

Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000118: Hidradenitis Suppurativa Area and Severity Index
(HASI)
Letter of Intent

Administrative Structure:

Description of the submitter including, but not limited to, principal investigator(s), working group member(s), institutions, and contact information not contained within the cover letter.

The submitting group is an international assembly of clinicians and researchers with expertise related to the condition of interest (hidradenitis suppurativa [HS]). The principal investigators are Joslyn Kirby and Noah Goldfarb and senior investigators are Michelle Lowes and Afsaneh Alavi. The group members, their institutions, and contact information are listed below.

United States: Joslyn S. Kirby¹, Noah Goldfarb², Michelle Lowes³

- 1) Penn State University, Department of Dermatology, Hershey, Pennsylvania
- 2) University of Minnesota, Department of Dermatology, Minneapolis, Minnesota
- 3) Rockefeller University, Department of Dermatology, New York, New York

Canada: Afsaneh Alavi⁴

- 4) University of Toronto, Department of Medicine, Division of Dermatology, Ontario, Canada

Concept(s) of Interest (COI) for Meaningful Treatment Benefit:

A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities).

The HASI is a measure of disease activity and assesses the severity and extent of active (inflamed) HS, rather than changes due to skin damage. The tool was designed to capture signs of inflammation that are most apt to change with treatment intervention, especially in the setting of a clinical trial. Recently, an international multi-stakeholder group reached consensus on a core outcome set of domains for HS clinical trials and made recommendations for assessments of HS physical signs.¹⁻³ The recommendations specifically suggested that physical signs include assessment of anatomic location and surface area.¹ In contrast, the vast majority of existing HS disease activity instruments do not incorporate surface area, but rely on specific terminology to categorize lesions, require discrimination among lesion morphologies, and lesion counting for each type of lesion – all of which can be problematic.⁴⁻¹¹ First, the terminology used to classify lesions has been vague and agreement among experts on interpretation has been poor.¹² Secondly, physician's ability to clinically classify lesion type is poor, as judged by sonographic evaluation.¹³ Also, counting lesions of any type can be difficult, even for clinical lesions that are relatively more defined, such as acne¹⁴ and actinic keratosis¹⁵. Supporting this, recent studies have shown that Hurley staging and other common measures used in clinical trials have generally moderate intra-rater and inter-rater reliability.^{16,17}

Provide a conceptual framework for the COA(s)

The HASI is designed to assess constructs of HS that are dynamic and indicate meaningful treatment benefit. Focus groups and interviews with clinicians and researchers, as well as review of the extant literature, were the basis for the design. The themes that arose were related to assessment of HS surface

area, as well as signs of disease activity including erythema, induration, and open skin. Surface area assessment is performed of several distinct anatomical areas, separately for the right and the left of some sites, and includes body sites not expressly measured many extant measures. Intensity scores for Inflammatory Color Change (redness or violaceous coloration), Inflammatory Induration, Open Skin Surface, and Tunnels are assigned for each.

Context of Use for COA Qualification:

Targeted study population including a definition of the disease and selection criteria for clinical trials (e.g., baseline symptom severity, patient demographics, comorbidities, language/culture groups).

The targeted study population includes adults, with HS, who are participating in a clinical trial. The HASI is designed to be completed by a trained clinician, who can read and write fluently in English. HS is defined by chronic outbreaks of boils or nodules over 6 or more months with a minimum of at least two boils in the axilla, groin, genitals, under the breasts, perianal, neck, and/or abdomen.¹⁸

Targeted study design and statistical analysis plan (includes the role of the planned COA in future drug development clinical trials, including the planned set of primary and secondary endpoints with hierarchy, if appropriate).

The HASI is being developed for use as a primary or secondary outcome measure in HS clinical trials to demonstrate changes in the HS clinical severity.

