STATISTICAL ANALYSIS PLAN
24 February 2020 DRAFT

CONFIDENTIAL

A Multicenter, Randomized, Open-label, Phase 3 Long-term Safety Study of Topically Applied Sofpironium Bromide (BBI-4000) Gel, 5% and 15% in Subjects with Axillary Hyperhidrosis

PROTOCOL NUMBER: BBI-4000-CL-303

SPONSOR:

Brickell Biotech, Inc.
5777 Central Ave., Suite 102
Boulder, CO 80301

NCT03627468

PREPARED BY

Rho, Inc.
2635 E NC Hwy 54
Durham, NC 27713
Telephone: (919) 408-8000
Fax: (919) 408-0999

Version: 0.3

DOCUMENT VERSION CONTROL

Version Number	Date	Comments/Changes
0.1	08 August 2019	First Draft
0.2	17 September 2019	Draft 2
0.3	09 October 2019	Draft 3
1.0	24 February 2020	Version 1.0

APPROVALS

Approved:

DocuSigned by:
Julian Garro
Signer Name: Julian Garro
Signing Reason: I approve this document
Signing Time: 25-Feb-2020 | 10:13:57 AM EST
CF556F08608345CA8FD9B40F656D28C3

Date: _____

Julian Garro

Senior Biostatistician III, Rho, Inc.

DocuSigned by:
Ping-Yu Liu
Signer Name: Ping-Yu Liu
Signing Reason: I approve this document
Signing Time: 24-Feb-2020 | 4:17:01 PM PST
76E122BB8DDB418CB857A9ED299F7617

Date: _____

Ping-Yu Liu

Biostatistician Consultant for Brickell Biotech, Inc.

DocuSigned by:
Deepak Chadha
Signer Name: Deepak Chadha
Signing Reason: I approve this document
Signing Time: 24-Feb-2020 | 4:33:49 PM PST
0392923DE86241A9B1C102CDDDC97EA1

Date: _____

Deepak Chadha

Chief Research and Development Officer, Brickell Biotech, Inc.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AE	Adverse event
ATC	Anatomic Therapeutic Chemical
BBI-4000	Sofpironium bromide
BMI	Body mass index
BP	Blood pressure
CRF	Case report form
CSR	Clinical study report
DLQI	Dermatology Life Quality Index
EOT	End of Treatment
FOCBP	Female of childbearing potential
HDSM-Ax	Hyperhidrosis Disease Severity Measure-Axillary
HDSM-Ax-11	Hyperhidrosis Disease Severity Measure-Axillary 11 item total
HDSM-Ax-7	Hyperhidrosis Disease Severity Measure-Axillary 7 item total
HidroQoL	Hyperhidrosis Quality of Life Index
HR	Heart rate
ICH	International Council on Harmonisation
IP	Investigational Product
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
PE	Physical exam
PGI-C	Patient Global Impression of Change
PGI-S	Patient Global Impression of Severity
PP	Per-Protocol
RR	Respiratory rate
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SE	Standard error
SI	Systeme International
TEAE	Treatment-emergent adverse event
TESAE	Treatment-emergent serious adverse event

UPT	Urine pregnancy test
WHO	World Health Organization

LIST OF IN-TEXT TABLES

1. PURPOSE OF THE ANALYSES

This statistical analysis plan (SAP) contains detailed information to aid in the implementation of the statistical analyses and reporting of the study data for use in the clinical study report (CSR) for study BBI-4000-CL-303. This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonisation (ICH) E9 Guideline, entitled Guidance for Industry: Statistical Principles for Clinical Trials, and the most recent ICH E3 Guideline, entitled Guidance for Industry: Structure and Content of Clinical Study Reports.

This SAP describes the data sets that will be used for analysis, as well as subject characteristics, safety, and clinician-reported and patient-reported perception of disease severity and improvement parameters. The details of the specific statistical methods stated in the protocol will be provided and any changes from the protocol-specified analyses will be documented in the SAP prior to database lock. If additional analyses are required to supplement the planned analyses described in this SAP after the database lock, they may be completed and will be described in the CSR. Table, figure, and listing specifications are provided as an attachment in a separate document. This SAP is based on the latest version of the BBI-4000-CL-303 protocol (Amendment 4) dated 6 May 2019.

2. PROTOCOL SUMMARY

The purpose of this Phase 3 study is to assess the long-term safety, local tolerability, and efficacy of sofpironium bromide gel, 5% and 15% when applied topically in subjects with axillary hyperhidrosis.

2.1 Study Objectives

Primary:

To evaluate the long-term safety and local tolerability of sofpironium bromide gel, 5% and 15% when applied topically in subjects with axillary hyperhidrosis.

Secondary:

- To evaluate the long-term effect of topically applied sofpironium bromide gel, 5% and 15% on Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax©) in subjects with axillary hyperhidrosis.
- To evaluate the long-term effect of topically applied sofpironium bromide gel, 5% and 15% on patient reported Dermatology Life Quality Index (DLQI) in subjects with axillary hyperhidrosis.

Other:

To evaluate the effect of topically applied sofpironium bromide gel, 5% and 15% on the Hyperhidrosis Quality of Life Index (HidroQoL©) in subjects with axillary hyperhidrosis. Only the first 100 subjects enrolled will complete this assessment.

2.2 Study Endpoints

2.2.1 Primary Endpoints

Primary endpoints include evaluation of the long-term safety and local tolerability of 5% and 15% sofpironium bromide gel when applied topically in subjects with axillary hyperhidrosis. Assessments will include:

- Adverse events
- Local tolerability assessments
- Vital signs (blood pressure, pulse rate, respiratory rate, and temperature)
- Laboratory tests (hematology, chemistry, and urinalysis) and pregnancy testing in Females of child-bearing potential (FOCBP)

2.2.2 Secondary Endpoints

The following secondary, efficacy endpoints will be analyzed:

- The proportion of subjects achieving ≥1-point improvement in HDSM-Ax-11 (11-item total) from baseline to end of treatment

- The proportion of subjects achieving ≥1.5-point improvement in HDSM-Ax-11 from baseline to end of treatment
- The proportion of subjects achieving ≥2-point improvement in HDSM-Ax-11 from baseline to end of treatment
- Change of HDSM-Ax-11 from baseline to end of treatment as a continuous measure

