Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000120: Scratch Sensor
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.

Principal Investigator: Steve Xu MD FAAD
Institutions:

- Sonica LLC
- Northwestern University Feinberg School of Medicine | Department of Dermatology

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).

Quantification of pruritus by measuring scratching behavior

Provide a conceptual framework for the COA(s)

Itch, similar to pain, is challenging to quantify objectively. Existing patient reported outcomes (PROs) for itch are subjective and suffer inter- and intra-patient variability—this is particularly true in pediatric patients who are disproportionately affected by atopic dermatitis. Measuring and quantifying scratching and rubbing motions, natural responses to itch, offers an objective method to quantify scratch in a patient's naturalistic environment.

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).

Pediatric (2 years to 11 years), adolescents (12 to 17 years), and adults with mild, moderate, or severe atopic dermatitis. Subjects of any language/cultural group, baseline severity, demographic group, or comorbidities would qualify.

***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*).**

We foresee this COA to act as either a primary, secondary, or exploratory endpoint of the efficacy of topical, oral, or injectable therapeutics for atopic dermatitis.

We will test the performance of this COA in assessing scratch time and scratch events in pediatric (2-11 years), adolescent (12-17 years), and adult patients with mild, moderate, or severe atopic dermatitis. The diagnosis of atopic dermatitis (AD) will be confirmed by a board-certified dermatologist using the American Academy of Dermatology diagnostic guidelines.[1] In this validation cohort, we will use direct

visualization by infrared camera during sleep for AD patients as well as direct visual observation and/or video recording during the day whenever feasible. This may occur in the home setting or in the inpatient setting. The sensor's quantification of scratch time and scratch events will then be compared against clinical research assistant coding of scratching time and scratching events observed on video camera footage.

The outputs of the sensors to act as a primary, secondary, or exploratory endpoints are as follows:

- Scratch time: this is an aggregate of time spent scratching with intervals reported in 0.1 seconds.
- Scratch events: this is an event where scratching is detected for at least 1 second without a gap of more than 0.5 seconds in scratching.
- Scratch intensity: this is determined by assessing the absolute displacement of the internal inertial motion unit of the sensor, which relates to the rigor of any individual scratching behavior.

We foresee the ability of this COA to data to demonstrate changes in scratch time, scratch events, and scratch intensity between an intervention group and a placebo group across time.

Our validation algorithm was completed with 200 minutes of scratch data. Thus, we propose at least 200 minutes of validation scratch data in the affected population. This is in line with previously reported systems for scratch algorithm validation using an wrist-watch actigraph where a total of 282 minutes of scratching data was obtained from 18 atopic dermatitis patients and 6 healthy normal (11.7 minutes per subject night for atopic dermatitis patients).[1] The overall accuracy for actigraphy to measure scratch has been disappointing. We hypothesize that the wide range of sampling frequencies in the ADAM sensor will exceed the accuracy of actigraphy based systems.

We propose conducting an n=20 test in atopic dermatitis patients where at least 30% (6 subjects) of subjects are pediatric (2 years to 11 years) and 30% (6 subjects) are adolescents (12-17 years of age). A single sensor placed on the dorsum of the dominant hand is proposed. Prior works have demonstrated that sensor placement on the dominant upper extremity limb is sufficient to capture total scratching behavior; in other words, sensors placed on all extremities provide only a marginal amount of additional information.[2]

Each subject will contribute between 1-7 subject nights (at least 21 subject nights). Sub-group analysis will be conducted on the sensor and algorithm's performance for total aggregate subject nights, age groups, and an individual patient basis. Bland-Altman plots will be generated for all comparisons with visually coded infrared camera to determine the presence or absence of fixed bis. In addition, patients will be surveyed for device usability and software ease of use via the Systems Usability Index®, a well-established tool to assess the complexity of technology.

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***
  We expect this tool to be used in any geographic location, language or cultural group. There is no available evidence suggesting that scratching is dependent on culture or demographics.

- ***Other study setting specifics (e.g., inpatient versus outpatient)***
  We expect this tool to be used in both inpatient, outpatient, and home settings.

COA Type: Digital Health Technology (DHT) COA

References:

1. Moreau A, Anderer P, Ross M, Cherny A, Almazan T, Peterson B. Detection of Nocturnal Scratching Movements in Patients with Atopic Dermatitis Using Accelerometers and Recurrent Neural Networks. *IEEE Journal of Biomedical and Health Informatics.* 2017;22(4):2168-2194.
2. Noro Y, Omoto Y, Umeda K, et al. Novel acoustic evaluation system for scratching behavior in itching dermatitis: rapid and accurate analysis for nocturnal scratching of atopic dermatitis patients. *J Dermatol.* 2014;41(3):233-238.