# STATISTICAL ANALYSIS PLAN
# PHASE II

**VERSION: 3.0**

**DATE:**

**January 12, 2022**

**BASED ON:**

*Protocol Version Amendment 3 Date: 28-FEB-2020*

*Data Management Plan Final Version 2 Date: 10-JUL-2020*

**Study Drug:**

*B244 Topical application*

**Protocol Number:**

*PRB244-01*

**Study Title:**

*A Phase II, Randomized, Double-Blind, Vehicle Controlled Study of the Efficacy, Safety, and Tolerability of B244 Topical Spray for the Treatment of Pruritus in Adults with a History of Atopic Dermatitis*

**Sponsor:**

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STATISTICAL ANALYSIS PLAN REVIEW AND APPROVAL

This Statistical Analysis Plan has been prepared in accordance with team reviewers' specifications.

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# 1 LIST OF ABBREVIATIONS

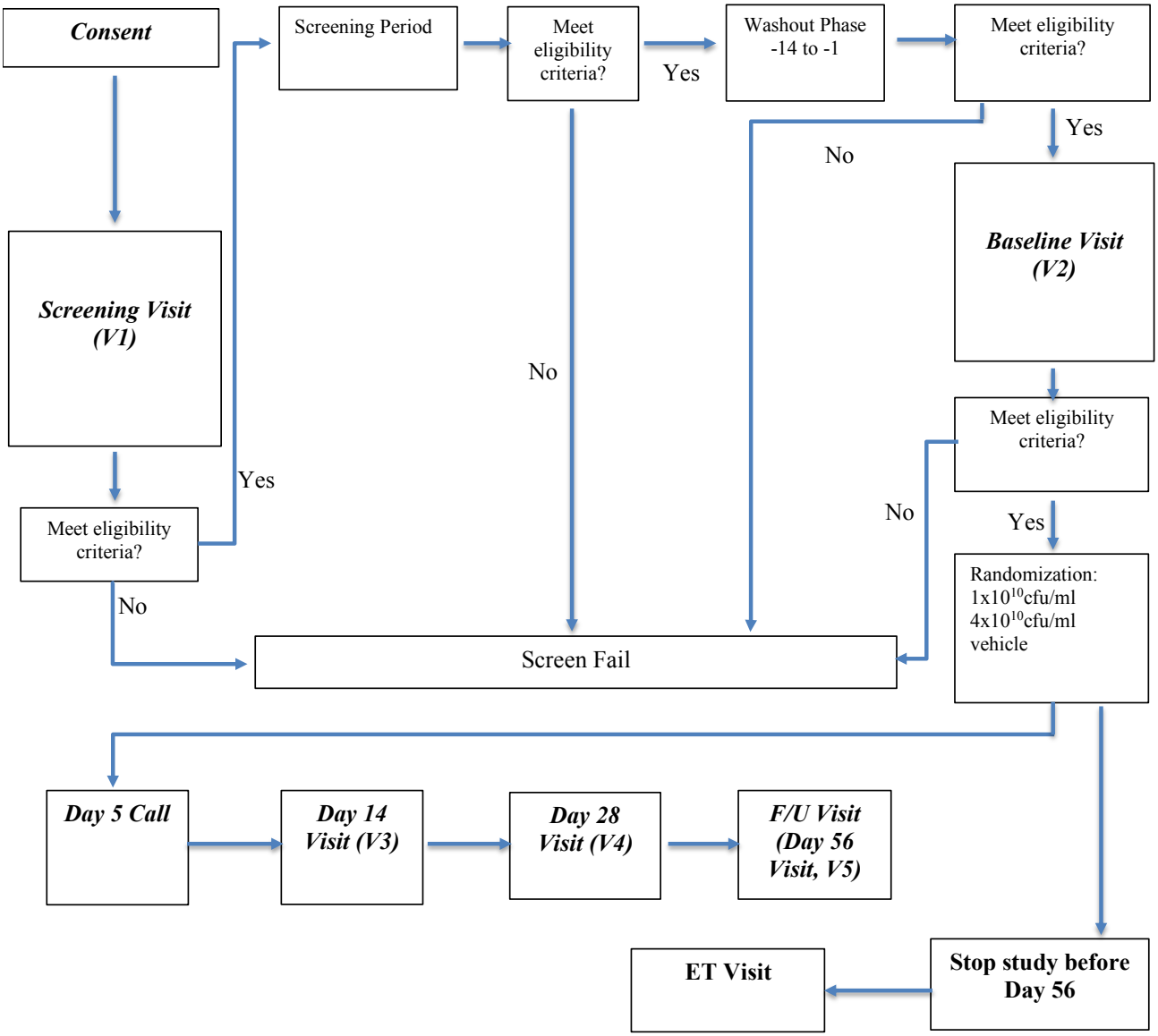
| Abbreviation | Full Form |
|---|---|
| AD | Atopic Dermatitis |
| ADaM | Analysis Data Model |
| AE | Adverse Event |
| AI | Average Itch |
| AI-NRS | Average Itch – Numeric Rating Scale |
| AMO | Ammonia Monooxygenase |
| ANCOVA | Analysis of Covariance |
| AOB | Ammonia Oxidizing Bacteria |
| ATC | Anatomical Therapeutic Chemical Classification System |
| BID | Twice-Daily |
| BMI | Body Mass Index |
| BSA | Body Surface Area |
| CDISC | Clinical Data Interchange Standards Consortium |
| COA | Clinical Outcome Assessment |
| CRF | Case Report Form |
| EASI | Eczema Area and Severity Index |
| E/T | Early Termination |
| FDA | Food and Drug Administration |
| HAO | NH2OH oxidoreductase |
| HbsAg | Hepatitis B Virus Surface Antigen |
| HCV Ab | Hepatitis C Virus Antibody |
| HIV | Human Immunodeficiency Virus |
| ICH | International Conference on Harmonization |
| IEC | Independent Ethics Committee |
| IGA | Investigator Global Assessment |
| IP | Investigational Product |
| IRB | Institutional Review Board |
| ITT | Intention to Treat |
| IWRS | Interactive Web Response System |
| MedDRA | Medical Dictionary for Regulatory Activities |
| mITT | Modified Intention to Treat |
| NH2OH | Hydroxylamine |
| NH3 | Ammonia |
| NO | Nitric oxide |
| NO2- | Nitrite |
| NRI | Non-Responder Imputation |
| NRS | Itch Numeric Rating Scale |
| PCP | Primary Care Physician |
| POEM | Patient Oriented Eczema Measure |
| PRO | Patient Reported Outcomes |

| | |
|---|---|
| PP | Per Protocol |
| PT | Preferred Term |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SDTM | Study Data Tabulation Model |
| SOA | Schedule of Assessments |
| SOC | System Organ Class |
| SPM | Study Procedures Manual |
| TEAE | Treatment Emergent Adverse Event |
| TESAE | Treatment Emergent Serious Adverse Event |
| WI-NRS | Worst Itch – Numeric Rating Scale |
| WHO | World Health Organization |
| WOCBP | Women of Childbearing Potential |

# 2 INTRODUCTION

This document describes the statistical methods and data presentations to be used in the summary and analysis of data from Protocol PRB244-01. Background information is provided for the overall study design and objectives. The study conduct and study details can be found in the protocol[1] and electronic case report forms (eCRFs).

## 2.1 Study Flowchart



## 2.2 Schedule of Activities

| Visit Name# | Screening | Washout phase | Baseline Day 0 | Day 5 | Day 14 (Week 2) | Day 28 (Week 4) | Day 56 (Week 8) | Early Termination Visit |
|---|---|---|---|---|---|---|---|---|
| Visit Number | V1 | | V2 | | V3 | V4 | V5 | |
| Visit Window in days | -21 to -14 | -14 to -1 | 0 | +/-2 | +/-2 | +/-2 | +/-3 | |
| Informed Consent | X | | | | | | | |
| Inclusion / Exclusion Criteria | X | | X | | | | | |
| Demographics | X | | | | | | | |
| Medical History | X | | X | | | | | |
| Concomitant Medications | X | | X | | X | X | X | X |
| Physical Exam | X | | | | | | X | X |
| Vital Signs | X | | X | | X | X | X | X |
| eDiary | X | X | X | X | X | X | X | X |
| POEM | X | | X | | X | X | X | X |
| 5-D Pruritus Scale | X | | X | | X | X | X | X |
| IGA | X | | X | | X | X | X | X |
| EASI | X | | X | | X | X | X | X |
| Itch Numeric Rating Scale (NRS) | X | X | X | X | X | X | X | X |
| Clinical Labs | X | | | | | X | | X* |
| Urine pregnancy test for WOCBP | X | | X | | | X | X | X |
| IWRS | | | X | | | | | |
| Investigational Product compliance | | | X | | X | X | | X |
| Dispense study drug | | | X | | X | | | |
| Application of study drug | | | X | X | X | X | | |
| Phone call to subjects | | X | | X | | | | |
| Collect study drug | | | | | X | X | | X |
| Study counseling | X | X | X | X | X | X | | |

| Visit Name# | Screening | Washout phase | Baseline Day 0 | Day 5 | Day 14 (Week 2) | Day 28 (Week 4) | Day 56 (Week 8) | Early Termination Visit |
|---|---|---|---|---|---|---|---|---|
| Visit Number | V1 | | V2 | | V3 | V4 | V5 | |
| Visit Window in days | -21 to -14 | -14 to -1 | 0 | +/-2 | +/-2 | +/-2 | +/-3 | |
| AE monitoring | X | | X | | X | X | X | X |