2.2.3 Other Endpoints

- The proportion of subjects achieving ≥1-point improvement in HDSM-Ax-7 (7-item total) from baseline to end of treatment
- The proportion of subjects achieving ≥1.5-point improvement in HDSM-Ax-7 from baseline to end of treatment
- The proportion of subjects achieving ≥2-point improvement in HDSM-Ax-7 from baseline to end of treatment
- Change of HDSM-Ax-7 from baseline to end of treatment as a continuous measure
- The proportion of subjects achieving ≥1-point improvement in the HDSM-Ax-11 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥1.5-point improvement in the HDSM-Ax-11 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥2-point improvement in the HDSM-Ax-11 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- Change in HDSM-Ax-11 from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and 52) as a continuous measure
- The proportion of subjects achieving ≥1-point improvement in the HDSM-Ax-7 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥1.5-point improvement in the HDSM-Ax-7 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥2-point improvement in the HDSM-Ax-7 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- Change in HDSM-Ax-7 from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and 52) as a continuous measure
- DLQI from baseline to each of Visits 5, 10, and 16 (Weeks 2, 6, 24, and 48)
- Patient Global Impression of Severity (PGI-S) summarized as frequency counts and percentages for each category (none, mild, moderate, severe, very severe) at each assessment, change from baseline as a 5x5 table with frequency counts and percentages at each post-baseline assessment
- Patient Global Impression of Change (PGI-C) summarized as frequency counts and percentages for each category (very much better, moderately better, a little

better, no change, a little worse, moderately worse, very much worse) at Visits 10 and 16 (Weeks 24 and 48)

Exploratory Efficacy Endpoint
HidroQoL from baseline to each of Visits 3 and 5 (Weeks 2 and 6); only the first 100 subjects enrolled in the study were to be eligible complete this assessment.

2.3 Overall Study Design and Plan

This is a multicenter, randomized, open-label, Phase 3 long-term safety study of topically applied sofpironium bromide gel, 5% and 15% in subjects with axillary hyperhidrosis.

A maximum of 300 subjects, at approximately 30 clinical sites, will be enrolled to obtain approximately 150 subjects that have completed 12 months of dosing and clinical assessments.

Subjects will be randomized 1:2 to receive either sofpironium bromide gel, 5% or 15% (100 subjects dosed with 5% gel and 200 subjects dosed with 15% gel). Subjects will apply the investigational product once daily at bedtime, to their axillae for 48 weeks.

Vital signs and adverse events will be collected at each visit. Local tolerability assessments will be collected at each post-Screening visit. Blood and urine samples will be collected and analyzed at Screening and then Week 6 (Visit 5), Week 24 (Visit 10), and Week 48 (Visit 16) for routine hematology, chemistry, and urinalysis parameters. Additionally, a urine pregnancy test for females of child-bearing potential will be collected and analyzed at each visit except at Week 2 (Visit 3), Week 6 (Visit 5), and Week 52 (Visit 17). Patient-reported outcomes HDSM-Ax, PGI-S, PGI-C, and DLQI will be recorded during the study at predefined time points. HidroQoL will be recorded at baseline, Week 2, and Week 6; only the first 100 subjects eligible and enrolled in the study will complete this assessment.

A total of 17 scheduled visits will take place over approximately 52 weeks.

2.4 Study Population

Subjects aged ≥9 years with a diagnosis of axillary hyperhidrosis.

2.5 Treatment Regimens

Either sofpironium bromide gel, 5% or 15%, will be topically applied to both axillae once daily at bedtime for 48 weeks.

2.6 Sample Size Determination

A maximum of 300 subjects, at approximately 30 clinical sites, will be randomized to receive either 5% or 15% sofpironium bromide gel in a 1:2 ratio to obtain approximately 150 subjects (50 subjects dosed for 48 weeks with 5% gel and 100 subjects dosed for 48

weeks with 15% gel) who have completed 12 months of dosing and clinical assessments. No formal sample size calculations were performed.

3. GENERAL ANALYSIS AND REPORTING CONVENTIONS

3.1 Reporting Conventions

The following is a list of general analysis and reporting conventions to be applied to this study, unless otherwise specified.

All data displays (tables, listings, and figures) will have a header showing the sponsor company name, protocol number, page number, and display status (i.e. "DRAFT" or "FINAL"), as well as a footer indicating path, file name, and run date/time. Summary tables and data listings will be summarized by treatment. All data collected per-protocol and all derived variables will be listed.

Categorical variables will be summarized using counts (n) and percentages (%) and will be presented in the form "n (xx.x)." If a count is 0, 0% will be shown for the percentage. If a percentage is 100%, 100% will be shown with no decimal place. To ensure completeness, summaries for categorical variables will include all categories, even if no subjects had a response in a particular category. Unless otherwise specified, the denominator for each percentage will be based on the number of subjects with available data in the population being summarized. If missing values are present, counts will be shown but will not be included in percentage calculations.

Continuous variables will be summarized using mean, standard deviation (SD), minimum, maximum, median, and number of subjects. The mean and median will be reported to an additional level of precision than the original observation in its rawest form (i.e. on the Case report form (CRF)), and the SD and other measures of variability (e.g. standard error (SE)) will be reported to two additional levels of precision than the original observations. The minimum and maximum will be the same precision as the original data. In general, any calculated values, such as those due to unit conversion, will be rounded to the same number of decimal places as the original data.

No tests of hypothesis of treatment group differences are planned; however, should they be performed as part of exploratory and ad hoc analyses, the associated p-value will be reported. All p-values will be rounded to 4 decimal places. P-values less than 0.0001 will be presented as "<0.0001" ; p-values greater than 0.9999 will be displayed as ">0.9999". Any p-values generated will be considered descriptive in nature; there will be no adjustments for multiple comparisons.

Summary tables and data listings:

- No preliminary rounding will be performed; rounding will only occur after analysis.

- Data from subjects excluded from an analysis population will be presented in the data listings but will not be included in the calculation of summary statistics, where applicable.

- Data from each subject will be separated by a blank line. Within a data listing, if a descriptive item appears line after line (e.g., repetition of a subject number, date, visit, etc.), only the first occurrence will be displayed (e.g., in Listing of Vital Signs, subject number, date and visit will only be displayed on first row when presenting all parameters collected at same visit). Repetition of actual results or outcomes (e.g., Adverse Events (AEs), lab results, vital sign values, etc.) will not be collapsed.

- Data listings will be sorted by site, subject, treatment, and week and/or time of assessment, unless otherwise noted.

- When change from baseline is calculated, baseline is the last observation obtained prior to dosing of the study drug.

Mock tables and data listings will be provided as attachments to this analysis plan. Minor changes to the mocks after formal SAP approval will not necessitate re-approval unless changes to the text of the SAP are required.

All statistical deliverables will be produced, validated, and reviewed for accuracy/consistency in accordance with Rho, Inc. standard operating procedures and the processes described in the statistical validation plan.

SAS® (SAS Institute, Cary, North Carolina) statistical software, version 9.4 or later, will be used for all analyses. Adverse Events and Medical History will be coded using the most recent version of the Medical Dictionary for Regulatory Activities (MedDRA). Concomitant medications will be coded using the latest version of the World Health Organization (WHO) Drug and Anatomic Therapeutic Chemical (ATC) classification and preferred term.

