Optimizing Intralesional Triamcinolone Dosing for Hidradenitis Suppurativa Protocol

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Contents

1.0 BACKGROUND/SIGNIFICANCE

Hidradenitis suppurativa (HS) is a chronic recurrent inflammatory disease of hair follicles primarily localized to the axillae, inframammary folds, suprapubic and inguinal skin, upper inner thighs, perineum, and buttocks. Early manifestations of HS include tender nodules that may progress into fluctuant abscesses. As the disease advances, recurrent inflammatory nodules and abscesses may develop permanent connecting dermal tracts ("tunnels").[1] Although the pathogenesis is poorly understood, HS is considered a disorder of follicular occlusion.[2] The most recent estimate of HS prevalence in the United States is 0.10%; however, African Americans, females, and young adults are disproportionately affected.[3] The median age of onset in females is 19 years and in males is 23 years. However, cases are reported in pediatric patients as early as 13 years old.[4] Furthermore, HS is associated with a wide range of comorbidities, including cardiovascular, endocrine, gastrointestinal disorders, and psychiatric comorbidities, such as depression, anxiety, bipolar illness, and schizophrenia.[5-7] There is not only greater disability and decreased quality of life compared to all other dermatologic conditions, but also the complexity and profound debilitation make management difficult and costly.[8]

For more than 50 years, a standard therapy for acute HS flares has been the subcutaneous injection of triamcinolone, a fluorinated corticosteroid, into inflammatory nodules, abscesses and sinus tracts. The proposed mechanism involves activation of the glucocorticoid receptor, which blocks synthesis of leukotrienes and reduces the production of proinflammatory cytokines, including interleukin-1. Additionally, this therapy is may inhibit cytotoxic T-cell activation.[9]

Previous studies documented the efficacy of intralesional triamcinolone in decreasing erythema, edema, suppuration, and size of lesion, as well as patient-reported pain.[10] Despite the proposed benefits of therapy, no standard effective dose has been established. Riis et al.[10] conducted a prospective case series utilizing 10 mg/mL with the volume of injection based on patient lesion size, while Alvarez et al.[11] performed a prospective open-label study injecting 40 mg/mL with a volume of 0.2-1 mL per fistulous tract.

At the Albert Einstein College of Medicine-Montefiore Hidradenitis Suppurativa Center (HSC), high-dose intralesional triamcinolone (20-40 mg/mL) is consistently used for hundreds of patients with inflammatory lesions. In an earlier retrospective review, it was reported that patients receiving high-dose intralesional triamcinolone (ILTAC) experienced improvement of disease state, quality of life, and overall satisfaction.[12] Additionally, the majority of patients were interested in receiving future ILTAC injections as clinically indicated. Given the immense disease burden of HS, optimizing ILTAC dosing may dramatically improve medical management and quality of life (QOL) for our patients. We are seeking to determine optimal dosing by comparing response parameters of low dose (10 mg/mL) versus two concentrations of high-dose (20mg/mL and 40 mg/mL) triamcinolone injections in HS patients with active inflammatory lesions.

Due to the complex pathophysiology of HS, treatment poses a formidable challenge, incorporating antibiotics, anti-androgens and anti-inflammatory drugs. The latter includes systemic biologics and local corticosteroid injections.[13] The standard corticosteroid used for acute nodules, abscesses, and draining sinus tracts reduces pain, redness, and swelling in 12- to

24-hours. Although ILTAC is considered a standard of care for acute flares in HS, studies documenting efficacy and side effect profile at varying doses are remarkably sparse.

Fajgenbaum et al.[14] performed a double-blinded, randomized, placebo controlled trial comparing normal saline (NS), intralesional TAC 10 mg/mL (ILTAC-10), and intralesional TAC 40 mg/mL (ILTAC-40). There were no statistically significant differences between the varying concentrations and normal saline.[14] However, the study was seriously under powered given the subject and lesion randomization parameters. Another major flaw in the study design was the randomization of lesions as opposed to participants. With this approach, systemic effects of the injection were not taken into account and likely obscured interpretation of the results. Additionally, they did not compare to an intralesional TAC 20 mg/mL (ILTAC-20) group, which limits the insight into varying concentrations of high-dose triamcinolone injections. Perhaps, the most disastrous failing of the study design was limiting the injection volume to 0.1 mL regardless of lesion size. Pain reduction and patient satisfaction were evaluated from paper surveys mailed to participants at the conclusion of the study but the potential for recall bias undermined the data integrity. Markers of inflammation and side effects of ILTAC were not addressed. It is noteworthy that one prospective study showing the benefit of ILTAC-40 based the volume injected on lesion size, using up to 2 mL per lesion.[11]

