prior to recruitment of participants.
The Investigator or his/her approved designee must explain the nature of the study protocol and associated risks to the potential study participant. The potential participant must be allowed to review the study information and to ask questions before being asked to sign the Informed Consent Form.

Signed informed consent must be provided by the potential study participant prior to initiation of any screening evaluations or other study-related procedures. The signature, date, and name of the individual at the site who obtained the informed consent will be recorded in the participant's source record. After written informed consent is obtained, a copy of the signed form will be provided to the patient to keep. The participant will then be assigned a participant number.

6.4.2.1 SCREENING

All participants will be screened prior to enrolment in the study. The following procedures must be conducted at the screening visit.

- Written informed consent
- Review of eligibility (diagnosis, inclusion and exclusion criteria)
- Medical history (including previous psoriasis treatments)
- Physical Examination
- Vital Signs (Respiratory rate, heart rate, tympanic temperature, blood pressure)
- Weight
- Height
- HS severity score baseline measurements

6.4.2.2 VISIT 1 (WEEK 0)

This visit occurs no later than 28 days from Screening visit. The visit may occur on the same day as the screening visit provided i) the participant was given sufficient time to read through the patient information and consent form and ii) seek advice from their primary physician, family and/or friend and iii) have had their questions answered by the investigator adequately.

- Review of inclusion and exclusion criteria

- Review of medical history
- Review of adverse events (if any)
- Concomitant medication collection
- Vital Signs (Respiratory rate, heart rate, tympanic temperature, blood pressure)
- Physical Examination
- Weight
- Review of HS progress
- Follicular unit extraction and sample analysis (if intervention group)
- HS severity score assessment s

6.4.2.3 VISIT 2 (WEEK 6)

- Review of withdrawal criteria
- Review of adverse events (if any)
- Review of HS progress
- Concomitant medication collection
- Vital Signs (Respiratory rate, heart rate, tympanic temperature, blood pressure)
- Physical Examination
- HS severity score assessments

6.4.2.4 VISIT 3 (WEEK 12)

- Review of adverse events (if any)
- Review of HS progress
- Concomitant medication collection
- Vital Signs (Respiratory rate, heart rate, tympanic temperature, blood pressure)
- Physical Examination
- HS severity score assessments

6.4.2.5 VISIT 4 (WEEK 24)

- Review of adverse events (if any)
- Review of HS progress
- Concomitant medication collection
- Vital Signs (Respiratory rate, heart rate, tympanic temperature, blood pressure)
- Physical Examination
- HS severity score assessments

6.5 STANDARD CARE AND ADDITIONAL TO STANDARD CARE PROCEDURES

Standard Care Procedures		
Procedure	**Time/Visit**	**Dosage/Volume**
Resorcinol 15%/topical clindamycin	Week 0	Applied to affected area as needed when there is flare.

Additional To Standard Care		
Procedure	**Time/Visit**	**Dosage/Volume**
FUE	Visit 1	NA

6.6 RANDOMISATION

A staff member of Sinclair Dermatology not involved in this study will randomise participants into the intervention and controlled group using the program from www.randomizer.org in a 1:1 stratification ratio. The treatment group will be treated with follicular unit extraction. Due to the study design, investigators and participants are unable to be blinded as to which participants will be in the treatment or control group. As there will be 24 participants in this study, numbers 1-24 will be randomly allocated to either control or treatment group using randomizer.org prior to recruitment of the study. Participants will then be allocated a number in the order in which they are recruited in the study and subsequently will be placed in the group that the number has been randomised into.

6.7 STUDY METHODOLOGY

Participants will be taken to the procedure room. Local anaesthesia will be injected into diseased hair-bearing area on affected axillae or groin on both sides. FUE will be performed by the investigator (who is experienced in FUE) using 0.8/0.9/1.0 mm Ertip® punch. The extracted hair follicular unit samples will be analysed histologically to confirm complete removal of the pilosebaceous units. Specimens are not kept for future analysis as they will be discarded.

At each study visit, the dermatologist will count the number of abscesses and nodules (as part of standard routine care) and will document this in their medical record. This will help to also score the HiSCR, IHS4, HS-PGA4 and participants will ask to rate their pain using the numerical pain score. Scoring will be done by the principle investigator as well as another dermatologist at Sinclair Dermatology.