3.2 Standard Calculations

Unless otherwise noted, baseline is defined as the last observed data value prior to the receiving the first application of treatment for treated subjects, and the last observed data value prior to the randomization date for randomized subjects who were not treated. The baseline derivation can include unscheduled visits.

Study day will be determined as:

- The assessment/event date minus the date of first dose of gel, if the assessment/event date is prior to the date of first dose of gel; and

- The assessment/event date minus the date of first dose of gel + 1, if the assessment/event date is on or after the date of first dose of gel.

Note that if the subject is randomized but not treated then the randomization date will be substituted for first dose date of gel.

Change from baseline will be calculated as the post-baseline data value minus the baseline value. Percent change from baseline will be calculated as the change from baseline divided by the baseline value, multiplied by 100.

At any particular time point, for ranked transformation of any data item of interest, all observed data will be ranked together without regard to treatment assignment, from smallest to highest value. The smallest observation will be assigned the rank of 1, the second smallest the rank of 2, and so on. Average ranks will be used for tied observations.

Unless otherwise noted, values reported as greater than or less than some quantifiable limit (e.g., "< 2.0") will be summarized with the symbol suppressed in summary tables and figures, which will use the numeric equivalent.

Partial or missing dates used in calculations of duration may be imputed with logic similar to that of Adverse Events (Section 9.1.1).

4. ANALYSIS POPULATIONS

Identification of the subjects to be included in each analysis population will be determined and finalized prior to database lock. Subjects will be classified into the Safety, Intent-to-Treat (ITT), Per Protocol (PP), and HidroQoL (HQL) populations according to the following definitions:

Safety Population
The Safety Population will include all subjects randomized in the study who received study drug at least once. Subjects will be included in the treatment group based on the majority of actual treatment they received (even if not the treatment group to which they were randomized).

ITT Population
The ITT Population will include all subjects who were randomized. Subjects will be included in the treatment group to which they were randomized, regardless of the treatment received.

PP Population
The PP Population will be a subset of the ITT Population and will include subjects who meet the following criteria:

- Meets the inclusion/exclusion criteria
- Has not taken or applied any interfering concomitant medications.
- Completed the following visits:
  - Visit 1 (Screening) and the required HDSM-Ax data collection
  - Visit 2 (Baseline) and the required HDSM-Ax data collection
  - Visit 4 (Week 4), and the required HDSM-Ax data collection
  - Visit 7 (Week 12), and the required HDSM-Ax data collection
  - Visit 10 (Week 24), and the required HDSM-Ax data collection
  - Visit 16 (Week 48), and the required HDSM-Ax data collection
  - Visit 17 (Week 52), and the required HDSM-Ax data collection
- Treatment received per randomization assignment

HQL Population
The HQL Population will be used for HidroQol analyses. Subjects with "Yes" noted for the question "Subject flagged for the Baseline-Visit 5 HidroQol Protocol" on the Subject CRF page are included. The first 100 subjects ≥ 17 years of age enrolled were eligible for this population.

5. STUDY SUBJECTS

5.1 Disposition of Subjects

Subject disposition will be summarized for all randomized subjects by treatment group. Summaries will include the number and percentage of subjects in each analysis population, reason for exclusion from the PP population, completing treatment, completing the study, and discontinuing the study early by the primary reason for discontinuation. Analysis populations are defined in Section 4. Treatment completers are subjects with "Yes" noted for the question "Did the subject complete treatment?" on the Study Disposition CRF page. Study completers are subjects with "Normal Study Completion" noted for the question "Subject's Status or Primary Reason for Early Termination" on the Study Disposition CRF page. Study discontinuers are subjects with any response to "Subject's Status or Primary Reason for Early Termination" other than "Normal Study Completion" on the Study Disposition CRF page.

All subject disposition data will be listed for all randomized subjects.

5.2 Protocol Deviations

Major protocol violations will be summarized by treatment group for the Safety Population. Major protocol violations may include, but will not be limited to the following:

- Violation of eligibility criteria;
- Randomization error;
- Non-compliance with study drug dosing;
- On-study administration of a prohibited medication;
- Unauthorized changes to protocol procedure that could potentially affect subject safety or are a flagrant deviation of protocol defined procedures.

All major protocol violations will be determined and appropriately categorized by the sponsor prior to database lock. The number and percentage of subjects with any major protocol violations as well as the number and percentage of subjects with violations within each category will be presented. A by-subject listing will be provided for all protocol violations, major or minor, for the Safety Population.

6. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic variables including age, sex, ethnicity, race, and predominant race, will be summarized by treatment group for the Safety, ITT, and PP Populations.

Age in years will be summarized using descriptive statistics. Age will also be categorized into 9-12, 13-16, and ≥ 17 years of age. Age groups, sex, ethnicity, race, and predominant race will be summarized with the number and percentage of subjects in each parameter category. If more than one race is reported, subjects will be counted in each relevant category.

Baseline characteristics include medical history, height, weight, time since onset of axillary hyperhidrosis symptoms, and body mass index (BMI). Medical history will be summarized for the Safety Population. Other baseline characteristics will be summarized for the Safety, ITT, and PP Populations by treatment group.

Height, weight, BMI, and time since onset of axillary hyperhidrosis symptoms at baseline will be summarized using descriptive statistics. BMI will be calculated as: weight (kg) / (height (cm) / 100)^2. If height is entered in inches, height is converted to cm by Height (cm) = 2.54 *Height (inches). If weight is entered in lbs, weight is converted to kg by Weight (kg) = 1/(2.2046)*Weight (lbs). Time since onset of axillary hyperhidrosis symptoms will be reported in months and calculated by dividing the duration in days by (365.25 / 12). Duration in days will be calculated as (date of informed consent – start date of axillary hyperhidrosis symptoms + 1).

Medical history events will be coded to system organ class using the most current version of MedDRA. Frequency counts and percentages will be used to summarize subjects reporting abnormal medical history by system organ class. Subjects reporting more than one event for a given system organ class will be counted only once for that system organ class.

All demography, baseline characteristics, and medical history data collected will be presented in listings.

7. MEASUREMENTS OF TREATMENT COMPLIANCE

Study drug compliance will be calculated as the percentage of study drug taken for each subject. Percentage of study drug taken will be calculated by taking into account whether a subject took all doses of study drug as instructed, including protocol indicated dosing modifications collected on the Dosing CRF page. For each dosing entry, percentage of study drug taken will be determined as the total number of doses received divided by the number of expected doses, multiplied by 100.

Expected doses for the study will be calculated as the sum of the expected dose per dosing period (i.e. a 28-day treatment period). The expected dose per dosing period will be calculated as the end date of the period minus the start date of the period, plus one, times a multiplier as shown in the table below. The prescribed frequency for dosing and the multiplier are based on dose reductions allowed per protocol Section 8.1.4.