2.0 STUDY DESIGN

a) Study Design

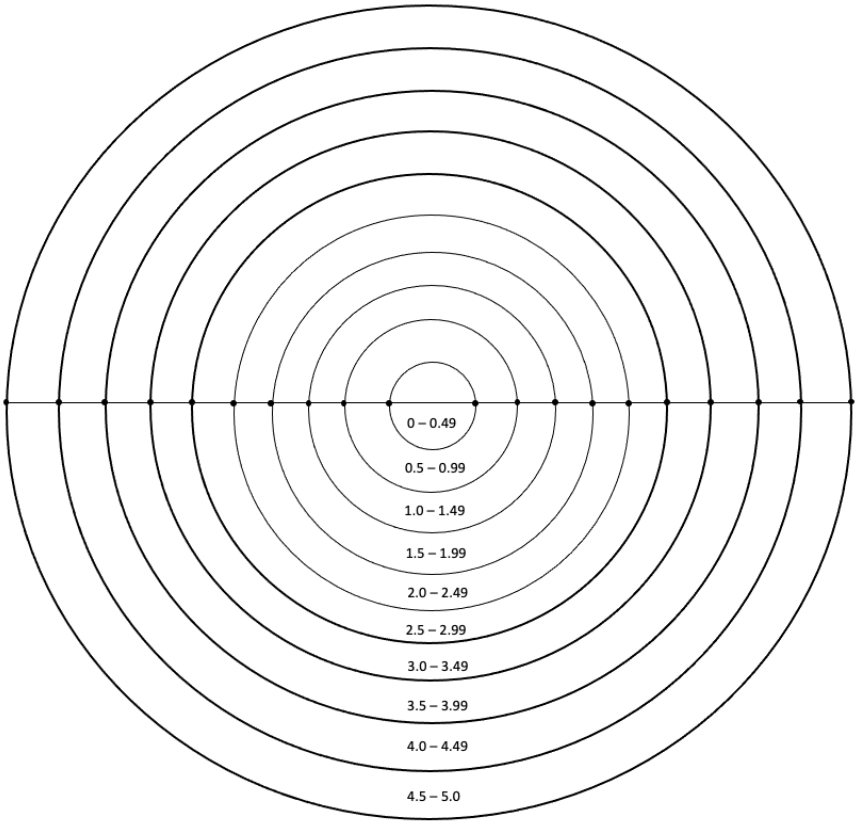
A double-blinded, randomized, placebo-controlled study examining the relative efficacy of ILTAC-10, ILTAC-20, and ILTAC-40 versus placebo for acute flares of HS in subjects with moderate to severe HS.

The duration of the study will be approximately 4 weeks for each enrolled patient and will include an initial screening/randomization/treatment visit and a 4-week follow-up period.

During the initial visit, subjects who meet the study's eligibility criteria will be randomized to receive either ILTAC-10, ILTAC-20, ILTAC-40, or normal saline (NS) placebo in a 1:1:1:1 ratio. The volume of ILTAC or NS administered is calculated based on the largest dimension of the HS lesion, which is measured by its greatest width in mm. For example, if a lesion is irregular in shape, measuring 22mm by 18mm, 22mm will be the largest dimension used for calculating volume. The administered volume (ml) is scaled by increments of 0.2ml, which corresponds to the HS lesion size, and ranges from 0.2ml to 2.0ml. The maximum volume of either ILTAC-10, ILTAC-20, ILTAC-40 or NS administered to any given HS lesion is 2.0ml.

Figure 1. Hidradenitis Suppurativa Lesion Size and Volume of administration of ILTAC-10, ILTAC-20, ILTAC-40, or normal saline placebo.

HS lesion size (cm)	Volume (ml)
0.0 – 0.49	0.2
0.5 – 0.99	0.4
1.0 – 1.49	0.6
1.5 – 1.99	0.8
2.0 – 2.49	1.0
2.5 – 2.99	1.2
3.0 – 3.49	1.4
3.5 – 3.99	1.6
4.0 – 4.49	1.8
4.5 – 5.0	2.0



Follow-up

The follow-up period will be of 4 weeks and will consist of 2 phone calls and 2 live visits, at week 2 and 4 after randomization.

A schedule of activities is shown in Section 5.0f.

Study Objectives

Aim 1

- To compare the efficacy of ILTAC-10, ILTAC-20, and ILTAC-40 versus placebo for the treatment of acute HS flares.

Aim 2

- To investigate the side effect profile of ILTAC-10, ILTAC-20, and ILTAC-40 in the treatment of acute HS flares.

Aim 3

- To compare patient reported satisfaction and impact on quality of life regarding ILTAC-10, ILTAC-20, ILTAC-40 versus placebo for the treatment of acute HS flares.

Hypothesis

Given the generally accepted anti-inflammatory property of fluorinated corticosteroids, it is anticipated that treatment with ILTAC will be superior to normal

saline for both acute HS flares, as well as patient reported outcome measures including HS-related pain and satisfaction after treatment. Additionally we expect a dose-depending response when ILTAC-40 is compared to ILTAC-20 and ILTAC-10. Our preliminary findings[12] suggest there will be no difference in subject side effect profile between the ILTAC and normal saline treatment arms.

Target population and recruitment methods

The target population will include patients over the age of 13 receiving care at the HSC for mild to advanced HS disease experiencing an acute flare. Patients will be recruited by the PI and study personnel (recruitment strategies are detailed in section 4).

Inclusion Criteria

- Age > 13 years old.
- Subject must voluntarily sign and date an informed consent, approved by an independent ethics committee / institutional review board.
- Subject is willing to comply with the procedures in this protocol.
- The subject must be diagnosed with HS and receiving care at HSC
- Subjects with Hidradenitis Suppurativa Physician Global Assessment (HS-PGA) score between 2 and 5 (Appendix A).[15]
- The subject must have an inflamed nodule or abscess at the time of enrollment.

Exclusion Criteria

- The subject has an HS-PGA score of 0 or 1
- The subject has received ILTAC less than 8 days prior to the initial visit.
- The subject does not have capacity to consent to the study.
- The subject is has taken systemic steroids at least 4 weeks prior to the time of enrollment.
- The subject has a known allergy or history of adverse reaction to steroids.
- The subject is pregnant.
- Subjects who have received a biologic therapy two weeks before and during the study period.