#: Comments/clarification to visits in table below.
*: if visit occurs before Day 28

| Visit Name | Comments/Clarification |
|---|---|
| Informed Consent | Informed consent will occur prior to any protocol-mandated procedures, including the stopping of any excluded therapies. |
| Vital Signs | Height and weight will be assessed at Screening; BP, pulse, respiration rate, and temperature will be assessed at each visit. Smoking status will be recorded at Screening |
| eDiary | Subjects will be provided eDiary to be completed at home daily and in-clinic. At home eDiary will include WI-NRS, AI-NRS, rescue medication, dose administration, and local skin tolerability. In clinic eDiary will include POEM and 5-D Pruritus Scale. eDiary will be reviewed at the Baseline visit to determine eligibility. |
| POEM | Patient reported assessment by ePRO |
| 5-D Pruritus Scale | Patient reported assessment by ePRO |
| IGA | Clinician assessment by eCOA |
| EASI | Clinician assessment by eCOA |
| Itch Numeric Rating Scale (NRS) | Patient reported assessment by ePRO |
| Clinical Labs | Patients should fast for at least 8 hours before the test but optional at Screening. Blood and urine for clinical chemistry will be shipped to the central lab for processing. Chemistry, Hematology, Lipid Panel, and Urinalysis will be done at Screening and Day 28. Serology will only be done at Screening. Kits and lab manuals will be provided by a central lab. |
| Investigational Product compliance | Weights of dispensed and collected bottles to be recorded following instructions provided to sites. |
| Application of study drug | First application of study drug will occur in the office under the supervision of the study staff. |
| Phone call to subjects | Call to initiate washout phase will be placed once results of screening clinical labs are finalized. Call on Day 5 will be made to counsel subjects on the use of IP and eDiary recordings, as well as answer any questions. |
| Study counseling | Subjects will be counseled at each visit on the appropriate use of IP, eDiary entries and use. |
| AE monitoring | AE will be monitored from screening to follow-up. After informed consent, but prior to study drug administration, only SAEs caused by a protocol-mandated intervention will be collected |

## 2.3 Schedule of eDiary and Efficacy Assessments

eDiary (ePRO) is provided to subjects at the screening visit for daily entry at home (e.g., application on smartphone). Questionnaires and clinician assessments are recorded via ePRO/eCOA (e.g., tablet) or CRF during the site visits per schedule of events. Additional patient reported information include rescue medication use, dose administration confirmation, and adjunctive therapy use.

| Device | Assessment | Frequency and Duration of Assessment |
|---|---|---|
| eDiary | WI-NRS | Once daily from Screening visit through the Follow-up visit |
| eDiary | AI-NRS | Once daily from Screening visit through the Follow-up visit |
| eDiary | Patient Reported Local Tolerability | Once daily from Day 1 to Day 7 of treatment |
| eDiary | POEM | Patient reported at site visits |
| eDiary | 5-D Pruritus Scale | Patient reported at site visits |
| eCOA/CRF | IGA | Clinician assessment at site visits |
| eCOA/CRF | EASI | Clinician assessment at site visits |

# 3 STUDY OBJECTIVE AND ENDPOINTS

## 3.1 Study Objectives

### 3.1.1 Primary Objective

To assess the efficacy of B244 in the treatment of pruritus in adults with a history of atopic dermatitis.

### 3.1.2 Secondary Objectives

To assess the safety and tolerability of B244 in adults with a history of atopic dermatitis.

## 3.2 Study Endpoints

### 3.2.1 Efficacy - Primary Endpoint

The primary efficacy endpoint is:

- Mean change (absolute) in WI-NRS from Baseline to Week 4

### 3.2.2 Efficacy - Secondary Endpoints

The secondary efficacy endpoints are:

- Proportion of subjects with ≥4point improvement in WI-NRS from Baseline to Week 4
- Proportion of subjects with any improvement in WI-NRS from Baseline to Week 4
- Mean change (absolute and percent) in AI-NRS from Baseline to Week 4
- Proportion of subjects with ≥4 point improvement in AI-NRS from Baseline to Week 4
- Proportion of subjects with any improvement in AI-NRS from Baseline to Week 4
- Mean change (absolute and percent) in WI-NRS from Baseline to Week 2
- Proportion of subjects with ≥4 point improvement in WI-NRS from Baseline to Week 2
- Mean change (absolute and percent) in POEM from Baseline to Week 4
- Mean change (absolute and percent) in 5-D Pruritus Scale from Baseline to Week 4

The endpoints will be reported for all weeks or all visits. The primary endpoint of mean change in WI-NRS is also presented at all weeks for both absolute and percent change. Absolute change will be considered the primary endpoint with percent change as supportive. Any improvement in WI-NRS and AI-NRS is defined as ≥1 point improvement from Baseline.

### 3.2.3 Efficacy - Exploratory Endpoints

- Mean change (absolute and percent) in IGA from Baseline to Week 4
- Mean change (absolute and percent) in EASI from Baseline to Week 4

- Proportion of subjects with IGA of Clear or Almost Clear and ≥2 point improvement from Baseline to Week 4
- Proportion of subjects with IGA of Clear or Almost Clear at Week 4
- Proportion of subjects with any improvement in IGA from Baseline to Week 4
- Proportion of subjects with ≥50% Improvement in EASI (EASI-50) from baseline to Week 4
- Proportion of subjects with ≥75% Improvement in EASI (EASI-75) from baseline to Week 4
- Proportion of subjects with ≥90% Improvement in EASI (EASI-90) from baseline to Week 4.

The endpoints will be reported for all visits. Absolute change will be considered the primary endpoint with percent change as supportive. Any improvement in IGA is defined as ≥1 point improvement from Baseline.

### 3.2.4 Safety & Tolerability

Safety and tolerability endpoints include the following:

- Incidence of TEAEs and SAEs
- TEAEs leading to discontinuation
- Changes in vital signs and clinical laboratory parameters following study drug exposure
- Changes in local skin tolerability following application of study drug

# 4 STUDY DESIGN

## 4.1 General Study Design and Plan

This is a prospective, vehicle-controlled, double-blind, multicenter, randomized phase II trial, comparing the effect of twice daily B244 applications for 4 weeks vs vehicle applications on treatment of mild to moderate pruritus associated with atopic dermatitis.

Approximately 576 subjects are planned to be enrolled.

The total duration of the study will be approximately 11 weeks. Participants will report for a Screening visit and if all inclusion/exclusion criteria are met, subjects will go through a two-week washout phase before reporting for a Baseline visit.

After Screening and Baseline, participants will be randomized to one of two doses of B244 or vehicle application for 4 weeks.

Randomization will be 1:1:1 so that an equal number of patients will be treated in each arm of the study.

All B244 randomized subjects will be treated at the dose of $1x10^{10}$ cells/ml (O.D. 5.0) or $4x10^{10}$ cells/ml (O.D. 20.0).

Subjects must be willing and able to complete diary within a consistent time frame on a daily basis and to comply with restrictions on allowable therapies for the duration of the study.

All subjects will attend a Screening visit not more than 21 days prior to Baseline (Day 0).

Subjects will be required to return to the clinic at Baseline, Day 14 (Week 2) and Day 28 (Week 4) visits. All subjects will be asked to attend a Week 8 follow-up visit 4 weeks (28 (±3) days) after the last dose of study medication.

Subjects will apply a total of 10 pumps of IP per application across all affected areas twice-a-day (i.e., 10 pumps in the morning and 10 pumps again at night) for 4 weeks.

Safety evaluations will consist of review of participant's medical history at screening and on-going assessment of adverse events reported throughout the study duration.

### 4.1.1 Inclusion-Exclusion Criteria and General Study Population

#### *4.1.1.1 Inclusion Criteria*

Deviations from inclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability, or participant safety. Therefore, adherence to the criteria as specified in the protocol is essential.

Participants eligible for enrollment in the study must meet all the following criteria:

1. Male and female subjects 18 to 65 years of age.
2. Pruritus of at least 4 weeks duration prior to the initial Screening visit and during the 2 week washout period.
    a. Subjects using stable doses of oral H1 antihistamines at the initial Screening visit must be willing to continue these at the same doses and frequencies throughout the study inclusive of the follow-up period.
3. Worst Itch Numeric Rating Scale (WI-NRS) score ≥ 7 in the 24-hour period prior to the initial Screening as well as Baseline visits.
4. Average weekly WI-NRS score ≥6 for each week of the washout period, as recorded in the eDiary.
5. A history of atopic dermatitis for greater than 12 months consistent with a diagnosis of atopic dermatitis, as defined by the 2014 American Academy of Dermatology (AAD) Guidelines of Care for the Management of Atopic Dermatitis[2].
    a. Subjects using bland emollients at the initial Screening visit will be allowed to continue to use their emollient of choice at a similar dose and frequency throughout the study, if used.

   b. Subjects using low- to mid-potency topical corticosteroids at the initial Screening visit will be allowed to use their topical corticosteroid of choice at the same dose and frequency no more than 7 days per month throughout the study as rescue medication.
6. A minimum of 10% and not more than 40% of the subjects' BSA affected by atopic dermatitis (*affected* is defined by physical examination findings: erythema, edema, scaling, lichenification, excoriation, with the excoriation serving as the physical examination correlate of pruritus) at Screening and Baseline.
   a. Subjects' BSA can include face and body OR body alone BUT NOT face alone.
7. An Investigator Global Assessment (IGA) score of 2-3 at Screening and Baseline.
8. Willing and able to complete once-daily eDiary entries within a consistent timeframe for the duration of the study and have ≥80% eDiary compliance rate during the washout period.
9. Judged to be in good health in the investigator's opinion.