Table 1. Prescribed Frequencies, compliance dosing multiplier, and reasoning

Prescribed Frequency for Dosing Period	**Dosing Multiplier**	**Reasoning**
Daily	2	Drug applied once daily per axilla (2)
PI Withheld	0	No dose administered
Every Other Day	1	Drug applied every other day (0.5), once per axilla (2)
Divided Daily	1	Half (0.5) of drug applied, once daily per axilla (2)
Divided Every Other Day	0.5	Half (0.5) of drug applied, once every other day (0.5), per axilla (2)

The total number of doses received will be calculated as the sum of the number of doses received during the dosing period. The number of doses received during the dosing period will be calculated as the expected dose for the period minus the number of missed doses recorded on the Dosing CRF page for that period.

Percentage of study drug taken over the course of the study will be calculated at the subject-level (i.e. across all dosing entries) and will be summarized by treatment arm using descriptive statistics based on the Safety Population.

8. EFFICACY EVALUATION

8.1 Overview of Efficacy Analysis Issues

The primary objective of this study is to evaluate long-term safety and tolerability of 5% and 15% sofpironium bromide gel. Primary endpoints are safety parameters and are described in Section 9.

Efficacy is of secondary importance for the study; all efficacy endpoints are described below.

8.1.1 Handling of Dropouts or Missing Data

Missing data will not be imputed for any of the efficacy endpoints.

8.1.2 Multicenter Studies

This is a multicenter study, with approximately 30 sites expected to participate. Data collected from all sites will be pooled for data analysis.

8.1.3 Assessment Time Windows

Allowable windows for each study visit are laid out in the Schedule of Events in Section 18.1. Assessments that occur outside of the allowable window for each study visit will be flagged as protocol deviations, but will be used in all analyses. In general, all data will be associated with the nominal study visit for which it was intended. Repeat assessments and unscheduled visits will be included in study listings, but will not be used in place of nominal timepoint data. It is not expected that there will be multiple measurements that occur within the same assessment time window. Should that occur, the closest measurement will be used in the analysis; an earlier measure will be used in case of a tie.

8.1.4 Definitions

For the purposes of analysis, Baseline and End of Treatment (EOT) definitions for HDSM-Ax as well as the other efficacy parameters of interest are defined below.

HDSM-Ax

The HDSM-Ax 11-Item scale (HDSM-Ax-11) will be defined as mean of the items in sections No. 1, 2, and 3 of the HDSM-Ax (11 sub-items in total). This will be applied to both the ≥ 12 years of age scale and the child scale. The mean will be derived by taking the total score and dividing by the number of questions answered. Subjects must answer at least 6 of the 11 sub-items to be evaluable for HDSM-Ax-11 total score.

The HDSM-Ax 7-Item scale (HDSM-Ax-7) will be defined as the mean of the items in section No. 1 and questions 2a. through 2e. of the HDSM-Ax (7 sub-items in total). This will be applied to both the ≥ 12 years of age scale and the child scale. The mean will be

derived by taking the total score and dividing by the number of questions answered. Subjects must answer all of the 7 sub-items to be evaluable for HDSM-Ax-7 total score.

Baseline and EOT values are defined as follows:

- Baseline = Visit 2 (Day 1) assessment
- EOT = Visit 16 (Week 48) assessment

HidroQoL

The HidroQoL is split up into two domains. The Daily Life Activities domain is derived as the sum of questions 1 through 6, and the Psychosocial Life domain is derived as the sum of questions 7 through 18, where the answers are coded as such:

"Very Much" = 2
"A little" = 1
"No, not at all" = 0

The HidroQoL total score is derived as the sum of the 2 domain scores (range 0 to 36).

DLQI

The DLQI total score is calculated by summing answers to questions 1 through 10, including both parts of Question 7. All questions must be answered at the first DLQI assessment. Subsequent DLQI assessments with a single missing answer will be scored 0 for that question and totaled. Subjects with more than one missing question will have the instrument dropped for that visit. The DLQI answers are coded as such:

"Very much" = 3
"A lot" = 2
"A little" = 1
"Not at all" = 0
"Not relevant" = 0
Question 7, 'prevented work or studying' = 3

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

PGI-S and PGI-C

PGI-S will be defined as Question #6 of the HDSM-Ax at each assessment. PGI-C will be defined as Question #7 of the HDSM-Ax at the Day 43 visit only.

8.2 Secondary Efficacy Endpoints

The following secondary efficacy endpoints will be analyzed:

- The proportion of subjects achieving ≥1-point improvement in HDSM-Ax-11 (11-item total) from baseline to end of treatment
- The proportion of subjects achieving ≥1.5-point improvement in HDSM-Ax-11 from baseline to end of treatment
- The proportion of subjects achieving ≥2-point improvement in HDSM-Ax-11 from baseline to end of treatment
- Change of HDSM-Ax-11 from baseline to end of treatment as a continuous measure

8.2.1 Other Efficacy Endpoints

The following other efficacy endpoints will be analyzed:

- The proportion of subjects achieving ≥1-point improvement in HDSM-Ax-7 (7-item total) from baseline to end of treatment
- The proportion of subjects achieving ≥1.5-point improvement in HDSM-Ax-7 from baseline to end of treatment
- The proportion of subjects achieving ≥2-point improvement in HDSM-Ax-7 from baseline to end of treatment
- Change of HDSM-Ax-7 from baseline to end of treatment as a continuous measure
- The proportion of subjects achieving ≥1-point improvement in the HDSM-Ax-11 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥1.5-point improvement in the HDSM-Ax-11 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥2-point improvement in the HDSM-Ax-11 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- Change in HDSM-Ax-11 from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and 52) as a continuous measure
- The proportion of subjects achieving ≥1-point improvement in the HDSM-Ax-7 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥1.5-point improvement in the HDSM-Ax-7 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- The proportion of subjects achieving ≥2-point improvement in the HDSM-Ax-7 score from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and Week 52)
- Change in HDSM-Ax-7 from baseline to each of Visits 2-15 and 17 (Weeks 2-44 and 52) as a continuous measure
- DLQI from baseline to each of Visits 5, 10, and 16 (Weeks 2, 6, 24, and 48)
- PGI-S summarized as frequency counts and percentages for each category (none, mild, moderate, severe, very severe) at each assessment, change from baseline as a 5x5 table with frequency counts and percentages at each post-baseline assessment

- PGI-C summarized as frequency counts and percentages for each category (very much better, moderately better, a little better, no change, a little worse, moderately worse, very much worse) at Visits 10 and 16 (Weeks 24 and 48)

8.2.2 Exploratory Efficacy Endpoints

Exploratory efficacy endpoints to be analyzed include the following:

- HidroQoL from baseline to each of Visits 3 and 5 (Weeks 2 and 6); only the first 100 subjects ≥ 17 years of age enrolled in the study were to complete this assessment, and an exploratory analysis was performed.