Outcomes

Primary Outcome

- Change from baseline in NRS pain scale at week 4 (Appendix B).[16]

Secondary Outcomes

- Change from baseline in NRS pain scale at days 2, 6, and 14.
- Difference in change from baseline in NRS pain scale at days 2, 6, 14, and 28 between ILTAC-10, ILTAC-20, ILTAC-40.
- Change from baseline in HS-PGA score at week 2 and 4.
- Difference in change from baseline in HS-PGA score at week 2 and 4 between ILTAC-10, ILTAC-20, ILTAC-40.
- Change from baseline in objective markers of inflammation (c-reactive protein [CRP], erythrocyte sedimentation rate [ESR], and interleukin-6 [IL-6]) at week 2 and 4.

- Change from baseline in subjective markers of inflammation (erythema, edema, and suppuration) at week 2 and 4.
- Change from baseline in lesion size at week 2 and 4.
- Difference in change from baseline in lesion size at week 2 and 4 between ILTAC-10, ILTAC-20, ILTAC-40.
- Change from baseline in Patient-Reported Outcomes Measurement Information System (PROMIS) measure of physical functioning at days 2, 6, 14, and 28. [17]
- Difference in change from baseline in PROMIS at days 2, 6, 14, and 28 between ILTAC-10, ILTAC-20, ILTAC-40.
- Proportion of subjects reporting side effects at days 2, 6, 14, and 28.
- Difference in proportion of subjects reporting side effects at days 2, 6, 14, and 28 between ILTAC-10, ILTAC-20, ILTAC-40.
- Baseline patient satisfaction.
- Change from baseline in patient satisfaction at days 2, 6, 14, and 28.
- Serum cortisol and ACTH levels at week 2 and 4.
- Change in serum cortisol and ACTH levels from week 2 to 4.

Number of Treatment Groups

This study is a parallel study with 4 treatment groups: normal saline, ILTAC-10, ILTAC-20, or ILTAC-40, receiving 2 mL of assigned treatment in up to 3 anatomic areas (maximum of 3 mL per patient).

Randomization and Blinding

The groups will be randomized in a 1:1:1:1 ratio and the total volume injected will be recorded at each visit. Randomization and treatment preparation will be performed by the Montefiore Research Pharmacy. Clinical assessments will be conducted by an assessor blind to the treatment allocation. The assessor will undergo training to achieve consistent, unbiased clinical assessments, including HS-PGA, subjective markers of inflammation, and survey administration. The unblinded study team member will maintain confidentiality with respect to participant allocation.

Safety Outcomes

Ongoing monitoring for Adverse Events (AEs), as defined by Albert Einstein College of Medicine's "Reportable Events Policy[18]," will occur throughout the study. Adverse events will be reported to the IRB.

Data Safety Monitoring Plan

Monitoring will be performed following the "Data and Safety Monitoring Policy" required by the Albert Einstein College of Medicine Institutional Review Board. The Data Safety Monitoring Committee (DSMC) will consist of Dr. Holly Kanavy and Dr. Juan Lin. They will have the responsibility for ensuring data and safety monitoring along with the PI who is ultimately responsible for the ongoing monitoring and safety of clinical protocols. The primary functions of the DSMC are as follows:

1. Review/assure protocol compliance.
2. Review all internal and external serious adverse reports, investigator alerts, action letters, and other safety reports.

3. Implement and determine the adequacy of DSM plans of all approved protocols.

The committee will meet quarterly or more frequently as needed. They will review serious (grade 3 or higher) adverse events from the study. In the event that the DSMC decides that a revision is warranted the committee will immediately notify the PI of the study. The DSMC has the authority to close trials to patient accrual should the risk to patients be excessive or outweigh the potential benefits of the study. All study suspensions and closures will be forwarded to the IRB from the DSMC.

b) Schedule of Study Visits

- Visit 1 (Initial visit)

  Participant eligibility will be assessed according to inclusion and exclusion criteria in 2.0a. A member of the study team will describe the study and answer any of the participant's questions. The participant will then be consented and enrolled. The initial visit and all subsequent visits will include documentation of NRS pain scale (Appendix B), HS-PGA, Hurley Stage (Appendix C), clinical markers of inflammation, and lesion size (as specified in our standard approach to care.[19] Photographs of the lesions will be obtained. The study personnel will administer a patient satisfaction survey and the PROMIS questionnaire, which will take 15 minutes to complete (Appendix D and Appendix F [or Appendix G if pediatric]). Chart review will record demographic information (age, gender, race, ethnicity, smoking status, and BMI) and complete blood count (CBC), basic metabolic profile (BMP), liver function tests (LFT), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), and interleukin-6 (IL-6). The lab work is a standard of care at the HSC independent of research objectives. The patient will receive an injection, not to exceed 2 mL per anatomic area, in up to 3 anatomic areas (total of 3mL). The patient will be counseled regarding potential side-effects of the treatment (Appendix H) and asked to monitor accordingly. No other changes to the patient's HS medication regimen will be made for the duration of the study.

- Phone Contact 1 (2-day post-treatment)

  Since triamcinolone has a half-life of 18 to 36 hours, the initial patient follow-up will be a phone call at 2 days post-injection, lasting 15 minutes. Study personnel will administer a patient satisfaction survey and the PROMIS questionnaire (Appendix D, and Appendix F [or Appendix G if pediatric]). Additionally, patients will be asked if they experienced any side effects, including thinning/atrophy of skin, acneiform lesions, capillary dilation, and/or dyschromia.

- Phone Contact 2 (6 days post-injection)

  This 15 minute phone call will be 6 days post-injection and will involve administering the patient satisfaction survey, the PROMIS questionnaire, and questions about side effects.