#### *4.1.1.2 Exclusion Criteria*

Deviations from exclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability or participant safety. Therefore, adherence to the criteria as specified in the protocol is essential.

Participants will be excluded from the study if any of the following criteria are met:

1. Clearly defined etiology for pruritus other than atopic dermatitis. These include but are not limited to urticaria, psoriasis or other non-atopic dermatologic conditions, hepatic or renal disease, psychogenic pruritus, drug reaction, untreated hyperthyroidism, parasite presence and presence of acute infection either systemically or in the AD lesions.
2. Presence of any acute condition which may risk inducing an atopic dermatitis flare during the course of the study, such as impetigo or active herpes simplex infection.
3. Treatment with systemic corticosteroids within 4 weeks prior to randomization.
4. Treatment with Class III or higher potency topical corticosteroids or any topical anti-pruritic therapies (other than stable doses of low- or mid-potency topical corticosteroids or bland emollients) within 4 weeks prior to randomization.
5. Treatment with systemic therapies with recognized anti-pruritic (e.g. tricyclic antidepressants, sedatives, tranquilizers, gabapentin, marijuana or other cannabinoids, opioid receptor agonists/antagonists) or pruritic (e.g. opioids, angiotensin-converting enzyme inhibitors, cocaine, antimalarials) properties within 4 weeks prior to randomization.
   a. Stable doses of H1 antihistamines will be permitted. Subjects must be willing to continue these at the same doses and frequencies throughout the study inclusive of the follow-up period.
6. Any clinically significant changes in type, dose, or frequency of bland emollients, low- or mid-potency corticosteroids, and/or oral H1 antihistamines throughout the study from screening to follow-up.
7. Treatment with systemic immunosuppressive/ immunomodulatory therapies within 4 weeks prior to randomization (including but not limited to phosphodiesterase-4

inhibitors, cyclosporine, mycophenolate-mofetil, methotrexate, azathioprine, interferon-gamma, or phototherapy).
8. Treatment with biologic therapies within 12 weeks or 5 half-lives prior to randomization, whichever is longer.
9. Use of an indoor tanning facility within 4 weeks prior to randomization.
10. Treatment with any investigational therapy within 4 weeks prior to randomization.
11. Allergen immunotherapy within 6 months prior to randomization.
12. Prior use of AO+ Mist.
13. History of malignancy within 5 years prior to randomization, with the exception of completely treated and non-metastatic basal cell carcinoma or squamous cell carcinoma of the skin.
14. History of a major psychiatric condition (including major depressive disorder, bipolar disorder, or schizophrenia), suicidal ideation, or suicide attempt.
15. Known active hepatitis infection.
16. Known history of human immunodeficiency virus (HIV) infection.
17. Presence of any medical condition or disability that, in the investigator's opinion, could interfere with the assessment of safety or efficacy in this trial or compromise the safety of the subject.
18. Currently pregnant or breastfeeding, or male subject with a pregnant or breastfeeding partner.
19. Females of childbearing potential who are unable or unwilling to practice highly effective contraception (pregnancy prevention); fertile males who are unable or unwilling to use condoms with female partners of childbearing potential.

#### *4.1.1.3 General Study Population*

Subjects with pruritus and a history of atopic dermatitis will be randomized into this study.

## 4.2 Study Withdrawal and Withdrawal from Investigational Product and Stopping Criteria

A participant may withdraw from the study at any time at his/her own request or may be withdrawn at any time at the discretion of the Investigator.

Reasons for withdrawal (participants who refuse to complete any remaining study visits) or discontinuation (participants who prematurely stop the application) at any time during the study may include, but are not limited, to the following:

- For safety reasons, either at the discretion of the Investigator or at the participant's request
- For protocol violations at the discretion of AOBiome
- Withdrawal of consent by the Subject
- Lost to follow-up

- Due to use of concomitant therapy that could interfere with the results of the study (the Investigator will report all such information through the CRF and decide, in accordance with AOBiome, whether the participant is to be withdrawn).

The reason for participant study withdrawal will be recorded in the electronic Case Report Form (eCRF). Data from participants withdrawing from the study will be considered evaluable up to the point at which they are withdrawn using the same criteria for evaluability as for participants who complete the study.

Study stopping rules will be implemented to stop the study for safety review in the event that:

- 1 subject reports death, or
- >2 subjects report an SAE, or
- >4 subjects experience grade 3 AEs of a similar type, or
- >6 subjects experience grade 2 AEs of a similar type

when the reported SAEs or AEs are considered possibly, probably, definitely or related to the investigational product.

Atopic Dermatitis is an active disease with known seasonal and personal histories of flares and exacerbations of the patient's underlying disease state. This includes personal histories of worsening itch and itch-scratch cycles, which can lead to localized infection and localized cellulitis. A subject's known and collected clinical history should be considered by the principal investigator when determining relationship of event to the investigational product.

### 4.3 Early Termination

Early termination from the study may occur due to loss to follow-up or withdrawal of consent by the subject. Participants who have discontinued the study early will be evaluated by the Investigator at the Early Termination Visit. See the list of assessments to be performed at the Early Termination Visit in the Time and Events Table (Section 2.2). Participants with ongoing AEs or SAEs believed to be possibly related to investigational product (IP) will continue to be followed until resolution or for 30 days as warranted by the nature of the AE.

## 5 PLANNED ANALYSIS

### 5.1 Final Analysis

Final analysis is planned for the study after the database lock. The final analysis will follow instructions presented in this SAP. No interim reporting is planned.

## 6 GENERAL CONSIDERATIONS

### 6.1 General Summary Tables and Individual Subject Data Listings

Summary tables and listings (e.g., post text tables and individual subject data listings) are prepared according to ICH Guideline E3 and include a "footer" providing explanatory notes that indicate as a minimum the SAS program name and the date of output generation.
Post text tables also include reference(s) to the subject data listing(s) that supports the summary data and the subject data listing(s) reference the input data source(s).

Post text tables will be organized with respect to treatment group and the order of drug presentation will be the low-dose group first, followed by the high-dose group, the pooled IP treatment group, then the vehicle control. The summary tables clearly indicate the number of subjects to which the data apply and unknown or not performed are distinguished from missing data.

Summary tables for medications and medical conditions are coded according to the WHO Drug Dictionary. Adverse event preferred terms and body/organ systems are coded using the MedDRA dictionary. The MedDRA dictionary can be used, as well, in the coding of signs and symptoms, medical history, physical examination abnormalities, and clinical diagnoses.

Supportive individual subject data listings, as a minimum, are sorted and presented by treatment group and subject ID. Listings also include visit number, visit date, and days relative to the initiation of double-blind treatment.

## 6.2 Data Management

Biorasi will create SDTM and ADaM data sets, perform statistical analyses, and create resulting outputs using (SAS®) software version 9.4 or above.

## 6.3 Data Presentation Conventions

The data analysis will be conducted on all participant data when the trial ends. Subjects will be pooled across all sites. Data will be presented by treatment group and pooled B244 treatment.

All data collected will be documented using summary tables, figures, and/or patient data listings.

Continuous variables (e.g., age) are summarized using descriptive statistics (the number of subjects with available data, the mean, standard deviation (SD), median, minimum and maximum). Categorical variables (e.g., race) are summarized using counts and percentages. Percentages are calculated using the total subjects per treatment group.

The following conventions are applied to all data presentations and summaries:

- For continuous variables, all mean and median values are formatted to one more decimal place than the measured value. Standard deviation values are formatted to two more decimal places than the measured value. Minimum and maximum values are presented with the same number of decimal places as the measured value.

- For categorical variables, the number and percentage of responses are presented in the form XX (XX.X %) where the percentage is in the parentheses.

- Date variables are formatted as DDMMMYYYY for presentation. Time is formatted in military time as HH:MM for presentation.

- P-values, if applicable, will be presented to 4 decimal places. If the p-value is less than 0.0001 then it will be presented as <0.0001.

The statistical test for the primary endpoint will use a one-sided 90% CI. All other statistical tests performed will use a two-sided 95% CI.

The table and listing shells and table of contents as part of this SAP provide the expected layout and titles of the tables, listings, and figures. Any changes to format, layout, titles, numbering, or any other minor deviation will not necessitate a revision to the SAP nor will it be considered a deviation from planned analyses. Only true differences in the analysis methods or data handling will necessitate such documentation. The appropriate listings supporting the tables will be included and are not specified in the individual sections throughout the document.

## 6.4 Baseline Definition

The day of first dose of study medication is Day 0 in the Schedule of Assessments (SOA) per protocol but will be considered relative study Day 1 in the SAP in order to construct Clinical Data Interchange Standards Consortium (CDISC) compliant datasets.

The Baseline visit (Day 0 per protocol) will take place once the results of Screening assessments are obtained, suggesting that the subject is eligible for entering the study. During this visit, those subjects who qualify for entering the study will be randomized to one of the study arms in a ratio of 1:1:1.

For all safety analyses, Baseline will be defined as the most recent measurement prior to the first administration of study drug.