Participants will be given a sheet (Appendix 3) where they can complete a diary of whenever they have a flareup which will identify the date of the flareups, which side and their pain level. This will be reviewed at each study visit.

Biospecimens are not kept by the investigators and are discarded once reviewed to confirm removal of pilosebaceous units.

7. STUDY POPULATION

This study will enroll male and female patients aged ≥18 years who are diagnosed with mild to moderate HS.

The study will consist of 24 recruited participants.

7.1 Recruitment Procedure

Participants will be recruited through Sinclair Dermatology.

7.2 Inclusion Criteria

Participants eligible for inclusion in the study must fulfil all the following criteria:

1. Male and female patients with HS aged ≥18 years.
2. Mild-moderate HS defined by Hurley stage 1 up to 2A
3. Minimum diagnosis of 3 months prior to baseline
4. Active HS present for at least 3 months from initial diagnosis.

7.3 Exclusion Criteria

Participants fulfilling any of these criteria are not eligible for inclusion in this study:

1. Current treatment with antibiotics, retinoids, immunosuppressants or biologic agents at the discretion of the investigator/research team.
2. Extensive scarring.
3. Absence of terminal hairs in target areas.
4. Previous laser hair removal in target areas.
5. Pregnant or lactating women.

7.4 Consent

An informed consent form will be provided by the investigator to be used in the patient informed consent process. As per clinical investigation regulations, written informed consent must be obtained prior to participation in the study.

The information will be given in both written and oral form. This communication will be in a language understandable to the patient and may not include any language that seems to waive any of the patient's legal rights to release the Investigator, Sponsor or the Institution from liability or negligence.

The Investigator must provide sufficient time for a prospective patient to consider whether or not to participate and must completely answer any questions raised by the patient. The investigator will explain to the patient that withdrawal from the study will be possible at any time without detriment to the participants' current or prospective medical care.

The procedure as well as topical clindamycin will be performed free of cost to the participants. Following conclusion of the study, any consequent follow-up visits and or consultations with associated medical personnel, not directly related to the study will be charged at their normal costing schedules. An example is continuing to visit the appropriate dermatologist for treatment and management of other dermatological conditions.

8. Participant Safety and Withdrawal

8.1 Risk Management and Safety

As part of standard routine care, the treating dermatologist will enquire about the patient's current medications, allergies and past medical history to ensure the procedure is appropriate. Furthermore, the participants will be given local anaesthetic to minimize pain from follicular unit extraction. Participants, as part of standard routine care, may also be given pain analgesia to manage their as well as other medications to manage the inflammation in their hidradenitis suppurativa.

8.2 Handling of Withdrawals

Participants are free to withdraw from the study at any time without providing reason(s) for withdrawal and without prejudice to further treatment. The reason(s) for withdrawal will be documented in the CRF.

Collected data from study visits will be stored at Sinclair Dermatology Clinical Trials Unit for 5 years then discarded. Samples and data will not be kept for future separate studies.

8.2.1 Withdrawal Criteria

Participants may be considered withdrawn if they state an intention to withdraw, fail to return for visits, or become lost to follow-up for any other reason.

The investigator should withdraw the subject from study if he/she believes that there is insufficient response to follicular unit extraction or that continuation would be detrimental to the subject's well-being. The investigator has the right to terminate the study at any time in case of a serious adverse event (SAE) or if special circumstances arise that may disadvantage the participant, making further treatment impossible.

They may be withdrawn from the study for any of the following reasons:

- consumption of medication which may interfere with study measurements
- severe AE assessed as treatment-related by the investigator
- non-compliance with protocol
- unsatisfactory therapeutic effect
- Lost to follow-up
- Withdrawal for another reason

Participants withdrawing from the study will be encouraged at the time of withdrawal, to complete the evaluations listed for the Unscheduled visit with an explanation as to why the participant is withdrawing from the study. The aim is to record data in the same way as for participants who have completed the study.

Even if participants are not withdrawn from the study, they can choose to withdraw their permission for their anonymous data and de-identified samples to be kept for future study use.

Any adverse events (AE)s that are continuing at the time of withdrawal from the study, should, wherever possible, be followed to resolution or stabilization, whichever is earlier.

Reasonable efforts will be made to contact participants who are lost to follow-up. These must be documented in the participant's file.