- Visit 2 (2 weeks post-injection)
  - The initial screening visit examination will be repeated at week 2. Additionally, the patient will be asked to identify side effects. A patient

satisfaction survey as well as the PROMIS questionnaire will also be administered, again lasting 15 minutes. Blood count (CBC), basic metabolic profile (BMP), liver function tests (LFT), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), and interleukin-6 (IL-6) will be routinely obtained at the two week visit. Serum 8 AM cortisol and ACTH will also be routinely obtained at the two week visit. The two week visit and lab draw are the standard of care for HS patients independent of research objectives.

- Visit 3 (Final visit - 4 weeks post-injection)
    - The initial screening visit examination will be repeated at week 4. Additionally, the patient will be asked to identify side effects. A patient satisfaction survey as well as the PROMIS questionnaire will also be administered, again lasting 15 minutes. Blood count (CBC), basic metabolic profile (BMP), liver function tests (LFT), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), and interleukin-6 (IL-6) will be routinely obtained at the four week visit. Serum 8 AM cortisol and ACTH will also be routinely obtained at the four week visit. The four week visit and lab draw are the standard of care for HS patients independent of research objectives.

Intralesional Triamcinolone Treatment Administration

While HS patients may have multiple sites of symptomatic disease, participants on this protocol will only receive treatment in up to three anatomic regions. These will generally be the most bothersome lesions to the patient. Networks of sinus tracks or the confluence of multiple nodules will be excluded as target treatment sites.

Treatment will only be administered by the blinded clinician on this study. Additionally, the clinical assessor and the patient will be blinded to the treatment group assigned. The patient will either receive normal saline, ILTAC-10, ILTAC-20, or ILTAC-40. Each lesion will be injected with up to 2 mL in up to 3 anatomic areas. The maximum treatment volume is 3 mL.

c) Outcome Measures Pertaining to Each Aim

- *Aim 1:* To compare efficacy of ILTAC-10, ILTAC-20, and ILTAC-40 versus placebo, we will measure the change from baseline in pain, objective and subjective markers of inflammation, physical functioning, and lesion size as well as comparing these changes among the different treatment groups. Change from pain baseline will be quantified by comparison of the NRS pain scale across different treatment groups (Appendix B).[16] Objective markers of inflammation include c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and interleukin-6 (IL-6), which will be obtained from chart review of standard of care initial, 2 week, and 4 week follow-up HS visit. Erythema and edema will be measured clinically based on a 5-point ordinal scale (Appendix E). Suppuration will be measured on a dichotomous scale, by the presence or absence of purulent drainage from the lesion. Physical functioning will be measured by change from baseline in the Patient-Reported Outcomes Measurement Information System (PROMIS) measure of physical functioning.[17] Separate forms will be administered for adult and pediatric participants. A one point change, either positive (improvement) or negative (decline), will be considered clinically meaningful (Appendix F and Appendix G).[20] Lesion size will be measured in centimeters at baseline and during the week 2 and 4 visit.

- *Aim 2:* Side effects of ILTAC-10, ILTAC-20, and ILTAC-40 that will be investigated include thinning/atrophy of the skin, acneiform lesions, capillary dilations, and dyschromia.[21] Hypothalamic-pituitary-adrenal (HPA) axis suppression will be obtained through chart review of standard of care serum 8 AM cortisol and ACTH levels at week 2 and 4 follow-up HS visits. Self-evaluations will be conducted by the patient and documented via telephone interviews. Clinical-evaluations will be conducted at the follow-up visits.
- *Aim 3:* To measure the patient's satisfaction after treatment, we will compare the results from the satisfaction survey between the different treatment groups at baseline, day 2, day 6, week 2, and week 4. The patient satisfaction survey will address disease control, and response to injection (in terms of pain, drainage, and lesion size), and quality of life (Appendix D).

3.0 STUDY POPULATION

a) Study Population: The study population includes patients >13 years old with HS by a physician. All patients with HS-PGA greater than 2 will be included, regardless of comorbidities.

b) Sample Size/Power Calculation: The primary outcome of our trial is a reduction in pain measures before and after treatment. We will have 4 groups: normal saline, ILTAC-10, ILTAC-20, and ILTAC-40. Of importance, these ILTAC doses are currently used for HS flares and are standard treatment for other dermatologic conditions, such as keloids.[10, 11, 14, 22] To estimate the sample size needed in each arm, we assumed that the pain score in our patients is normally distributed. The mean difference in pain score between normal saline and ILTAC-10 is estimated to be 1, with a standard deviation of 1, at baseline and also two days later, as is consistent with our clinical experience. We also assumed a range of correlations (0.1-0.9) that may be observed for a patient's pain score at the multiple follow-up points. When comparing normal saline and ILTAC-10, the most conservative of the treatment arms in terms of pain change, it is shown that at least 30 participants per arm are required to detect the anticipated effects (see Table 1 below for power calculations). Additionally, given that we expect to see a greater reduction in pain with ILTAC-20 and ILTAC-40, we will be more than sufficiently powered to detect the large pain reductions anticipated in the ILTAC-20 and ILTAC-40 groups. This conservative approach allows for the detection of a clinically meaningful change, as any substantial reduction in pain would result in clinical utilization of ILTAC.