The patient reported local tolerability diary for the first 7 days of treatment will be reported as relative study Day 1 to Day 7 in the eDiary, which corresponds to Day 0 to Day 6 per protocol. For the patient reported local tolerability diary, the first measurement occurs at the end of the first day of treatment (Day 0 Baseline visit per protocol, equivalent to relative study Day 1 reported in the patient reported local tolerability diary) and solicits subjects to record any changes in local tolerability symptoms compared to the previous day prior to treatment. Relative study Day 2 to Day 7 patient reported local tolerability diary entries (Day 1 to Day 6 per protocol) solicit subjects to record any changes in local tolerability symptoms compared to the previous day of treatment.

For all efficacy analysis derived from patient reported daily diary entries (e.g., WI-NRS, AI-NRS), Baseline period is defined as the average of the 1-week period before randomization (Day

-7 to -1) where the subject is observed for their medical condition (see also Section 6.5.3). For the primary analysis, at least 1 day of daily diary entry is required to calculate the Baseline WI-NRS and AI-NRS. For the sensitivity analysis, at least 4 days of daily diary entries are required.

Baseline WI-NRS = (Sum of daily WI-NRS scores from Day -7 to Day -1) / (Total number of WI-NRS diaries entered from Day -7 to Day -1)

Baseline AI-NRS = (Sum of daily AI-NRS scores from Day -7 to Day -1) / (Total number of AI-NRS diaries entered from Day -7 to Day -1)

For efficacy analysis derived from on-site visit assessments (e.g., BSA, IGA, EASI, 5-D Pruritus Scale, POEM), Baseline is defined as the most recent measurement prior to the first administration of study drug (i.e., assessment at the Baseline visit on Day 0 per protocol or relative study Day 1).

For the rescue medication diary, the Baseline rescue medication days is the number of rescue medication days recorded during the 2 weeks (Day -14 to Day -1) prior to the Baseline visit.

## 6.5 Derived and Transformed Data

### 6.5.1 Baseline Age

Subject's age in years will be calculated based on the date of the Baseline visit date using the following formula:

Age (years) = FLOOR ((INTCK ('month', Date of Birth, Date of Baseline Visit) - (DAY(Date of Baseline Visit) < MIN(DAY(Date of Birth), DAY (INTNX ('month', Date of Baseline Visit, 1) - 1)) ) /12 ); where:

- FLOOR () is a SAS function that returns the largest integer that is less than or equal to the argument.
- INTCK () is a SAS function that returns the number of interval boundaries of a given kind that lie between two dates, times, or datetime values.
- DAY () is a SAS function that returns the day of the month from a SAS date value.
- INTNX () is a SAS function that increments a date, time, or datetime value by a given time interval, and returns a date, time, or datetime value.

### 6.5.2 Study Day

Day 1 is defined as the day of the Baseline visit when the subject will receive the first dose after the subject is randomized. Day 2 is defined as the day after the Baseline visit when the subject is on the second day of treatment.

- For a visit date on or after the date of the first dose:
  Study Day = (date of interest – date of first dose) + 1

- For a visit date before the date of the first dose:
  Study Day = (date of interest – date of first dose)

### 6.5.3 Weekly Average WI-NRS and AI-NRS

For WI-NRS and AI-NRS the weekly average is calculated from the daily scores. For the primary analysis the weekly average will be calculated when there is at least one recorded daily score in the corresponding week. Values from study day (as defined above) Day 1 to 7 contributes to Week 1 average, Study Day 8 to 14 to Week 2, etc. Baseline is derived as the average of the daily scores for Day -7 to -1. The average will be derived as the mean of all non-missing values during the respective time period.

Week 1 WI-NRS = (Sum of daily WI-NRS scores from Day 1 to Day 7) / (Total number of WI-NRS diaries entered from Day 1 to Day 7)

Week 2 WI-NRS = (Sum of daily WI-NRS scores from Day 8 to Day 14) / (Total number of WI-NRS diaries entered from Day 8 to Day 14)

Week 3 WI-NRS = (Sum of daily WI-NRS scores from Day 15 to Day 21) / (Total number of WI-NRS diaries entered from Day 15 to Day 21)

Week 4 WI-NRS = (Sum of daily WI-NRS scores from Day 22 to Day 28 or Day of Visit 4 – 1, whichever is earlier) / (Total number of WI-NRS diaries entered from Day 22 to Day 28 or Day of Visit 4 – 1, whichever is earlier)

Week 5 WI-NRS = (Sum of daily WI-NRS scores from Day of Visit 4 to Day of Visit 4 + 6) / (Total number of WI-NRS diaries entered from Day of Visit 4 to Day of Visit 4 + 6)

Week 6 WI-NRS = (Sum of daily WI-NRS scores from Day of Visit 4 + 7 to Day of Visit 4 + 13) / (Total number of WI-NRS diaries entered from Day of Visit 4 + 7 to Day of Visit 4 + 13)

Week 7 WI-NRS = (Sum of daily WI-NRS scores from Day of Visit 4 + 14 to Day of Visit 4 + 20) / (Total number of WI-NRS diaries entered from Day of Visit 4 + 14 to Day of Visit 4 + 20)

Week 8 WI-NRS = (Sum of daily WI-NRS scores from Day of Visit 4 + 21 to Day of Visit 4 + 27 or Day of Visit 5 – 1, whichever is earlier) / (Total number of WI-NRS diaries entered from Day of Visit 4 + 21 to Day of Visit 4 + 27 or Day of Visit 5 - 1, whichever is earlier)

The same conventions are used to calculate Week 1 to Week 8 AI-NRS.

Week 1 AI-NRS = (Sum of daily AI-NRS scores from Day 1 to Day 7) / (Total number of AI-NRS diaries entered from Day 1 to Day 7)

Week 2 AI-NRS = (Sum of daily AI-NRS scores from Day 8 to Day 14) / (Total number of AI-NRS diaries entered from Day 8 to Day 14)

Week 3 AI-NRS = (Sum of daily AI-NRS scores from Day 15 to Day 21) / (Total number of AI-NRS diaries entered from Day 15 to Day 21)

Week 4 AI-NRS = (Sum of daily AI-NRS scores from Day 22 to Day 28 or Day of Visit 4 – 1, whichever is earlier) / (Total number of AI-NRS diaries entered from Day 22 to Day 28 or Day of Visit 4 – 1, whichever is earlier)

Week 5 AI-NRS = (Sum of daily AI-NRS scores from Day of Visit 4 to Day of Visit 4 + 6) / (Total number of AI-NRS diaries entered from Day of Visit 4 to Day of Visit 4 + 6)

Week 6 AI-NRS = (Sum of daily AI-NRS scores from Day of Visit 4 + 7 to Day of Visit 4 + 13) / (Total number of AI-NRS diaries entered from Day of Visit 4 + 7 to Day of Visit 4 + 13)

Week 7 AI-NRS = (Sum of daily AI-NRS scores from Day of Visit 4 + 14 to Day of Visit 4 + 20) / (Total number of AI-NRS diaries entered from Day of Visit 4 + 14 to Day of Visit 4 + 20)

Week 8 AI-NRS = (Sum of daily AI-NRS scores from Day of Visit 4 + 21 to Day of Visit 4 + 27 or Day of Visit 5 – 1, whichever is earlier) / (Total number of AI-NRS diaries entered from Day of Visit 4 + 21 to Day of Visit 4 + 27 or Day of Visit 5 – 1, whichever is earlier)

Sensitivity analysis will be performed on a restricted weekly average, requiring at least 4 responses in the 7 days for each respective time period. Subjects with fewer than 4 responses during the 7-day time period(s) will have their weekly average set to missing.

### 6.5.4 Derivation of ≥4 Point and Any Improvement in WI-NRS and AI-NRS

The proportion of subjects with ≥4 point and any improvement (≥1 point) in WI-NRS and AI-NRS from Baseline will be derived from the weekly averages containing at least one daily score and at least 4 daily scores (as discussed in section 6.5.3 for primary and sensitivity analyses, respectively) and will be presented for each week (Weeks 1 to 8).

### 6.5.5 Percent Change from Baseline

Percent change from Baseline will be derived for continuous (WI-NRS, AI-NRS) endpoints and for the total score for ordinal endpoints (IGA, EASI, 5-D Pruritus Scale, POEM). Percent change from Baseline will be derived as: [(Post-Baseline value – Baseline value) / Baseline value] * 100.

For EASI, percent change from Baseline will be derived to indicate subjects who have obtained 50%, 75%, and 90% improvement.

### 6.5.6 Rescue Medication During Treatment Period

The treatment period (also referenced as "on-treatment") begins on date of subject's first dose and ends on Day of Visit 4 – 1, even if the subject has applied IP on Day of Visit 4.

Based on recorded use of rescue medication the following variables will be derived and normalized as described in section 7.5.4 for all subjects:

- Number of days in a month with rescue treatment (for Week 1 to Week 4 and Week 5 to Week 8)
- Number of days every 2 weeks with rescue treatment (for Day -14 to -1 for Baseline, Day 1 to Day of Visit 3 -1 for Week 2, Day of Visit 3 to Day of Visit 4 -1 for Week 4, Day of Visit 4 to Day of Visit 4 + 13 for Week 6, and Day of Visit 4 + 14 to Day of Visit 5 – 1 for Week 8)

Proportion of subjects with rescue treatment, and the above two variables (number of days in a month with rescue treatment and number of days every 2 weeks with rescue treatment) will be derived and normalized for subjects with recorded use of rescue medication.