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***
- ***Other study setting specifics (e.g., inpatient versus outpatient)***

COA Type: ClinRO

1. Thorlacius L, Ingram JR, Villumsen B, et al. A core domain set for hidradenitis suppurativa trial outcomes: an international Delphi process. *Br J Dermatol*. 2018.
2. Thorlacius L, Ingram JR, Garg A, et al. Protocol for the development of a core domain set for hidradenitis suppurativa trial outcomes. *BMJ open*. 2017;7(2):e014733.
3. Thorlacius L, Garg A, Ingram JR, et al. Towards global consensus on core outcomes for Hidradenitis Suppurativa research: An update from the HISTORIC consensus meetings I and II. *Br J Dermatol*. 2017.
4. Grant A, Gonzalez T, Montgomery MO, Cardenas V, Kerdell FA. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled crossover trial. *J Am Acad Dermatol*. 2010;62(2):205-217.
5. Sartorius K, Emtestam L, Jemec GB, Lapins J. Objective scoring of hidradenitis suppurativa reflecting the role of tobacco smoking and obesity. *Br J Dermatol*. 2009;161(4):831-839.

6. Sartorius K, Lapins J, Emtestam L, Jemec GB. Suggestions for uniform outcome variables when reporting treatment effects in hidradenitis suppurativa. *Br J Dermatol*. 2003;149(1):211-213.
7. Chiricozzi A, Faleri S, Franceschini C, Caro RD, Chimenti S, Bianchi L. AISI: A New Disease Severity Assessment Tool for Hidradenitis Suppurativa. *Wounds : a compendium of clinical research and practice*. 2015;27(10):258-264.
8. Zouboulis CC, Tzellos T, Kyrgidis A, et al. Development and validation of the International Hidradenitis Suppurativa Severity Score System (IHS4), a novel dynamic scoring system to assess HS severity. *Br J Dermatol*. 2017;177(5):1401-1409.
9. Kimball AB, Jemec GB, Yang M, et al. Assessing the validity, responsiveness and meaningfulness of the Hidradenitis Suppurativa Clinical Response (HiSCR) as the clinical endpoint for hidradenitis suppurativa treatment. *Br J Dermatol*. 2014;171(6):1434-1442.
10. Ingram JR, Hadjieconomou S, Piguet V. Development of core outcome sets in hidradenitis suppurativa: systematic review of outcome measure instruments to inform the process. *Br J Dermatol*. 2016;175(2):263-272.
11. Hessam S, Scholl L, Sand M, Schmitz L, Reitenbach S, Bechara FG. A Novel Severity Assessment Scoring System for Hidradenitis Suppurativa. *JAMA Dermatol*. 2018;154(3):330-335.
12. Lipsker D, Severac F, Freysz M, et al. The ABC of Hidradenitis Suppurativa: A Validated Glossary on how to Name Lesions. *Dermatology (Basel, Switzerland)*. 2016;232(2):137-142.
13. Wortsman X, Moreno C, Soto R, Arellano J, Pezo C, Wortsman J. Ultrasound in-depth characterization and staging of hidradenitis suppurativa. *Dermatol Surg*. 2013;39(12):1835-1842.
14. Lucky AW, Barber BL, Girman CJ, Williams J, Ratterman J, Waldstreicher J. A multirater validation study to assess the reliability of acne lesion counting. *J Am Acad Dermatol*. 1996;35(4):559-565.
15. Ianhez M, Fleury Junior LF, Bagatin E, Miot HA. The reliability of counting actinic keratosis. *Archives of dermatological research*. 2013;305(9):841-844.
16. Ovadja ZN, Schuit MM, van der Horst C, Lapid O. Inter- and Intrarater Reliability of the Hurley Staging for Hidradenitis Suppurativa. *Br J Dermatol*. 2018.
17. Thorlacius L, Garg A, Riis PT, et al. Interrater agreement and reliability of outcome measurement instruments and staging systems used in hidradenitis suppurativa. *Br J Dermatol*. 2019.
18. Zouboulis CC, Del Marmol V, Mrowietz U, Prens EP, Tzellos T, Jemec GB. Hidradenitis Suppurativa/Acne Inversa: Criteria for Diagnosis, Severity Assessment, Classification and Disease Evaluation. *Dermatology (Basel, Switzerland)*. 2015;231(2):184-190.