Table 1. Tests for Two Groups of Pre-Post Scores. Numeric Results for Comparing Mean Change in a Repeated Measures Design. Null Hypothesis: $\delta = 0$. Alternative Hypothesis: $\delta \neq 0$. Results assuming a t-test. [23]

Target Power	Actual Power	N1	N2	N	δ	σ(T1)	σ(T2)	ρ	σ(Diff)	Alpha
0.8	0.81021	30	30	60	1	1	1	0.1	1.342	0.05
0.8	0.81347	27	27	54	1	1	1	0.2	1.265	0.05
0.8	0.8004	23	23	46	1	1	1	0.3	1.183	0.05
0.8	0.80321	20	20	40	1	1	1	0.4	1.095	0.05
0.8	0.80704	17	17	34	1	1	1	0.5	1	0.05
0.8	0.81254	14	14	28	1	1	1	0.6	0.894	0.05
0.8	0.82111	11	11	22	1	1	1	0.7	0.775	0.05
0.8	0.83633	8	8	16	1	1	1	0.8	0.632	0.05
0.8	0.87068	5	5	10	1	1	1	0.9	0.447	0.05

- Report Definitions
    i. Target Power is the desired power value (or values) entered in the procedure. Power is the probability of rejecting a false null hypothesis. Actual power is the power obtained in this scenario. Because N1 and N2 are discrete, this value is often (slightly) larger than the target power. N1 and N2 are the number of items sampled from each population. N is the total sample size, N1 + N2. δ is mean change of group 2 minus the mean change of group 1 assuming the alternative hypothesis. σ(T1) and σ(T2) are the standard deviations of measurements at time 1 and time 2, respectively. P is correlation between a pair of observations made on the same subject. σ(Diff) is the standard deviation of the paired differences, assumed equal for the two groups. Alpha is the probability of rejecting a true null hypothesis.
- Summary Statements
    i. A 2-by-2 repeated measures design consists of two groups of subjects, each measured at two time points. In this case, the primary goal of the study is to compare the change across time in group 1 to the change across time in group 2. Sample sizes of 30 in group 1 and 30 in group 2 achieve 81% power to detect a difference in mean changes of 1.0 with a standard deviation of 1.0 at the first time point, a standard deviation of 1.0 at the second time point, and a correlation between measurement pairs of 0.100. The significance level (alpha) is 0.050 using a two-sided, two-sample t-test.

c) Inclusion Criteria
- Age > 13 years old.
- Subject must voluntarily sign and date an informed consent, approved by an independent ethics committee / institutional review board.
- Subject is willing to comply with the procedures in this protocol.

- The subject must be diagnosed with HS and receiving care at HSC
- Subjects with Hidradenitis Suppurativa Physician Global Assessment (HS-PGA) score between 2 and 5 (Appendix A).[15]
- The subject must have an inflamed nodule or abscess at the time of enrollment.

Exclusion Criteria

- The subject has an HS-PGA score of 0 or 1
- The subject has received ILTAC less than 8 days prior to the initial visit.
- The subject does not have capacity to consent to the study.
- The subject is has taken systemic steroids at least 4 weeks prior to the time of enrollment.
- The subject has a known allergy or history of adverse reaction to steroids.
- The subject is pregnant.
- Subjects who have received a biologic therapy two weeks before and during the study period.

d) Justification of exclusion of pregnant patients: ILTAC-40 is pregnancy category C.
e) Subjects who do not have the capacity to consent will not be enrolled in the study.
f) The sources of research material include the photographs and patient surveys, which will be obtained by individually identifiable living human subjects. The photographs are part of routine clinical care. The patient surveys will be for the specific purpose of research.

4.0 PARTICIPANT RECRUITMENT

a) Those receiving care through the HSC at Montefiore Medical Center will be invited to enroll in the trial. It is estimated that that the research team will have the capacity to screen and enroll 5 new patients per clinic. The day prior to each clinic, research personnel will use a random number generator to identify 8 potentially eligible patients based on inclusion/exclusion criteria, considering refusals or ineligibility, during the screening. After obtaining informed consent, patients will be enrolled in the study.
b) We will register our study on https://clinicaltrials.gov.
c) It will be explained that treatment will not be different for patients who do not wish to enroll in the study. Study participation is completely voluntary, and patients can choose to withdraw at any time.
d) Patients privacy will be protected by assigning each participant a unique identifier for any analysis (see below for details).

5.0 INFORMED CONSENT

a) Informed Consent containing all of the necessary elements is provided.
b) The Informed Consent Process
   - The PI or clinician will obtain informed consent.
   - Prior to the initiation of any study related procedures, the potential subjects will be given a copy of the most recent IRB stamped and approved informed consent to read.
   - The PI or clinician will discuss the specifics of the study including but not limited to the purpose of the research, procedures, time commitment, required tasks, alternative

treatments, benefits, risks, confidentiality, etc. in a comprehensible (non-scientific) manner, using language readily understandable by the subject.

- The person consenting will assure the voluntariness of the subject. Subjects will be told that participation is voluntary and that, if they do not consent, they will not be penalized in any way.
- A private, confidential setting will be provided for the potential subject to read and discuss the informed consent free from coercion, undue influence or constraints of time. All subjects will be given a chance to ask questions and express concerns. They will be given the option to take the consent home and discuss it with family, friends, and/or health care providers.
- After a subject and the person conducting the consenting signs and dates the consent, the subject will be given a copy of the signed informed consent form.
- An enrollment note will be written in the EMR document as to who obtained consent, how, when, were questions asked and answered, and that a copy of the informed consent was given to the subject.

c) No waiver/alteration of the informed consent process is requested.

d) Informed consent will be obtained by the parent or legal guardian of all minors. In addition minors between the ages of 13 to 17 who are capable to give assent with sign the same Informed Consent Document as the parent or legal guardian.