### 6.5.7 Missing Start and Stop Dates for Prior and Concomitant Medication

Start date:

- If start date is completely missing, start date will be imputed with the informed consent date.
- If year is present and month and day are missing, set month and day to January 1.
- If year and day are present and month is missing, set month and day to January 1.
- If year and month are present and day is missing, set day to the 1st day of month.

Stop date:

- If end date is completely missing, end date will not be imputed and medication will be assumed to be ongoing.
- If year is present and month and day are missing, set month and day to December 31st.
- If year and day are present and month is missing, set month and day to December 31st.
- If year and month are present and day is missing, set day to the last day of month.

### 6.5.8 Safety Parameters

Safety and tolerability endpoints will consist of all adverse events (AEs) reported during the study duration from the date of randomization through Week 8 (End of Study Visit). Specific AEs are defined below.

Treatment-Emergent Adverse Events (TEAE): Any AE with onset after the first dose of study medication through 28 days after the last dose of study medication.

Serious Adverse Event (SAE): An AE occurring at any dose that results in any of the following outcomes: death, a life-threatening AE, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

Associated with Use of the Study Drug: There is a reasonable possibility that the experience may have been caused by the study drug. If the Investigator does not know whether or not study drug caused the event, then the event will be handled as "related to study drug" for reporting purposes. The determination of whether an AE is related to study drug is as follows:

- Related: The AE has a missing, unknown, possible, probable or definite relationship to the study medication.
- Not related: The AE is unlikely or definitely unrelated to the study drug.

### 6.5.9 Missing Start and Stop Dates for Adverse Events

Start date:

- If start date is completely missing, start date is set to date of first dose.
- If (1) year is present and month and day are missing or (2) year and day are present and month is missing:
  - If year = year of first dose, then set month and day to month and day of first dose.
  - If year < year of first dose, then set month and day to December 31st.
  - If year > year of first dose, then set month and day to January 1st.
- If month and year are present and day is missing:
  - If year = year of first dose and
    - If month = month of first dose, then set day to day of first dose date.
    - If month < month of first dose, then set day to last day of month.
    - If month > month of first dose, then set day to 1st day of month.
  - If year < year of first dose, then set day to last day of month.
  - If year > year of first dose, then set day to 1st day of month.

Stop date:
If the outcome of the AE was ongoing or unknown, then the rules outlined below will not be applied.

- If stop date is completely missing, stop date is set to date of study discontinuation/end of study date.
- If (1) year is present and month and day are missing or (2) year and day are present and month is missing:
  - If year = year of study discontinuation, then set month and day to month and day of study discontinuation.
  - If year < year of study discontinuation, then set month and day to December 31$^{st}$.

- If year > year of study discontinuation, then set month and day to December 31st.

- If month and year are present and day is missing:
  - If year = year of study discontinuation/end of study date and
    - If month = month of study discontinuation/end of study date, then set day to day of study discontinuation date.
    - If month < month of study discontinuation/end of study date, then set day to last day of month.
    - If month > month of study discontinuation/end of study date, then set day to 1st day of month.
  - If year < year of study discontinuation/end of study date, then set day to last day of month.
  - If year > year of study discontinuation/end of study date, then set day to 1st day of month.

### 6.5.10 Visit Windows

It is expected that all visits should occur according to the protocol schedule. All visit data will be tabulated per the evaluation visit as recorded on the CRF even if the assessment is outside of the visit window. All ePRO/diary data will be tabulated per the weekly conventions defined in Section 6.5.3. In data listings, the relative day of all dates will be presented.

### 6.5.11 Categorization of Continuous Variables

For reporting and analysis purpose continuous variables may be categorized.

Age at Baseline will be categorized in 3 groups: 18 to 40 years, 41 to 54, 55 to 65 years.

BSA will be categorized in 3 groups: 10 to 20%, >20 to 30%, >30 to 40%. If subjects are admitted into the study with baseline BSA outside of these specified ranges, then the subject will be placed into the closest occurring category. For example, if a subject is admitted into the study with a baseline BSA of 50%, then they will be included in the >30-40% category. Footnotes will be added to relevant tables, listings, or figures (TLFs) noting how many subjects out of range were included in the analysis.

### 6.5.12 Site Related Baseline Covariates

Site may be included as a covariate in regression models. Additional covariates reflecting site, seasonality, and geographical variation may be derived and included in sensitivity analyses.

For pooling of sites, the following covariates may be defined:

- Enrollment low to high (for example, pool by number of subjects enrolled: 1-9, 10-15, 16-25, 26+)
- Enrollment gap (based on time between enrolled patients, one or more gaps of 56 days or above between enrollment v none)

For investigation of seasonality and geography effect the following covariates on site level will be defined:

- Colder v warmer months (randomized Oct. – Mar / Apr – Sep)
- Seasonal geographic locations (warm all year v cooler all year)

For IP effect the following covariates may be defined:

- IP lot used (subjects who use at least 2 kits from the same lot can be included in the lot analysis)

Above mentioned site related baseline covariates may be derived if post-hoc analyses are performed (see Section 7.4).

# 7 STATISTICAL ANALYSES

## 7.1 Sample Size Determination

Approximately 576 subjects may be enrolled to account for 16.7% drop out rate prior to completing the study. A total of 160 evaluable subjects per group (480 total) are required to achieve at least 80% power to detect a pairwise difference of 0.65 in mean WI-NRS change from Baseline to Week 4 between one of two active doses of B244 and vehicle control when assuming a standard deviation of 2.5 and applying a Dunnett Testing Method at a one-sided familywise error rate of 0.10.

## 7.2 Analysis Populations

Final analysis populations will be determined and agreed upon prior to database lock and patient unblinding as described in section 7.3.2.

### 7.2.1 Screen Failures

Investigators must account for all subjects who sign informed consent and will maintain an Enrollment Log capturing subjects screened and indicating who was enrolled or excluded and the reason why. If the subject is found not to be eligible prior to enrollment, the reason(s) for ineligibility must be documented by the Investigator.

These subjects will neither contribute to data presentations nor be included in formal statistical analyses. The number of screen failures will be included in the data disposition table. Subject Numbers assigned to subjects who fail Screening will not be re-used.

### 7.2.2 Subjects Enrolled and Subjects Not Assigned

Subjects are considered enrolled if they sign informed consent and meet all eligibility criteria. Randomization is not a requirement for subjects to be considered enrolled.

Any subject who meets eligibility criteria but is not randomized (e.g., withdrew from the study, lost-to-follow-up, etc.), will be classified as "Not Assigned" in the statistical outputs. This group of subjects will not include Screen Failures as those subjects will be reported separately.

Thus, enrolled subjects consist of randomized subjects and not assigned subjects.

### 7.2.3 Safety Population

The safety population includes all subjects who apply at least 1 dose of study medication. Subjects will be grouped as treated.

### 7.2.4 Modified ITT Population

Modified Intent to Treat (mITT): All randomized participants who apply at least 1 dose of study medication and have at least one post-baseline evaluation on-site visit. Subjects will be grouped as randomized.

This is a change from the protocol.

### 7.2.5 Per-Protocol (PP) Population

The PP population includes all subjects in the mITT population without any major protocol deviations that may have an impact on the efficacy assessments, who complete their Week 4 visit, and who administer at least 50% of investigational product (IP). Subjects will be grouped as treated.

### 7.2.6 Role of Populations in Analyses

The results in the mITT population will be considered definitive for superiority of each active treatment to vehicle with those in the PP population considered supportive. Safety analyses will be performed using the Safety population.

## 7.3 General Analysis

### 7.3.1 Subjects Disposition

The subject disposition summary will include the number screened, the number of screen failures, the number enrolled, the number in each patient population for analysis, the number who completed the study, the number who discontinued the study and reason for discontinuation from the study. Disposition data will be summarized by treatment and pooled B244 treatment arm.

A summary table of analysis populations and reasons for exclusion will be presented for all subjects enrolled.

A by-subject data listing of study completion information including the reason for study discontinuation will be presented. A by-subject listing of inclusion/exclusion criteria not met will also be presented.

### 7.3.2 Clinical Trial Protocol Deviations

A summary of all major protocol deviations for mITT and Safety populations by category will be generated. Protocol deviation data will be summarized by treatment and pooled B244 treatment arm. A by-subject data listing of all protocol deviations will also be presented. Protocol deviations will be categorized as major or minor per Protocol Deviation Guidance v2.1.
At the discretion of the Sponsor, major protocol deviations, as determined by a review of the data prior to unblinding of the study results and the conduct of statistical analyses, may result in the removal of a subject's data from the PP population. Biorasi and its data monitoring group as applicable will be responsible for producing the final protocol deviation file, in collaboration with Sponsor; this file will include a description of the protocol deviation and clearly identify whether or not this violation warrants exclusion from the PP population. This file will be finalized prior to hard database lock.

### 7.3.3 Demographic and Baseline Characteristics

Demographic and Baseline characteristic data summarization will be performed in order to descriptively assess the comparability of treatment groups. Data to be tabulated will include age, race, sex, ethnicity, height, weight, BMI, smoking status, and rescue medication days during the 2-weeks prior to baseline as well as Baseline WI-NRS, AI-NRS, IGA, EASI, BSA, 5-D Pruritus Scale, and POEM scores.

## 7.4 Efficacy Analysis

All efficacy analyses will be performed on the mITT population and PP population using the methods described below. Regression models will include all eligible subjects for the respective analysis, from the 3 treatment arms.