8.3 Analysis Methods

All secondary and other efficacy endpoints will be summarized using descriptive statistics by treatment group for the ITT and PP populations. For continuous measures, mean, standard deviation, median, minimum and maximum will be reported for results at time point and for change from baseline by visit as indicated in Section 8.2.1. For categorical measures, frequency and percentage of subjects will be reported by the visits indicated in Sections 8.2 and 8.2.1. The exploratory HidroQoL endpoint will be summarized by treatment group as a continuous measure using descriptive statistics. At each visit, both domain scores and the total score will be summarized for the HQL population. No formal hypothesis testing or modeling of efficacy endpoints will be performed. Figures for proportion of subjects achieving ≥1-point, ≥1.5-point, and ≥2-point imprpovment in HDSM-Ax (for both 7-Item and 11-Item) by visit will be provided. Additionally, figures of mean change from baseline over time for HDSM-Ax (for both 7-Item and 11-Item) will be provided.

9. SAFETY EVALUATION

9.1 Overview of Safety Analysis Methods

All safety data will be analyzed and presented by treatment received for the Safety Population.

9.1.1 Handling of Dropouts or Missing Data

All available information will be used for descriptive statistics. No imputation for missing data will be applied with the exception of the handling of partial dates.

Partial AE and concomitant medication start and end dates will be imputed as follows:

1. If the year and month are known:
    a. If the year and month are the same as the year and month of the treatment start date, impute to treatment start date and will therefore be recorded as TEAEs.
    b. Otherwise, use the 1st of the month.
2. If only the year is known:
    a. If the year is the same as the year of treatment start date, impute to treatment start date and will therefore be recorded as TEAEs.
    b. Otherwise, impute to January 1st of that year.
3. If the date is completely missing, impute to treatment start date.

Listings will show the actual dates collected and not the imputed dates.

9.1.2 Multicenter Studies

The study will be conducted at approximately 30 clinical sites. Data from the sites will be pooled.

9.1.3 Assessment Time Windows

Safety parameters will be collected according to the schedule of assessments in the Time and Events Table in Section 7 of the protocol (Appendix 18.1). No more/less than 14 ± 3 days may elapse between Visit 2 (Baseline) and Visits 3-6 (Weeks 2-8). No more/less than 28 ± 5 days may elapse between each of Visits 7-16 (Weeks 12-48). The End of Treatment visit may occur within ± 5 days of Week 52 (364 days). Summaries will be presented by planned visits where applicable.

9.2 Safety Variables

Primary endpoints include evaluation of the long-term safety and local tolerability of 5% and 15% sofpironium bromide gel when applied topically in subjects with axillary hyperhidrosis. Assessment will include:

- Adverse events
- Local tolerability assessments
- Vital signs (blood pressure, pulse rate, respiratory rate, and temperature)
- Laboratory tests (hematology, chemistry, and urinalysis) and pregnancy testing in FOCBP

9.3 Extent of Exposure

Extent of exposure to study treatment will be summarized for the Safety Population by treatment group. The duration of exposure will be presented in days and summarized using descriptive statistics. Drug (pump) dispensation will be provided in a listing, to include total drug delivered per subject. Each pump will be primed, then weighed, prior to dispensing pumps to subjects. Each pump will be weighed upon return. Total drug delivered will be calculated as the total weight of all pumps dispensed minus the total weight of all returned pumps.

9.4 Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as those adverse events (AEs) with onset after the first dose of study drug or existing events that worsened after the first dose during the study. Treatment-emergent AEs will be summarized by treatment group. Partial or missing start or end dates will be imputed per Section 9.1.1.

Verbatim terms on case report forms will be mapped to preferred terms and system organ classes using the latest version of MedDRA.

At Weeks 2, 4, 6, 12, 24, 48 and 52, treatment-emergent adverse events (TEAEs, i.e., AEs occurring during or after treatment initiation) will be summarized in the following tables: all reported TEAEs, all treatment-related TEAEs, severe TEAEs, TEAEs leading to dose interruption, TEAEs leading to dose modification, TEAEs leading to study discontinuation, TEAEs of special interest, and anticholinergic TEAEs. Two sets of the above tables will be produced: (a) for cumulative TEAEs up to the current visit reported by those making the visit, and (b) for cumulative TEAEs up to the current visit reported by all Safety Population subjects (including those absent from the current visit). At each of the 7 indicated weeks, each of the above tables will summarize the subject incidence (frequency count and %) for the specified TEAE, mapped to MedDRA System Organ Class and Preferred Term, according to the highest severity reported. Subjects with only unknown severity for a TEAE will be counted under the severity unknown category. Additionally, serious TEAEs and treatment-related serious TEAEs will be summarized in the same manner for all data through Week 52.

Summaries that are displayed by system organ class and preferred terms will be ordered by descending incidence of system organ class in the combined BBI-4000 group and preferred term within each system organ class. The combined BBI-4000 group will not be displayed and will only be used for sorting. TEAEs of special interest include the following:

- Vision blurred
- Mydriasis
- Urinary hesitation
- Pupils unequal

Adverse event data will be presented in data listings by subject, treatment group, and event. Serious TEAEs and TEAEs leading to discontinuation of the study will be presented in separate data listings. Death is not expected. However, should death occur on study, the event will be reported with detailed narratives.

9.5 Local Tolerability Assessments

Local tolerability assessments are performed for both axillae individually at all visits after screening (Visits 2-17). Visit 2 data are the baseline. Should Visit 2 data be missing, baseline will be derived as the last value prior to first dose and as such unscheduled visits may be included. Subjects rate the severity of any symptoms of burning, stinging, and itching at the application-site on a scale of 0 = absent, 1 = minimal, 2 = mild, 3 = moderate, and 4 = severe. Investigators assess the drug application site for the existence of significant local symptoms of scaling and erythema on a scale of 0 = absent, 1 = minimal, 2 = mild, 3 = moderate, and 4 = severe.

Subject and Investigator assessments will be included in tables and listings. At each visit, local tolerability assessments will be descriptively summarized by severity for each treatment group. At each post-baseline visit, local tolerability will be summarized as cumulative shift tables vs. baseline. Subject counts and percentages for each symptom will be cross-tabulated with baseline severity according to the maximum post-baseline severity reported for either axilla up to the current visit.

9.6 Clinical Laboratory Evaluation

Laboratory parameter results will be collected at the Screening Visit and Visits 3-16. Baseline will be derived as the last value prior to first dose and as such unscheduled visits may be included.

Laboratory parameters will be presented in Systeme International (SI) units and descriptively summarized for values at each visit and for changes from baseline at each

subsequent visit. In addition, at each post-baseline visit, parameter status (low, normal, high or normal, abnormal, as applicable) will also be summarized as shift tables vs. baseline status. Summary results will include the count and percentage of subjects within each shift category and treatment group. Unscheduled visits and early termination visits will be included in the shift tables.