8.3 Risk Management and Safety

If a participant becomes ill during the study, or in the event that they suffer an injury as a result of the study, participants will be advised to contact the study doctor. The study doctor will arrange for appropriate treatment.

Participants will be made aware there is a risk of embarrassment and discomfort arising from the disclosure of personal and sensitive information. The study site will ensure that all participants' personal information is de-identified in all study records and in any future publication of study results.

8.3.1 DEFINITIONS

An adverse event (AE) is any untoward, undesired, or unplanned event in the form of signs, symptoms, disease, or laboratory or physiologic observations occurring in a person given an investigational product (where applicable). The event does not need to be causally related to the investigational product (where applicable). An AE includes, but is not limited to, the following:

- Any clinically significant worsening of pre-existing condition
- An AE occurring from overdose of an investigational event (where applicable), whether accidental or intentional.
- An AE occurring from abuse (i.e., use for nonclinical reasons) of an investigational product/procedure (where applicable)

A serious adverse event (SAE) is an AE that:

- Results in death
- A life-threatening AE: An AE is considered 'life-threatening', if in the view of the investigator, it places the patient at an immediate risk of death.
- Requires inpatient hospitalization or an extension of an existing hospitalization
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect
- Results in an important medical event.

Important medical events are AE's that may not result in death, be life-threatening, or require hospitalization may be considered SAEs when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in hospitalization, or the development of drug dependency or drug abuse.

Hospitalization is the official admission to a recognized hospital. Hospitalization or prolongation of a hospitalization constitutes a criterion for an AE to be serious; however, it is not in itself considered an SAE. In the absence of an AE, any hospitalization or prolongation of a hospitalization should not be recorded by the investigator as a serious adverse event.

8.3.2 ADVERSE EVENT AND SERIOUS ADVERSE EVENT RECORDING AND REPORTING

Determination of AEs will be based upon the signs and symptoms identified during the physical examination and on clinical evaluation of the participant. The signs and symptoms will be recorded using standard medical terminology. Any identified AEs and SAEs will be reported from the signing of the informed consent form to the end of Week 24 (end of study). The investigator must instruct the patient to report any AEs and SAEs during this time period.

The investigator will also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse events to the regulatory and the Human Research Ethics Committee (HREC).

8.3.3 Adverse Event Follow Up

All AEs will be followed through the end of the study and be recorded as “continuing” if not resolved at the last study visit. All SAEs will be followed to resolution or stabilization.

8.3.4 Definition of Screening Failures

A “screening failure” is a participant from whom informed consent is obtained and documented in writing (that is, the subject or legally authorized representative as required by local law and regulations, and the participant’s carer has signed an informed consent form), but who has not commenced receiving the study medication.

8.3.5 Definition of completed participants

A participant will be deemed to have completed the study once the participant had follicular unit extraction or had topical clindamycin and followed up as part of standard routine care up to week 24.

8.4 Replacements

There will be no replacements if participants withdraw.

9. Statistical Methods

9.1 Sample Size Estimation & Justification

Given that this is a pilot study assessing the effectiveness of FUE for HS management, we have decided 24 participants is required as a pilot. The result of this study will be used to inform sample size calculations for future studies as well as account for 20% rate of lost to follow-up.

9.2 Power Calculations

This pilot study uses 12 participants in each group (intervention vs controlled) and results from this will allow us to calculate the sample size required for statistical power in future clinicals studies.

9.3 Statistical Methods To Be Undertaken

Abscess and nodule counts will be recorded and then compared at the study visits up to week 24. This will be done using the paired t test.

Paired t test will also be used to compare changes in HS-PGA, IHS4 and HiSCR scores between the treated and control sites.

10. Storage of Blood and Tissue Samples

10.1 Details of where samples will be stored, and the type of consent for future use of samples

Specimen collected from FUE will be used for histopathology analysis but will not be stored at Sinclair Dermatology. It will be discarded into the biohazard bins.

11. Data Security & Handling

11.1 Details of where records will be kept & How long will they be stored

Medical records including source documents and photography during the study visits at Sinclair Dermatology will be kept on Sinclair Dermatology premises within the Clinical Trials Unit and medical record keeping software. Records will be retained for 5 (five) years following completion and study close-out.