- *Primary Analysis*: Includes data for all subjects in the respective population (mITT/PP)
- *Sub-Analysis*: Excludes data collected on/after date of first on-treatment rescue medication use through the end of the study.
    - For WI-NRS/AI-NRS endpoints, excludes data from *week* of first on-treatment rescue medication use.
- *Non-Responder Imputation (NRI) Analysis*: Subjects who discontinue treatment early or who take on-treatment rescue medications will be imputed as a non-responder for assessments that occur on/after date of discontinuation/on-treatment rescue medication use through the end of the study.

- For WI-NRS/AI-NRS endpoints, excludes data from *week* of discontinuation/first on-treatment rescue medication use.
- Subjects who discontinue early should have at least one treatment-emergent adverse event (TEAE) leading to discontinuation in order to have their data imputed for NRI analysis.

Efficacy Analyses

| **Measure** | **Endpoints** | **Analysis** |
|---|---|---|
| WI-NRS/ AI-NRS* | Mean Change from Baseline | 1. Primary<br>2. Primary/Sensitivity<br>3. Sub-Analysis<br>4. Sub-Analysis/Sensitivity |
| WI-NRS/ AI-NRS* | Improvement (4-Point, Any) | 1. Primary<br>2. Primary/Sensitivity<br>3. Sub-Analysis<br>4. Sub-Analysis/Sensitivity<br>5. NRI<br>6. NRI/Sensitivity |
| 5D | Mean Change from Baseline | 1. Primary<br>2. Sub-Analysis |
| EASI | Mean Change from Baseline | 1. Primary<br>2. Sub-Analysis |
| EASI | Improvement (≥50%, ≥75%, ≥90%) | 1. Primary<br>2. Sub-Analysis<br>3. NRI |
| IGA | Mean Change from Baseline | 1. Primary<br>2. Sub-Analysis |
| IGA | Improvement (2-Point to Clear/Almost Clear, Clear/Almost Clear, Any) | 1. Primary<br>2. Sub-Analysis<br>3. NRI |
| POEM | Mean Change from Baseline | 1. Primary<br>2. Sub-Analysis |

*WI-NRS/AI-NRS analyses require at least 1 diary entry per week to calculate the weekly average, except for the sensitivity analyses, where at least 4 diary entries per week are required.

PP population excludes subjects with any major protocol deviation that may impact efficacy and safety analyses, including those with any confounding events or those over the rescue medication use limits but includes data for subjects below rescue medication use limits. Rescue medication

use below the allowed limit per protocol are considered minor protocol deviations, are considered non-confounding, and is included in the PP population.

The following events are confounding:

- Change in stable use of oral H1 antihistamines (e.g., change in type, dose, and frequency of medication)
- Change in stable use of bland emollients (e.g., change in type, dose, and frequency of treatment)
- Use of excluded medications during study
- Use of rescue medications over the allowed limit per protocol (over 3 rescue medication days during the 2-week washout period, over 7 rescue medication days during the 4-week treatment, and over 7 rescue medication days during the 4-week follow-up)

In the PP sub-analysis, all subject data over the rescue medication limits per the PP primary analysis will be excluded, but subject data below the rescue medication limits will be included up to the date or week that the first rescue medication is taken.

Hypothesis tests for the primary efficacy endpoint will be performed using a Dunnett Testing Method, applying pairwise comparisons of each respective B244 dose group to vehicle using a one-sided familywise error rate of 0.10. Section 7.4.2 provides further details. No additional adjustments will be made for multiple testing. As such, p-values from analysis of secondary and exploratory efficacy analyses must be interpreted in an exploratory fashion.

Supportive analyses may be performed for all efficacy analyses combining the B244 dose groups in comparison against vehicle and comparison of the B244 groups to one another.

Furthermore, stratified analyses will be performed by presenting descriptive statistics by age group, race, gender, IGA at Baseline (2 or 3), EASI at baseline (≤10 or >10), BSA range at Baseline (10 to 20%, >20 to 30%, >30 to 40%), rescue treatment used at Baseline (Yes, No), and rescue medication used while on treatment (Yes/No).

In case there are clear differences between groups in the stratified analyses, then post-hoc sensitivity analyses may be performed to control for those covariates in the appropriate statistical model. This post-hoc analysis may also include examination of outcome measures stratified by presence/absence of asthma at Baseline. Site related baseline covariates may also be analyzed post-hoc as described in Section 6.5.12. The effect of seasonality may also be investigated via seasonal pattern as one sine and one cosine function[3], if applicable, including interaction with site specific covariate. Post-hoc analysis may also include examination of outcome measures that include/exclude certain lots due to aging or stratified by investigational product lot.

### 7.4.1 Analysis of WI-NRS and AI-NRS

The primary endpoint of mean change from Baseline to Week 4 in WI-NRS will be analyzed using analysis of covariance (ANCOVA) models.

In addition, the continuous efficacy endpoints WI-NRS, AI-NRS will be summarized using descriptive statistics at Baseline, Week 1, Week 2, Week 3, Week 4, Week 5, Week 6, Week 7, and Week 8 for actual values and change from Baseline values.

The difference in treatment groups in change from Baseline values at post-baseline visits will be analyzed using a mixed model with repeated measures to account for within subject variability and including visit (Baseline vs. Week 1, Week 2, Week 3, Week 4, Week 5, Week 6, Week 7, Week 8), treatment group, visit-by-treatment interaction, and Baseline value as explanatory variables. The subject variability will be modelled using a compound symmetry covariance matrix. Other types of covariance structure may be applied should they provide a better model fit.

The frequency and rate of WI-NRS and AI-NRS responders at Week 1, Week 2, Week 3, Week 4, Week 5, Week 6, Week 7, Week 8 (≥4 point change from Baseline in WI-NRS and AI-NRS) and other responder endpoints (any improvement from Baseline in WI-NRS and AI-NRS, defined as ≥1 point change from Baseline) will be reported and compared between treatment groups using a logistic regression model by week. Generalized estimating equations to account for repeated measures and within-subject variability may also be applied. Responder status varies by outcome measure, endpoint, and visit. That is, a subject can be considered a responder at one visit, but not the next for a specific measure. Similarly, a subject can be considered a responder for one measure but not another at the same visit.

Additionally, daily WI-NRS and AI-NRS scores will be presented in by-subject data listings.

### 7.4.2 Analysis of Primary Endpoint of Change from Baseline to Week 4 in Weekly Average WI-NRS

The ANCOVA model for the primary endpoint change from Baseline to Week 4 in weekly average WI-NRS will have treatment group and Baseline weekly average WI-NRS as explanatory variables. Hypothesis testing will be done using a Dunnett Testing Method, applying pairwise comparisons of each respective B244 dose group to vehicle using a one-sided familywise error rate of 0.10. Treatment effect will be estimated as least squares means using vehicle as reference and adjusted for multiplicity according to the Dunnett Testing Method and presented with one-sided 90% CI.

Additionally, the two B244 dose groups will be compared by presenting the treatment difference estimated using least squares means.

Finally, in a separate analysis, the pooled B244 dose groups will be compared to vehicle using the same ANCOVA model.

### 7.4.3 Analysis of IGA, EASI, POEM, 5-D Pruritus Scale

The endpoints IGA, EASI, POEM, 5-D Pruritus Scale will be summarized using descriptive statistics and analyzed using a logistic regression model at each respective timepoints. Mean change from Baseline to Week 2, Week 4, and Week 8 in IGA, EASI, POEM, and 5-D Pruritus Scale, as well as IGA and EASI responders, will be analyzed for mITT and PP as described in section 7.4.

Responder status is determined by reaching a certain level of improvement as defined below. Responder status varies by outcome measure, endpoint, and visit. That is, a subject can be considered a responder at one visit, but not the next for a specific measure. Similarly, a subject can be considered a responder for one measure but not another at the same visit. Responder criteria for categorical measures are as follows:

- Proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and ≥2-point improvement from Baseline will be reported for Week 2, Week 4, and Week 8.
- Proportion of subjects with IGA 0 (clear) or 1 (almost clear) will be reported for Week 2, Week 4, and Week 8.
- Proportion of subjects with any improvement in IGA from Baseline (defined as ≥1 point change from Baseline) will be reported for Week 2, Week 4, and Week 8.
- Proportion of subjects with at least 50%, 75%, and 90% improvement in EASI (EASI-50, EASI-75, and EASI-90, respectively) from Baseline will be reported for Week 2, Week 4, and Week 8.

Each of these outcomes will be compared between treatment groups using a logistic regression model by week. Generalized estimating equations to account for repeated measures and within-subject variability may also be applied.

## 7.5 Safety Analysis

Safety analyses will be conducted using the Safety population.

### 7.5.1 Study Drug Exposure

Subject dosing/exposure is recorded in both the ERT (patient diary entries) and EDC (site entries). In case of any discrepancies of the first and/or last exposure date between ERT and EDC, the EDC date will be used. Only ERT records that fall within the first and last dosing dates reported in the EDC (inclusive) will be retained.

Each site participating in the trial will be instructed to assess subject's compliance by weighing the investigational product at the Baseline visit, Week 2 visit, and Week 4 visit and followed every time study medication is dispensed and returned.

At the Week 2 visit, subjects will return any empty bottle (likely Bottle 1 since each bottle should last approximately 10 days and the subject should be on Bottle 2 at the time of visit) to

the site for weight measurement. At the Week 4 visit, all used and unused bottles will be returned to the site for weight measurements.