e) The treatment is for research purposes and there will be no cost to the patient. The initial visit, the four week follow up, and the laboratory tests are standard clinical care and will be billed to the patient's insurance. No remuneration will be offered for participation. Montefiore HIPAA procedures and policies will be followed.

f) Study Calendar

	Enrollment	Day 2	Day 6	Week 2	Week 4
Photograph	X			X	X
HS-PGA	X			X	X
Treatment: NS, ILTAC-10, ILTAC-20 or ILTAC-40	X				
Patient Satisfaction Survey	X	X	X	X	X
PROMIS Survey	X	X	X	X	X
NRS Pain Scale	X	X	X	X	X
Side Effect Assessment		X	X	X	X

6.0 RISK/BENEFIT

a) The protocol here is considered greater than minimal risk, due to injection of medication or placebo. The initial risk of injection is temporary discomfort during the treatment. Potential side effects of the treatment include thinning/atrophy of the skin, acneiform lesions, capillary dilations, dyschromia, and HPA axis suppression. A psychological risk

of disappointment may occur if participation does not lead to a clinical improvement. Breach of confidentiality is a possible risk if data is lost or stolen.

b) Risk will be minimized as follows:
Confidentiality will be maintained by keeping records in secure areas in the clinic. Patient-identifiable materials, such as paper administered surveys and consent forms will be kept in secure areas, i.e., lockable storage rooms. Computer files are accessible via password-protected computers that kept in lockable rooms. All lab personnel that work with patient data have passed human subject protection courses, and certification of this is on file in the IRB office. No patient identifiers will be included in the analytic datasets. All results will be presented and published as aggregate results without patient identifiers.

c) In our experience to date, patients are pleased to be involved in the HSC and gratified to assist in further advancing our current knowledge of this poorly understood and immensely debilitating disease. Potential benefits for individual patients include improvement or resolution of HS symptoms. Additionally, patients will be receiving personalized care by a team of experts, as well as the psychological benefits of receiving care at a multidisciplinary treatment center. There will be additional benefit for the group of HS patients as we learn to optimize the treatment of acute flares.

d) Data will be stored in a de-identified manner, using a CGP-coding scheme. The Safe Harbor method will be used to de-identify one PHI specific identifier (patient name) by creating a unique code for each patient. The list of patient names and codes will be kept in a separate and secure location, on an Idrive on Montefiore Computer system, with restricted access only to approved individuals. The data will be carefully entered and analyzed in statistical programs. The data will be checked and edited by members of the research team. No individuals other than members of the research team, will have access to the data. All lab personnel that work with patient data or samples have passed human subject protection courses, and certification of this is on file in the IRB office. All physical data will be maintained at a designated site, in a locked cabinet, in a locked room.

7.0 DATA ANALYSIS

a) Statistical Methods
We will analyze the data from the study using an intention to treat approach. Categorical variables, including presence of side effects, drainage, and physical function, will be analyzed with chi square tests. Continuous variables, such as NRS pain scale, markers of inflammation, and lesion size, will be analyzed by T-test. Sensitivity analyses or exploratory analyses may be performed to examine the effect difference for race or gender. In the unlikely case patients do not receive the treatment they will still be randomized for analysis using a per protocol approach. All statistical tests will be 2-sided, with $p<0.05$ considered significant.

b) There will be no interim analysis or early stopping of the study.

c) Confounding and effect modification will be addressed by randomization of the subjects and blinding of both the investigators and the participants.

d) If subjects are lost to follow up, they will be analyzed in the group to which they were initially randomized.

8.0 DATA QUALITY CONTROL AND DATABASE MANAGEMENT

a) Data will be stored in a de-identified manner, with a CGP-coding scheme. The Safe Harbor method will be used to de-identify one PHI specific identifier (patient name) by creating a unique code for each patient. The list of patient names and codes will be kept in a separate and secure location, on an Idrive on Montefiore Computer system, with restricted access only to approved individuals. The data will be carefully entered and analyzed in statistical programs such as excel. The data will be checked and edited by the members of the research team. No individuals other than members of the research team will have access to the data. All lab personnel that work with patient data or samples have passed human subject protection courses, and certification of this is on file in the IRB office. All physical data are kept in a designated site, in a locked cabinet in a lockable room.

b) Subject treatment assignments will remain blinded until the final subject has completed follow up and all data has been recorded and validated. Urgent, immediate unblinding due to medical emergency may be authorized by the Investigator. All instances of subject unblinding will be documented in the study record.

9.0 REFERENCES

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10.0 APPENDICES

Appendix A: HS-PGA Score

Disease severity, measured by HS-PGA, is defined as follows:

- 0, clear
- 1, minimal: noninflammatory nodules
- 2, mild: fewer than 5 inflammatory nodules or 1 abscess/draining fistula with no inflammatory nodules
- 3, moderate: 5 or more inflammatory nodules, or 1 abscess/draining fistula and at least 1 inflammatory nodule, or 2 to 5 abscesses/draining fistulas and fewer than 10 inflammatory nodules
- 4, severe: 2 to 5 abscesses/draining fistulas and at least 10 inflammatory nodules
- 5, very severe: more than 5 abscesses/draining fistulas

Appendix B: NRS Pain Scale

The patient-reported NRS for pain is an 11-point NRS ranging from 0 (no pain) to 10 (worst possible pain).