Collected data will be kept in Microsoft Excel at Sinclair Dermatology clinical trials unit server as an electronic file. It will be password-protected as well as being stored in a password protected area of the server that only investigators will have access to this file.

11.2 Confidentiality and Security

The Investigator will assure that all participants' anonymity will be maintained and that their identities are protected from unauthorized parties. The disclosure of personal information from another party or organization to the investigators, even if for the purpose of seeking initial expression of interest in the clinical trial, must be authorized by each individual to whom the information relates. Study findings will be recorded on a computer and stored in accordance with local data protection laws. All data collected will be de-identified. Data security will be upheld by storing the hard copies in a securely locked patient file room. Security of the room is maintained through a password-protected lock. Only authorized study personnel will have access to the room.

11.3 Ancillary data

As part of standard routine care, participants may have photographs taken with their consent for medical care of their hidradenitis suppurativa, to allow comparisons after treatments. As such, collection of photos will be indefinite in the medical record keeping software. However, no additional photographs out of standard routine care is required for this clinical study.

12. Consumer Involvement

Participants involved in this study are consumers as we are improving their quality of life with a procedure. There has been no consumer input into the design of the study.

13. Direct access to source data/documents

The Principal Investigator and Associate Investigators involved in this study will permit study-related monitoring, audits, HREC review and regulatory inspection(s) as well as providing direct access to source data/documents.

14. ETHICS

14.1 ETHICAL CONDUCT OF THE STUDY

The study will be conducted in accordance with the protocol, legal and regulatory requirements, and the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice (ICH GCP), and the Declaration of Helsinki.

14.2 STUDY MONITORING

The Principal Investigator is responsible for the overall monitoring of the study. The Investigators will be responsible for ensuring the completeness, consistency, and compliance of the protocol. All Associate investigators will maintain patient confidentiality in accordance with local regulations. By agreeing to participate in this study, the investigators agree to ensure that any issues are resolved in a timely manner.

14.3 REPORTING OF SAFETY ISSUES AND SERIOUS BREACHES OF PROTOCOL OR ICH GCP

In the event of any prohibition or restriction imposed by an applicable regulatory authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the investigational product, HREC should be informed immediately.

In addition, the investigator will inform HREC immediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of ICH GCP that the investigator becomes aware of.

14.4 PROTOCOL AMENDMENTS

Any change in the study procedure and patient visits will require a protocol amendment. An investigator cannot make any changes without prior approval from HREC, unless it is done to eliminate or prevent any immediate danger to the patients. A protocol amendment made to eliminate an immediate danger to a patient may be implemented immediately, however the alteration must be documented, and submitted to the HREC within 5 working days. All protocol amendments must be reviewed and approved using the same process as the original protocol.

14.5 TERMINATION OF STUDY

Premature termination of this study may occur because of a regulatory authority decision, change in opinion of the institutional review board/ethics committee, or investigational product safety problems, or at the discretion of the Principal Investigator.

If the Principal Investigator terminates or suspends the study, the Investigator will inform the HREC and provide them with a detailed written explanation. Upon, study completion, the investigator will provide the HREC, and regulatory authorities with final reports and conclusions as required by regulations.

15. FUNDING

Dr Bevin Bhoyrul is the Principal Investigator of this study and is a consultant dermatologist at Dr Rodney Sinclair Pty Ltd, trading as Sinclair Dermatology. Follicular unit extraction and study visits will be conducted at Sinclair Dermatology. Dr Bhoyrul will bear the costs for activities conducted in the study.

No member of the research team will receive a personal financial benefit from this study other than their ordinary wages.

16. PUBLICATION POLICY

The authors will have the right to publish the procedure, results of and conclusions from this study, participant to this clause and in strict accordance with copyright law. Images taken during the study may be used in medical, scientific or non-scientific publications, including medical journals, textbooks and electronic publications. Study participants may choose to opt out of the use of their photographs in publications by not ticking the relevant box in the Consent Form page. All reasonable steps will be taken to de-identify participants' facial features and any other identifying features from such publications.