The cumulative amount of study drug exposure will be estimated by calculating the difference between the weight of all bottles of drug dispensed and the weight of all bottles returned. Differences will be summed together and reported as Net Weight of Study Drug.

The amount of product used per day will be estimated by dividing the change by the number of days the subject was on treatment. These weights will be compared to the weight of the product that would be used if the subject was compliant with the protocol. Percent compliance will be calculated as follows, with planned study drug use per day defined as 2.8g (0.14 g per pump x 10 pumps per application x 2 applications per day = 2.8 g) and number of days = 28 days:

$$\text{Percent compliance} = \frac{\text{Net Weight of Study Drug}}{[\text{Planned study drug use per day}] * \text{Numbers of days}} \times 100$$

The expected amount of study drug used over 4 weeks is approximately 0.14 g per pump x 10 pumps per application x 2 applications per day x 28 days of treatment = 78.4 g. The compliance will be calculated for Baseline to Week 4 visit.

The total dispensed and returned IP weights, the Net Weight of Study Drug, and the percent compliance during the treatment period will be summarized by treatment group and pooled B244 treatment and will be presented in a by-subject data listing. Percent compliance will be calculated for all subjects who received study drug, even if they did not return any/all of their study drug kits. Kits not returned will be assumed to be fully used and the return weight will be imputed as 0g. In the listing, the total weight dispensed, returned, net weight, and % compliance will be presented.

Dose compliance for each subject will also be calculated based on the number of daily study drug dosing diaries entered out of the total study drug dosing diaries available (2 study drug dosing diaries available per day x 28 days of treatment = 56 available entries). Only ERT dosing diary records from date of first dose through date of Visit 4-1 will be considered for calculating secondary compliance.

### 7.5.2 Adverse Events

Adverse events will be summarized by treatment group and pooled B244 treatment using the Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred term. Separate tabulations will be produced for all treatment-emergent AEs (TEAEs), treatment-related TEAEs (those considered by the Investigator as at least possibly drug related), treatment-emergent SAEs (TESAEs), discontinuation from study due to TEAEs, deaths due to TEAEs, TEAEs by severity, and TEAEs occurring in ≥ 2% of any study arm. By-subject listings will be provided for all treatment-emergent and non-treatment-emergent AEs.

Any treatment emergent AEs related to local safety (e.g., erythema, edema, induration, vesiculation, etc.) will be collected by the investigator during scheduled clinic visits. In addition, solicited patient assessment of local tolerability at application site (e.g., new itching, new rash, new pain/tenderness, new burning/stinging, new skin redness/color change, etc.) and grade will be collected during the first week of treatment using eDiary to inform local skin tolerability. Investigator will determine if any new local tolerability symptom or exacerbation of an existing symptom due to treatment warrants recording as an AE.

A summary of the incidence of any adverse event, SAE, and adverse events leading to discontinuation will be presented. Summaries will display, by treatment group and pooled B244 treatment, the incidence of patients with events, the frequency of patients with events within each primary system organ class and by preferred terms. For each preferred term and each system organ class a patient will be counted only once. For summaries on severe or drug-related AE, for a given patient, the highest severity or relationship for a specific preferred term will be considered.

### 7.5.3 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization (WHO) dictionary version Mar 2020 or later. Prior medication is defined as any medication with a stop date prior to the date of first dose of study drug. Concomitant medication is defined as any medication with a start date on or before the date of last dose of study drug and a stop date on or after the date of first dose of study drug.

Prior and concomitant medications will be summarized by Anatomic Therapeutic Class (ATC) Level 1 and Preferred Term by treatment group and pooled B244 treatment. Patients taking the same medication multiple times will be counted once per medication. Previous and concomitant medications will also be presented in a data listing.

### 7.5.4 Rescue Medications

The number of rescue medication days during the treatment period will be compared to the number of rescue medication days during the 2-week washout period (Day -14 to -1) using:

- 4-week treatment period:
  - Day 1 to Day of Visit 4 – 1 for all 4 weeks of treatment (Weeks 1 – 4)
- 2-week intervals of the treatment period:
  - Day 1 to Day of Visit 3 – 1 for first 2 weeks of treatment (Weeks 1 – 2)
  - Day of Visit 3 to Day of Visit 4 – 1 for last 2 weeks of treatment (Weeks 3 – 4)

- 4-week follow-up period:
  - Day of Visit 4 to Day of Visit 5 – 1 for all 4 weeks of follow-up (Weeks 5 – 8)
- 2-week intervals of the follow-up period:
  - Day of Visit 4 to Day of Visit 4 + 13 for first 2 weeks of follow-up (Weeks 5 – 6)

- Day of Visit 4 + 14 to Day of Visit 5 – 1 for last 2 weeks of follow-up (Weeks 7 – 8)

Each time interval will be normalized as a rate using the following formula:

$$\#\ rescue\ medication\ days = \left(\frac{\#\ days\ rescue\ medications\ used\ in\ interval}{\#\ actual\ days\ in\ interval}\right) * \#\ expected\ days\ in\ interval$$

For example, if there are 30 days in the Week 4 interval (the 2 weeks between visits 3 and 4), and a subject uses rescue medications for 7 of those 30 days, then the formula will be calculated as (7/30)*14=3.27. That is, 3.27 rescue medication days should be reported for the interval covering Weeks 3 and 4.

Change in rescue medication days from Baseline to each post-baseline visit will be tabulated. Number of rescue medication days per 2-week interval and per study period (treatment, follow-up) will be listed.

The use of any of the allowed rescue medications in the rescue medication diary data will be counted for the rescue medication days. If multiple rescue medications are reported on a single date, that date is still counted as only 1 rescue medication day. "Other" rescue medication selected in the daily diary will be confirmed to be one of the allowed rescue medications, and only the allowed rescue medications will be included as rescue medication days while others will not (such as other concomitant medications or prohibited medications).

### 7.5.5 Patient Reported Local Tolerability

Patient Reported Local Tolerability assesses the following local tolerability symptoms: skin redness and/or color change, itching, burning and/or stinging, pain and/or tenderness, and new or changing rash. Responses are provided according to the following scale:

0 = None
1 = Mild
2 = Moderate
3 = Severe

Each of the 5 questions for local skin tolerability will be summarized by day and treatment as categorical variable (grade) by day and as continuous variable using the score. Patient reported local tolerability will be reported from Day 1 to 7 and in shift tables. Day 1 is the first day of treatment in relation to the previous untreated day and the change in tolerability for subsequent days (Day 2 to Day 7) is in relation to the previous treated day.

### 7.5.6 Laboratory Data

Clinical laboratory values will be expressed in SI units reported by the central laboratory.

The actual value and change from screening will be summarized for each clinical chemistry, hematology, lipid panel, HbA1C and urinalysis parameters and by each visit. In the event of repeat values, the last non-missing value per visit will be used.

For clinical laboratory values with references ranges classifying the values as low/high/normal/abnormal, shift tables from Baseline to each post-baseline visit will be provided, where values of high and low will be classified as abnormal.

Sample for Serology was collected only at Baseline. Hence, Serology data will be only provided in a listing.

All laboratory data will be also provided in data listings. Values outside of the lab parameter's normal range will be flagged as high, low, or abnormal based on the range of the test.

### 7.5.7 Vital Signs and Physical Examination

Vital sign measurements will be presented for each subject in a data listing. Systolic blood pressure, diastolic blood pressure, heart rate, respiration rate, and temperature will be summarized as actual value and change from Baseline by visit.

All physical examination findings will be presented in a data listing.

### 7.5.8 Medical History

A by-subject data listing of medical history will be presented. Medical history will be coded using MedDRA v23.0 or higher, and the number and percentage of patients experiencing at least 1 such diagnosis by MedDRA System Organ Class (SOC) and Preferred Term (PT) will be reported.

### 7.5.9 COVID-19 Issues

By-subject data listings will be provided for COVID-19 test types and results, missed visits and assessments due to COVID-19 specifying reason not done, and adverse events related to COVID-19.

## 7.6 Handling of Dropouts or Missing Data

To account for missing daily diary entries for WI-NRS and AI-NRS, the average score for a week will be presented, where at least one score or four scores must be collected in a week for the primary and sensitivity analyses, respectively.

No other accommodations will be made for missing data other than those discussed in sections 6.5.7 and 6.5.9.

## 7.7 Changes to Planned Analyses

With respect to planned analyses in the protocol, the following changes have been made:

- Use of Modified Intent to Treat (mITT) population rather than Intent to Treat (ITT) population. Both populations consist of subjects who are enrolled and apply at least 1 dose of study treatment. mITT population also requires that at least one post-baseline evaluation visit occur.
- Reporting of endpoints for all visits have been added.
- Responder endpoints for EASI and IGA have been added.
- The protocol states that the treatment period is 28 days, yet the IP administration in the Schedule of Assessments covers a 29-day period (Visit 2 to Visit 4). In order to be consistent with the 28-day treatment period, the time frame of Visit 2 to Visit 4-1 will be used to report the following data:
    - NRS rating scores
    - "On-treatment" rescue medication use
    - Dosing diaries for secondary compliance

# 8 REFERENCES

1. Protocol Number PRB244-01, Amendment 3, Date 28-Feb-2020: "A Phase II, Randomized, Double-Blind, Vehicle Controlled Study of the Efficacy, Safety, and Tolerability of B244 Topical Spray for the Treatment of Pruritus in Adults with a History of Atopic Dermatitis."

2. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: Section 1: Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014; 70(2):338-351.