Appendix C: Hurley Staging

- Stage 1: Single of multiple abscesses without sinus tract formation or scarring
- Stage 2: Recurrent abscesses with one or more sinus tracts and scarring widely separated by normal skin
- Stage 3: Diffuse involvement with multiple sinus tracts and no intervening normal skin

Appendix D: Patient Satisfaction Survey

1. What is your race?
    a. Caucasian
    b. Black/African American
    c. American Indian/Alaska Native
    d. Asian Indian
    e. Chinese
    f. Filipino
    g. Japanese
    h. Korean
    i. Vietnamese
    j. Other Asian
    k. Native Hawaiian
    l. Guamanian/Chamorro
    m. Samoan
    n. Other Pacific Islander
    o. Other _____ (Please specify)

2. What is your ethnicity?
    a. Hispanic/Latinx/Spanish origin
    b. Not Hispanic/Latinx/Spanish origin

3. Please rate your current flare or lesions.
    a. Clear
    b. Minimal
    c. Mild
    d. Moderate
    e. Severe
    f. Very severe

4. On a scale from 0 to 10, with 0 being an example of someone with no pain and 10 being the worst pain possible, where would you rate your pain at rest?

5. On a scale from 0 to 10, with 0 being an example of someone with no pain and 10 being the worst pain possible, where would you rate your pain when HS lesions present today are touched?

6. How would you rate the drainage of your current flare?
   a. None
   b. A little
   c. Some
   d. A lot
   e. The most I've ever had

7. Using the following scale:

   (5) Excellent (4) Very good (3) Good (2) Fair (1) Poor

   how would you rate your current……

   a. Disease control?
   b. Mobility?
   c. Ability to sleep for the past two nights?
   d. Mood?
   e. Quality of life?

8. How satisfied are you with the steroid injections?
   1. Very satisfied
   2. Satisfied
   3. Neutral
   4. Dissatisfied
   5. Very dissatisfied

9. If response to number 8 was dissatisfied or very dissatisfied, please explain why.

10. Would you be willing to undergo steroid injections again?
    1. Yes
    2. No

10a. If response to number 10 was no, please explain why.

Appendix E: Ordinal Scale to Grade Erythema and Edema

Visual assessment ordinal scale to grade skin erythema

- 0, no erythema
- 1, very faint erythema: skin has a very light pink color
- 2, faint erythema, skin reaction is more apparent with clear borders but is still pink with more intensity
- 3, bright erythema, erythema is apparent in bright pink and borders are clearly defined
- 4, skin is bright red, borders are very well defined, capillaries and bruising may be visible

Assessment ordinal scale to grade edema

- 0, no edema (soft)
- 1, moderate to severe edema (soft to hard)
- 2, fluctuant

Appendix F: PROMIS – Adult Physical Functioning

PROMIS® Item Bank v2.0 – Physical Function – Short Form 10a

Physical Function – Short Form 10a

Please respond to each question or statement by marking one box per row.

		Not at all	Very little	Somewhat	Quite a lot	Cannot do
PFA1	Does your health now limit you in doing vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFC36r1	Does your health now limit you in walking more than a mile (1.6 km)?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFC37	Does your health now limit you in climbing one flight of stairs?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA5	Does your health now limit you in lifting or carrying groceries?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA3	Does your health now limit you in bending, kneeling, or stooping?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
		Without any difficulty	**With a little difficulty**	**With some difficulty**	**With much difficulty**	**Cannot do**
PFA11	Are you able to do chores such as vacuuming or yard work?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA16r1	Are you able to dress yourself, including tying shoelaces and buttoning your clothes?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB26	Are you able to shampoo your hair?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA55	Are you able to wash and dry your body?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFC45r1	Are you able to sit on and get up from the toilet?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Appendix G: PROMIS – Pediatric Physical Functioning

PROMIS Pediatric Item Bank v2.0 – Mobility– Short Form 8a

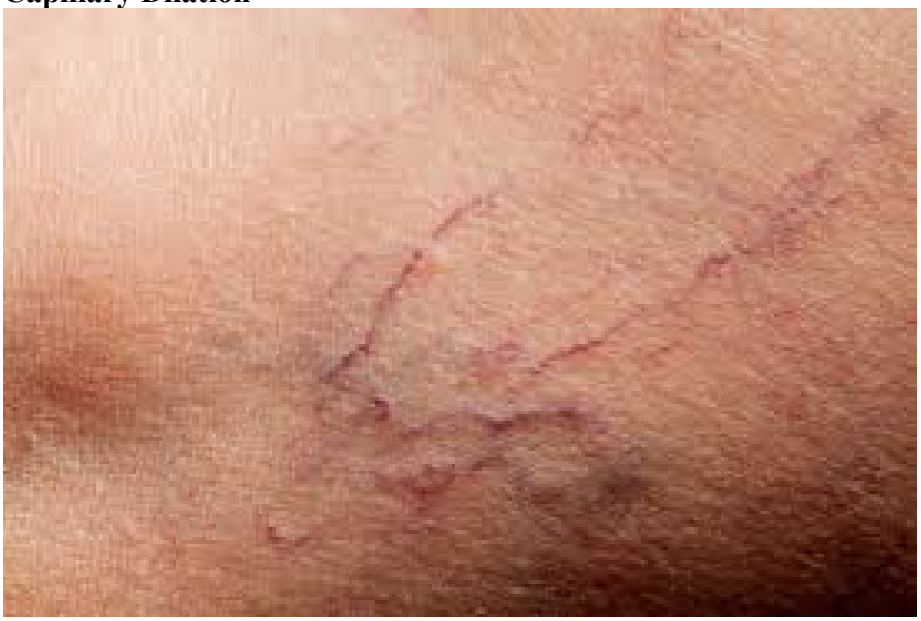
Pediatric Mobility – Short Form 8a

Please respond to each question or statement by marking one box per row.