Laboratory parameters to be summarized and listed include hematology, clinical chemistry, and routine urinalysis. Urine pregnancy test results will be a by-subject listing only. Laboratory measurements identified as abnormal (i.e., outside the normal range) will also be listed separately by subject, laboratory test, and unit.

9.7 Vital Signs, Physical Findings, and Other Observations Related to Safety

9.7.1 Vital Signs

Vital sign results will be collected at each visit. Visit 2 data are the Baseline. Should Visit 2 data be missing, baseline will be derived as the last value prior to first dose and as such unscheduled visits may be included. Vital sign measurements will include systolic and diastolic blood pressure, pulse rate, respiratory rate, and temperature. Vital sign parameters will be summarized with descriptive statistics for values at each visit and for changes from baseline at each subsequent visit. Vital signs will also be listed by subject.

9.7.2 Physical Examinations (PE)

Physical examination results will be collected at the Screening Visit and End of Study Visit. Physical examination will include assessments of the head, eyes, ears, nose, throat, skin, thyroid, neurological, lungs, cardiovascular, abdomen (liver and spleen), lymph nodes, and extremities. Height and weight will also be measured and recorded. Results of the physical examination will be presented in subject data listings by subject, study visit, and body system.

9.7.3 Other Safety Measures

9.7.3.1 Prior and Concomitant Medications

Medications will be coded using the latest version of the WHO drug dictionary. Medications entered on the CRF will be mapped to ATC drug class (level 4) and drug name.

Prior and concomitant medications will be summarized separately and the study phase of each medication will be determined programmatically based on medication start and end dates. Partial or missing start and end dates will be imputed according to Section 9.1.1.

A prior medication is defined as any medication administered prior to the date of the first dose of study drug. A concomitant medication is defined as any medication administered

on or after the date of the first dose of study drug. A medication may be defined as both prior and concomitant.

For the summary of both prior medications and concomitant medications, the number and percentage of subjects receiving any medication will be summarized by treatment group, as will the number and percentage receiving any medication by ATC drug class and generic drug name. Subjects reporting use of more than one medication at each level of summarization (any medication received, ATC class, and generic drug name) will be counted only once. ATC class terms will be displayed by descending order of incidence, as will generic drug names within each ATC class. The study phase during which each medication was received (e.g., prior, concomitant, or both) will be presented on the listing of prior and concomitant medications.

Prior or concomitant therapies and procedures will be listed only.

10. PHARMACOKINETIC/PHARMACODYNAMIC EVALUATION

Pharmacokinetic and pharmacodynamic analyses are not part of this study protocol.

11. OTHER ANALYSES

11.1 Psychometric Analysis of the HDSM-Ax

In parallel to the traditional statistical analysis, psychometric evaluation of the HDSM-Ax will be carried out to confirm the most appropriate HDSM-Ax scoring algorithm and to examine internal validity, construct validity (i.e., examination of the magnitude of correlation between the HDSM-Ax total score and key variable such as items 4 and 5 of the HDSM-Ax, PGI-S, and PGI-C), stability, reliability, ability to detect change, and interpretability of clinical trial results.

The details regarding psychometric analyses will be described in a separate analysis plan.

12. INTERIM ANALYSES AND DATA MONITORING

There is no plan to establish a data monitoring committee for this study.

There are no formal interim analyses planned, however the HidroQoL assessment was evaluated upon enrollment of 100 eligible subjects. The treatment groups were not blinded. The mean, standard deviation, median, minimum, maximum and the same summary statistics for change from baseline for the HidroQoL total score, Daily Life Activities Domain score, and Psychosocial Life Domain score were reported using the HQL Population. The results of this analysis are intended to be used to inform protocol development for subsequent studies.

13. CHANGES TO THE ANALYSES PLANNED IN THE PROTOCOL

Analyses specified in the protocol dated 6 May 2019 that have changed in this SAP include the following:

- Protocol Synopsis
    - The synopsis describes the baseline of HDSM-Ax as the average of Screening and Day 0. The baseline definition has been updated to be the Day 1 visit.
- Protocol Section 10.1 Analysis Populations
    - The definition of ITT population has been updated to include all subjects who were randomized.
- Protocol Section 10.2 Endpoints
    - For the exploratory efficacy endpoint, the protocol describes an interim analysis. It has been clarified in this SAP that the interim analysis was not formal and that the treatment groups were not blinded.
    - Endpoints have been added to the 'Other Efficacy Endpoint' section to capture the 11-item total of HDSM-Ax and the 7-item total of HDSM-Ax.
- Protocol Section 10.3 Safety Analysis
    - The protocol describes three sets of AE tables to be produced at each visit. The first set "(a) TEAEs reported at the current visit by those making the visit" will not be generated, as it will not provide any substantial information to the safety profile".
    - The protocol states that all SAEs will be summarized by the three sets of AE tables. Due to an expected low incidence, one SAEs table and one treatment-related SAEs table will be generated for all data through Week 52.

14. REFERENCES

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Statistical principles for clinical trials (E9). International Conference on Harmonization; 1998.

15. LIST OF PLANNED TABLES

Number	Title	Population
14.1.1.1	Summary of Subject Disposition	All Randomized Subjects
14.1.1.2	Summary of Major Protocol Deviations	Safety
14.1.2.1	Summary of Demographic Characteristics	Safety
14.1.2.2	Summary of Demographic Characteristics	ITT
14.1.2.3	Summary of Demographic Characteristics	Per Protocol
14.1.3.1	Summary of Baseline Characteristics	Safety
14.1.3.2	Summary of Baseline Characteristics	ITT
14.1.3.3	Summary of Baseline Characteristics	Per Protocol
14.1.4	Summary of Medical History	Safety
14.1.5	Summary of Prior Medications by Drug Class and Generic Drug Name	Safety
14.2.1.1.1	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-11 from Baseline to End of Treatment	ITT
14.2.1.1.2	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-11 from Baseline to End of Treatment	Per Protocol
14.2.1.2.1	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-11 from Baseline to End of Treatment	ITT
14.2.1.2.2	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-11 from Baseline to End of Treatment	Per Protocol
14.2.1.3.1	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-11 from Baseline to End of Treatment	ITT
14.2.1.3.2	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-11 from Baseline to End of Treatment	Per Protocol
14.2.1.4.1	Change from Baseline in HDSM-Ax-11 to End of Treatment	ITT
14.2.1.4.2	Change from Baseline in HDSM-Ax-11 to End of Treatment	Per Protocol
14.2.2.1.1	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-7 from Baseline to End of Treatment	ITT
14.2.2.1.2	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-7 from Baseline to End of Treatment	Per Protocol
14.2.2.2.1	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-7 from Baseline to End of Treatment	ITT
14.2.2.2.2	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-7 from Baseline to End of Treatment	Per Protocol
14.2.2.3.1	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-7 from Baseline to End of Treatment	ITT
14.2.2.3.2	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-7 from Baseline to End of Treatment	Per Protocol
14.2.2.4.1	Change from Baseline in HDSM-Ax-7 to End of Treatment	ITT
14.2.2.4.2	Change from Baseline in HDSM-Ax-7 to End of Treatment	Per Protocol
14.2.2.5.1	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-11 from Baseline by Visit	ITT