APPENDIX 1

a) Description of inflammatory and follicular pattern phenotype of hidradenitis suppurativa b) Hurley staging of hidradenitis suppurativa b) Hidradenitis suppurative- Physician's Global Assessment (HS-PGA) c) Numerical rating scale (NRS) for pain[19-23]

a) Description of follicular vs inflammatory phenotype

Follicular (Pattern A)	**Inflammatory (Pattern B)**
Follicular lesions on a background of comedones and nodules with occasional abscesses. More common in women, less commonly fistular (tunnel) formation, non-coalescent.	Predominately abscesses with occasional nodules in the absence of comedones. More frequently in men, more severe disease with more frequent fistulae and scarring

b) Hurley-staging.

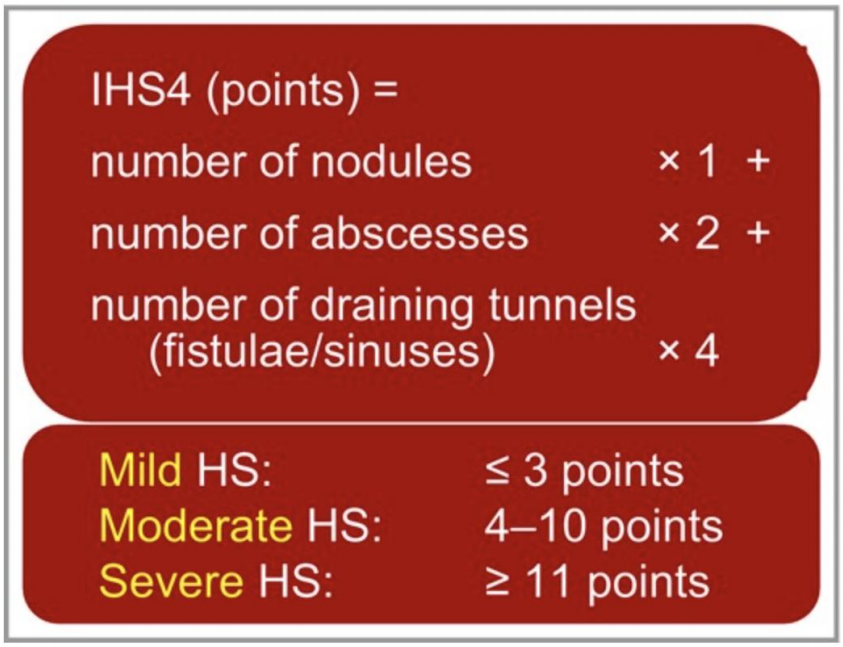
Hurley stage	
I	Abscess formation, single or multiple, without sinus tracts and cicatrization
II	Single or multiple, widely separated, recurrent abscesses with tract formation and cicatrization
III	Diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area

c) Hidradenitis Suppurativa Physician's Global Assessment (PGA)

HS-PGA	
Clear (score = 0)	0 abscesses, 0 draining fistulas, 0 inflammatory nodules, and 0 noninflammatory nodules
Minimal (score = 1)	0 abscesses, 0 draining fistulas, 0 inflammatory nodules, and presence of noninflammatory nodules
Mild (score = 2)	0 abscesses, 0 draining fistulas, and 1–4 inflammatory nodules; or 1 abscess or draining fistula and 0 inflammatory nodules
Moderate (score = 3)	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 (score = 4)	2–5 abscesses or draining fistulas and ≥ 10 inflammatory nodules

Very severe (score = 5)	severe	> 5 abscesses or draining fistulas

d) International Hidradenitis Suppurativa Severity Score System (IHS4)



e) Numerical rating scale (NRS)

APPENDIX 2

Schedule of assessments

Assessment/Procedure	Screening (Initial assessment)	Visit 1 (may occur same day as screening visit)	Visit 2	Visit 3	Visit 4
Demographic information and eligibility: **- Inclusion/exclusion criteria** **- Height and weight** **- Medical History** **- Concomitant medications** **- Weight**	**X**				
Consent	**X**	**X**			
Medical History and concomitant medications review		**X**	**X**	**X**	**X**
Clinical assessments (as part of standard routine care)	**X**	**X**	**X**	**X**	**X**
Follicular unit extractio n and sample analysis for intervention group		**X**			
Topical for controlled group		**X**			
Hidradenitis suppurativa assessment scores	**X**	**X**	**X**	**X**	**X**

Appendix 3: Diary sheet for documentation of flareups.

Date of flareup	Where is the flare up (e.g. right underarm, left underarm, left groin, right groin or other)? If other, please specify.	How would you rate this pain out of 10?

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