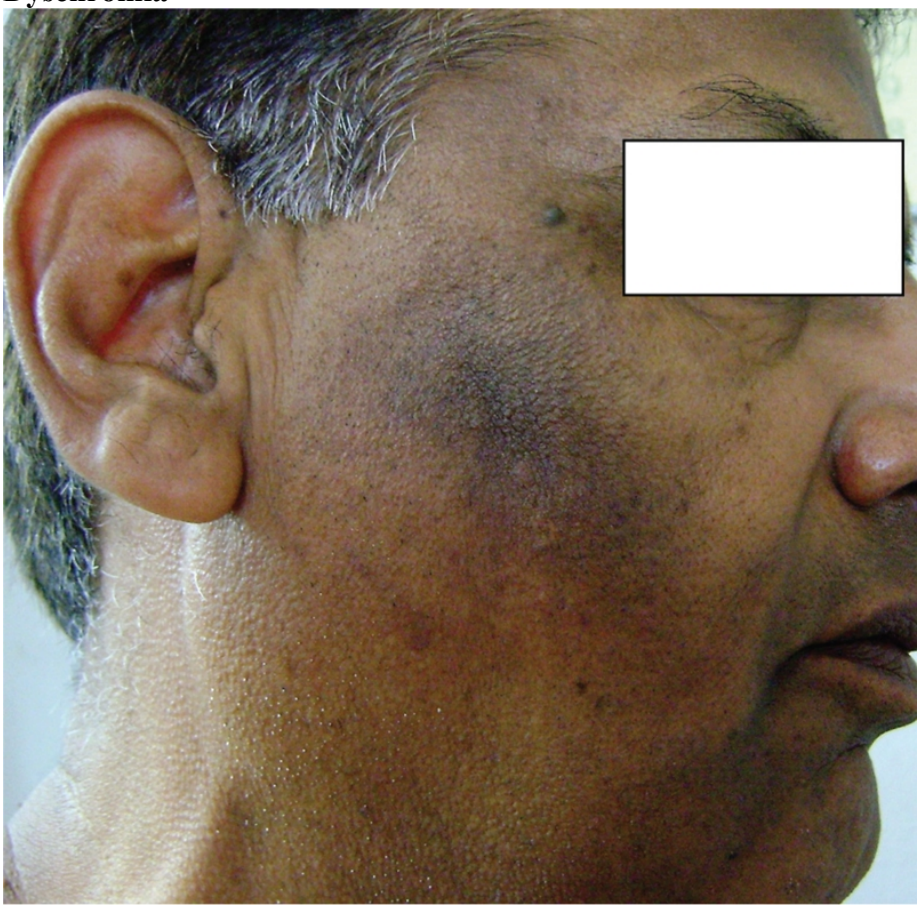
	In the past 7 days…	With no trouble	With a little trouble	With some trouble	With a lot of trouble	Not able to do
235R1r	I could do sports and exercise that other kids my age could do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
4124R1r	I could get up from the floor	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
236R1r	I could keep up when I played with other kids	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
3892R1r	I could move my legs	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
2646R1r	I could stand up by myself	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
4185R1r	I could stand up on my tiptoes	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
2707R2r	I could walk up stairs without holding on to anything	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
5023R1r	I have been physically able to do the activities I enjoy most	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Appendix H: Intralesional Triamcinolone Side Effects

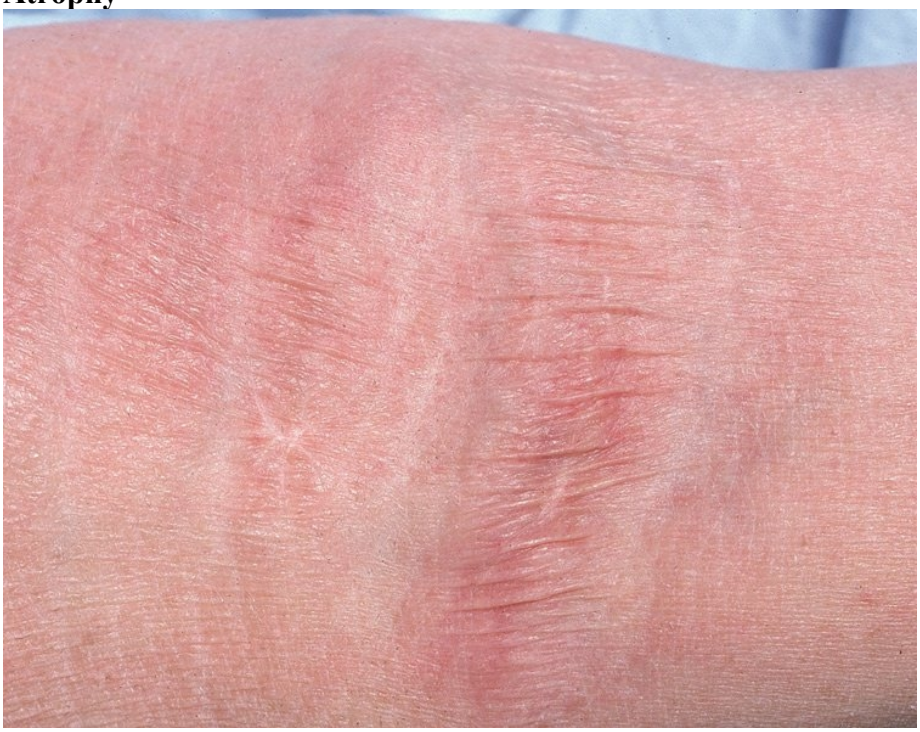
Capillary Dilation



Dyschromia



Atrophy



Acneiform Lesions