14.2.2.5.2	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-11 from Baseline by Visit	Per Protocol
14.2.2.6.1	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-11 from Baseline by Visit	ITT
14.2.2.6.2	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-11 from Baseline by Visit	Per Protocol
14.2.2.7.1	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-11 from Baseline by Visit	ITT
14.2.2.7.2	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-11 from Baseline by Visit	Per Protocol
14.2.2.8.1	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-7 from Baseline by Visit	ITT
14.2.2.8.2	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-7 from Baseline by Visit	Per Protocol
14.2.2.9.1	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-7 from Baseline by Visit	ITT
14.2.2.9.2	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-7 from Baseline by Visit	Per Protocol
14.2.2.10.1	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-7 from Baseline by Visit	ITT
14.2.2.10.2	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-7 from Baseline by Visit	Per Protocol
14.2.2.11.1	Change from Baseline in HDSM-Ax-11 by Visit	ITT
14.2.2.11.2	Change from Baseline in HDSM-Ax-11 by Visit	Per Protocol
14.2.2.12.1	Change from Baseline in HDSM-Ax-7 by Visit	ITT
14.2.2.12.2	Change from Baseline in HDSM-Ax-7 by Visit	Per Protocol
14.2.2.13.1	Change from Baseline in DLQI by Visit	ITT
14.2.2.13.2	Change from Baseline in DLQI by Visit	Per Protocol
14.2.2.14.1	Patient Global Impression - Severity (PGI-S) by Visit	ITT
14.2.2.14.2	Patient Global Impression - Severity (PGI-S) by Visit	Per Protocol
14.2.2.15.1	Patient Global Impression - Severity (PGI-S) Shift from Baseline to Each Visit	ITT
14.2.2.15.2	Patient Global Impression - Severity (PGI-S) Shift from Baseline to Each Visit	Per Protocol
14.2.2.16.1	Patient Global Impression of Change (PGI-C) by Visit	ITT
14.2.2.16.2	Patient Global Impression - Change (PGI-C) by Visit	Per Protocol
14.2.3	Change from Baseline in HidroQoL by Visit	HQL
14.3.1.1	Overall Summary of Treatment Emergent Adverse Events	Safety
14.3.1.2	Number and Percentage of Subjects with Serious Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity	Safety
14.3.1.3	Number and Percentage of Subjects with Serious Treatment-Related Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity	Safety

14.3.1.4.1	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.2	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)
14.3.1.4.3	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.4	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)
14.3.1.4.5	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.6	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)
14.3.1.4.7	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.8	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)
14.3.1.4.9	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.10	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)
14.3.1.4.11	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.12	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)

14.3.1.4.13	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.14	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)
14.3.1.4.15	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 2)
14.3.1.4.16	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 2 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 2 or Not)
14.3.1.5.1	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 4)
14.3.1.5.2	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.5.3	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 4)
14.3.1.5.4	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.5.5	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 4)
14.3.1.5.6	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.5.7	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 4)
14.3.1.5.8	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.5.9	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to	Safety (Subjects Reaching Week 4)

	Week 4 by System Organ Class, Preferred Term, and Maximum Severity	
14.3.1.5.10	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.5.11	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 4)
14.3.1.5.12	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.5.13	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 4)
14.3.1.5.14	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.5.15	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 4)
14.3.1.5.16	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 4 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 4 or Not)
14.3.1.6.1	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)
14.3.1.6.2	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.6.3	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)
14.3.1.6.4	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.6.5	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)

14.3.1.6.6	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.6.7	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)
14.3.1.6.8	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.6.9	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)
14.3.1.6.10	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.6.11	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)
14.3.1.6.12	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.6.13	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)
14.3.1.6.14	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.6.15	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 6)
14.3.1.6.16	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 6 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 6 or Not)
14.3.1.7.1	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)

14.3.1.7.2	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.7.3	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)
14.3.1.7.4	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.7.5	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)
14.3.1.7.6	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.7.7	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)
14.3.1.7.8	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.7.9	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)
14.3.1.7.10	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.7.11	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)
14.3.1.7.12	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.7.13	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)

14.3.1.7.14	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.7.15	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 12)
14.3.1.7.16	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 12 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 12 or Not)
14.3.1.8.1	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.2	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 24 or Not)
14.3.1.8.3	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.4	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 24 or Not)
14.3.1.8.5	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.6	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 24 or Not)
14.3.1.8.7	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.8	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 24 or Not)
14.3.1.8.9	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.10	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to	Safety (All Safety Subjects,

	Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Reaching Week 24 or Not)
14.3.1.8.11	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.12	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 24 or Not)
14.3.1.8.13	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.14	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 24 or Not)
14.3.1.8.15	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 24)
14.3.1.8.16	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 24 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 24 or Not)
14.3.1.9.1	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.2	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)
14.3.1.9.3	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.4	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)
14.3.1.9.5	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.6	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)

14.3.1.9.7	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.8	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)
14.3.1.9.9	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.10	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)
14.3.1.9.11	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.12	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)
14.3.1.9.13	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.14	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)
14.3.1.9.15	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 48)
14.3.1.9.16	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 48 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 48 or Not)
14.3.1.10.1	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.2	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)

14.3.1.10.3	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.4	Number and Percentage of Subjects with Treatment-Related Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)
14.3.1.10.5	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.6	Number and Percentage of Subjects with Severe Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)
14.3.1.10.7	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.8	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Interruption Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)
14.3.1.10.9	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.10	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Dose Modification Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)
14.3.1.10.11	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.12	Number and Percentage of Subjects with Treatment-Emergent Adverse Events Leading to Study Discontinuation Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)
14.3.1.10.13	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.14	Number and Percentage of Subjects with Treatment-Emergent Adverse Events of Special Interest Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)

14.3.1.10.15	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (Subjects Reaching Week 52)
14.3.1.10.16	Number and Percentage of Subjects with Anticholinergic Treatment-Emergent Adverse Events Cumulative to Week 52 by System Organ Class, Preferred Term, and Maximum Severity	Safety (All Safety Subjects, Reaching Week 52 or Not)
14.3.6.1	Worst Post-baseline Severity for Local Tolerability Assessments by Treatment Group	Safety
14.3.6.2	Worst Severity for Local Tolerability Assessments by Treatment Group and Visit	Safety
14.3.6.3	Summary of Vital Signs	Safety
14.3.4.1	Mean and Mean Change from Baseline in Serum Biochemistry Values by Visit	Safety
14.3.4.2	Mean and Mean Change from Baseline in Hematology Values by Visit	Safety
14.3.4.3	Mean and Mean Change from Baseline in Continuous Urinalysis Values by Visit	Safety
14.3.4.4	Categorical Urinalysis Values by Visit	Safety
14.3.4.5	Shift in Serum Biochemistry Results from Baseline to Each Visit	Safety
14.3.4.6	Shift in Hematology Results from Baseline to Each Visit	Safety
14.3.4.7	Shift in Continuous Urinalysis Results from Baseline to Each Visit	Safety
14.3.4.8	Shift in Categorical Urinalysis Results from Baseline to Each Visit	Safety
14.3.5	Study Drug Administration Exposure and Compliance	Safety
14.3.6.4	Summary of Concomitant Medications by Drug Class and Generic Drug Name	Safety

16. LIST OF PLANNED FIGURES

Number	Description	Analysis Set
14.2.1.1.1	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-11 by Visit	ITT
14.2.1.1.2	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-11 by Visit	Per Protocol
14.2.1.2.1	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-11 by Visit	ITT
14.2.1.2.2	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-11 by Visit	Per Protocol
14.2.1.3.1	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-11 by Visit	ITT
14.2.1.3.2	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-11 by Visit	Per Protocol
14.2.1.4.1	Mean Change from Baseline in HDSM-Ax-11 by Visit	ITT
14.2.1.4.2	Mean Change from Baseline in HDSM-Ax-11 by Visit	Per Protocol
14.2.2.1.1	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-7 by Visit	ITT
14.2.2.1.2	Proportion of Subjects Achieving ≥1-point Improvement in HDSM-Ax-7 by Visit	Per Protocol
14.2.2.2.1	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-7 by Visit	ITT
14.2.2.2.2	Proportion of Subjects Achieving ≥1.5-point Improvement in HDSM-Ax-7 by Visit	Per Protocol
14.2.2.3.1	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-7 by Visit	ITT
14.2.2.3.2	Proportion of Subjects Achieving ≥2-point Improvement in HDSM-Ax-7 by Visit	Per Protocol
14.2.2.4.1	Mean Change from Baseline in HDSM-Ax-7 by Visit	ITT
14.2.2.4.2	Mean Change from Baseline in HDSM-Ax-7 by Visit	Per Protocol

17. LIST OF PLANNED DATA LISTINGS

Number	Description	Analysis Set
16.2.1	Subject Disposition	All Randomized Subjects
16.2.2	Protocol Deviations	Safety
16.2.3	Analysis Populations	All Randomized Subjects
16.2.4.1	Demographic and Baseline Characteristics	Safety
16.2.4.2	Medical History	Safety
16.2.4.3	Prior and Concomitant Medications	Safety
16.2.6.1	Hyperhidrosis Disease Severity Measure-Axillary Results	ITT
16.2.6.2	Dermatology Quality of Life Index Results	ITT
16.2.6.3	Hyperhidrosis Quality of Life Index Results	HQL
16.2.7.1	All Adverse Events	Safety
14.3.2.1	Serious Adverse Events	Safety
14.3.2.2	Adverse Events Resulting in Study Discontinuation	Safety
14.3.2.3	Adverse Events Resulting in Death	Safety
16.2.7.2	Adverse Events of Special Interest	Safety
16.2.9.1	Local Tolerability Results	ITT
16.2.9.2	Vital Signs Results	Safety
16.2.9.3	Physical Examination Results	Safety
16.2.8.5	Pregnancy Results	Safety
16.2.8.1	Serum Biochemistry Results	Safety
16.2.8.2	Hematology Results	Safety
16.2.8.3	Urinalysis Results	Safety
16.2.8.4	Clinically Significant Laboratory Values	Safety
16.2.5.1	Study Medication Dosing	Safety
16.2.5.2	Study Drug Accountability	Safety
16.2.5.3	Exposure Parameters	Safety
16.2.9.4	Prior or Concomitant Therapies or Procedures	Safety
16.2.10	Subject Study Visits	All Randomized Subjects

18. APPENDICES

18.1 Schedule of Events

VISIT	1	2	3 – 6[1]	7 – 16[2]	17[3]
Time Point	Screening (-31 to 0 Days)	Baseline (Day 1)	Weeks 2, 4, 6, 8 ±3 days	Q4 Weeks (Weeks 12 – 48) ±5 days	End of Study Week 52 ±5 days
PROCEDURE					
Informed Consent	X				
Medical Hx, Demog	X				
I/E Criteria	X	X			
Randomization		X			
PE	X				X
Vitals (BP, HR, RR, Temp)	X	X	X	X	X
HDSM-Ax	X	X	X	X	X
PGI-S[4]	X	X	X	X	X
PGI-C[5]				X	
DLQI[6]		X	X	X	
HidroQoL[7]		X	X		
Optional End of Study Survey[8]					X
Local Tolerability[9]		X	X	X	X
Adverse Events[9]	X	X	X	X	X
UPT (FOCBP)[10]	X	X	X	X	
IP Dispensation/ Return/ Resupply[11]		X	X	X	
IP Weight[11]		X	X	X	

Compliance Training/Evaluation		**X**	**X**	**X**	**X**
Safety Labs (heme., chem., urine)[12]	**X**		**X**	**X**	
Conmeds	**X**	**X**	**X**	**X**	**X**

Abbreviations: BP = blood pressure; Chem. = chemistry; Conmeds = concomitant medications; DLQI = Dermatology Life Quality Index; FOCBP= females of child-bearing potential; HDSM-Ax = Hyperhidrosis Disease Severity Measure-Axillae; heme. = hematology; HR = heart rate; Hx = history; I/E = inclusion/exclusion; IP = investigational product; PE = physical examination; PGI-C = Patient Global Impression of Change; PGI-S = Patient Global Impression of Severity; RR = respiratory rate; UPT = urine pregnancy test, urine = urinalysis.

[1]No more than 14±3 days may elapse between Visit 2 (Baseline) and Visit 3 (Week 2).

[2]No more than 28±5 days may elapse between each of Visits 7-16 (Weeks 12-48).

[3]The End of Study Visit may occur ±5 days of Week 52.

[4]Administered as Question #6 of HDSM-Ax at every assessment.

[5]Administered as Question #7 of HDSM-Ax at Week 24 and Week 48 visits.

[6]Administered at Baseline, Weeks 2, 6, 24, and 48.

[7]Administered at Baseline, Week 2, and Week 6; only the first 100 subjects enrolled in the study will complete this assessment.

[8] Administered at Week 52 visit; the End of Study Survey is optional.

[9] Investigator local tolerability assessments to be performed after the Subject local tolerability assessments.

[10] Performed at Screening, Baseline, and then Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48.

[11] Performed at Baseline and then Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48.

[12] Performed at Screening and then Weeks 6, 24, and 48.

19. ATTACHMENTS

None.