3. Stolwijk AM, Straatman H, et al. Studying seasonality by using sine and cosine functions in regression analysis. J Epidemiol Community Health. 1999 Apr; 53(4): 235–238. doi: 10.1136/jech.53.4.235

# 1 APPENDIX

## 1.1 APPENDIX A: Tables

### 1.1.1 General

| Display Number | Title | Population | Unique/Repeat |
|---|---|---|---|
| 14.1.1.1 | Subject Enrollment and Disposition | All Subjects | Unique |
| 14.1.1.2 | Analysis Populations and Exclusions | All Enrolled Subjects | Unique |
| 14.1.2.1 | Summary of Major Protocol Deviations (PD)/Violations (PV) | mITT | Unique |
| 14.1.2.2 | Summary of Major Protocol Deviations (PD)/Violations (PV) | Safety | Repeat |
| 14.1.3.1 | Summary of Demographic and Baseline Characteristics | mITT | Unique |
| 14.1.3.2 | Summary of Demographic and Baseline Characteristics | PP | Repeat |
| 14.1.3.3 | Summary of Demographic and Baseline Characteristics | Safety | Repeat |
| 14.1.4.1 | Summary of Baseline Disease Status | mITT | Unique |
| 14.1.4.2 | Summary of Baseline Disease Status | PP | Repeat |
| 14.1.4.3 | Summary of Baseline Disease Status | Safety | Repeat |

Table 14.1.1.1
Subject Enrollment and Disposition
(All Subjects)

| Disposition | Statistic | B244 O.D. 5.0 | B244 O.D. 20.0 | Pooled B244 | Vehicle | All Subjects |
|---|---|---|---|---|---|---|
| Total Number of Subjects | | | | | | |
| Screened | n | | | | | xx |
| Screen Failures [1] | n (%) | | | | | xx (xx.x) |
| Enrolled [2] | n | xx | xx | xx | xx | xx |
| Not Assigned [3,4] | n (%) | | | | | xx (xx.x) |
| Randomized [4] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Treated [5] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Completed the Study [6,7] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Discontinued | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Study Population [8] | | | | | | |
| Safety (SAF) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Modified Intent-to-Treat (mITT) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Per Protocol (PP) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Reason for Early Study Discontinuation | | | | | | |
| Death | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Lost to Follow-up | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Withdrawal of Consent by Subject | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Investigator's Decision | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Adverse Event | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Pregnancy | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Significant Non-Compliance | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Significant Clinical Event | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Incident of Unblinding | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Failure to Meet Continuation Criteria | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Other | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

[1] Percentage based on the number screened.
[2] The number enrolled is equal to the sum of the number randomized and the number not assigned.
[3] Not Assigned includes subjects who passed the initial inclusion/exclusion assessment, but withdrew or were lost-to-follow-up prior to randomization.
[4] Percentage based on the number enrolled.
[5] Percentage based on the number randomized.
[6] Percentage and all subsequent percentages based on the number treated.
[7] Completed the Study indicates completion up to and including Week 8 visit.
[8] Safety Population: All subjects treated with at least 1 dose of IP.
Modified Intent-to-Treat Population: All randomized participants who apply at least 1 dose of IP and have at least one post-baseline evaluation visit.

Per Protocol Population: Includes all subjects in the mITT population who administered at least 50% of IP (based on the weight of IP used calculated using the algorithm: difference in weight of all bottles dispenced and weight of all bottles returned must be at least 50% of the initial theoretical product weight i.e.(0.14 g per pump x 20 pumps per day x 28 days = 78.4 g)), have completed their Week 4 visit and did not have any major protocol deviations.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Reason for Early Study Discontinuation response "Significant Clinical Event" corresponds to the CRF response "Any clinical AE, lab abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the subject."

Table 14.1.1.2
Analysis Populations and Exclusions
(All Enrolled Subjects)

| Number of Subjects | Statistic | B244 O.D. 5.0 | B244 O.D. 20.0 | Pooled B244 | Vehicle | All Subjects |
|---|---|---|---|---|---|---|
| Enrolled | n | xx | xx | xx | xx | xx |
| Randomized [1] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Included in Safety (SAF) [2,4] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Excluded from Safety (SAF) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| No IP Applied | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Included in Modified Intent-to-Treat (mITT) [3,5] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Excluded from Modified Intent-to-Treat (mITT) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| No Post-Baseline Evaluation Visit | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Included in Per Protocol (PP) [6] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Excluded from Per Protocol (PP) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Major Protocol Deviation | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Did Not Complete Week 4 Visit | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Applied < 50% IP | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

[1] Percentage based on number enrolled.
[2] Percentage based on the number randomized.
[3] Percentage and all subsequent percentages based on the number treated.
[4] Safety Population: All subjects treated with at least 1 dose of IP.
[5] Modified Intent-to-Treat Population: All randomized participants who apply at least 1 dose of IP and have at least one post-baseline evaluation visit.
[6] Per Protocol Population: Includes all subjects in the mITT population who administered at least 50% of IP (based on the weight of IP used calculated using the algorithm: difference in weight of all bottles dispenced and weight of all bottles returned must be at least 50% of the initial theoretical product weight i.e.(0.14 g per pump x 20 pumps per day x 28 days = 78.4 g)), have completed their Week 4 visit and did not have any major protocol deviations.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.1.2.1
Summary of Major Protocol Deviations (PD) / Violations (PV)
(Modified Intent-to-Treat Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Subjects with At Least One Major PD/PV [1,2] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| PD/PV Category 1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| PD/PV Category 2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| PD/PV Category 2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |

[1] Percentage and all subsequent percentages based on the number treated.
[2] Subjects are counted once per PD/PV category experienced.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.1.2.2 Summary of Major Protocol Deviation (PD) / Violations (PV) for Safety Population

Table 14.1.3.1
Summary of Demographic and Baseline Characteristics
(Modified Intent-to-Treat Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Age [1] | | | | | |
| 18 to 40 years | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| 41 to 54 years | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| 55 to 65 years | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Age | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Sex | | | | | |
| Male | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Female | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Ethnicity | | | | | |
| Hispanic or Latino | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Not Hispanic or Latino | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Race | | | | | |
| American Indian or Alaskan Native | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Asian | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Black or African American | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Native Hawaiian or Other Pacific Islander | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| White | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Other | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Height (cm) | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weight (kg) | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| BMI (kg/m2) | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |

| | | | | | |
|---|---|---|---|---|---|
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| BSA (%) [2] | | | | | |
| 10 – 20% | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| >20 – 30% | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| >30 – 40% | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| BSA (%) [2] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Smoking Status | | | | | |
| Yes | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| No | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Rescue Medication [3] | | | | | |
| Yes | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| No | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Rescue Medication Days [3] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] Percentage and all subsequent percentages based on the number treated.
[2] BSA: Body Surface Area. Measured at baseline. Four subjects in the mITT population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and two included in the >30-40% category (117001 [BSA=65%] and 150006 [BSA=56%]).
[3] Baseline rescue medication days is the number of rescue medication days recorded during the 2 weeks (Day -14 to Day -1) prior to the baseline visit.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.1.3.2 Summary of Demographic and Baseline Characteristics for Per Protocol Population
  - Footnote 2 will change to: "BSA: Body Surface Area. Measured at baseline. Three subjects in the PP population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and one included in the >30-40% category (150006 [BSA=56%])."
- Repeat for 14.1.3.3 Summary of Demographic and Baseline Characteristics for Safety Population
  - Footnote 2 will change to: "BSA: Body Surface Area. Measured at baseline. Five subjects in the SAF Population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and three included in the >30-40% category (117001 [BSA=65%], 138004 [BSA=70%], and 150006 [BSA=56%])."

Table 14.1.4.1
Summary of Baseline Disease Status
(Modified Intent-to-Treat Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| WI-NRS [1] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| AI-NRS [2] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| 5-D Pruritus Scale Total Score | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| EASI [3] | | | | | |
| ≤10 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| >10 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| EASI Total Score | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| IGA | | | | | |
| 2 – Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| 3 – Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| IGA | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| POEM Total Score | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] Baseline WI-NRS = (Sum of daily WI-NRS scores from Day -7 to Day -1) / (Total number of WI-NRS diaries entered from Day -7 to Day -1)

[2] Baseline AI-NRS = (Sum of daily AI-NRS scores from Day -7 to Day -1) / (Total number of AI-NRS diaries entered from Day -7 to Day -1)
[3] Percentage and all subsequent percentages based on the number treated.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.1.4.2 Summary of Demographic and Baseline Characteristics for Per Protocol Population
- Repeat for 14.1.4.3 Summary of Demographic and Baseline Characteristics for Safety Population

### 1.1.2 Efficacy

| Display Number | Title | Population | Unique/Repeat |
|---|---|---|---|
| *DESCRIPTIVE* | | | |
| 14.2.1.1.1 | Summary of Values and Change from Baseline for WI-NRS | mITT | Unique |
| 14.2.1.1.2 | Summary of Values and Change from Baseline for WI-NRS | PP | Repeat |
| 14.2.1.1.3 | Summary of Values and Change from Baseline for WI-NRS by Age Group | mITT | Repeat |
| 14.2.1.1.4 | Summary of Values and Change from Baseline for WI-NRS by Age Group | PP | Repeat |
| 14.2.1.1.5 | Summary of Values and Change from Baseline for WI-NRS by Sex | mITT | Repeat |
| 14.2.1.1.6 | Summary of Values and Change from Baseline for WI-NRS by Sex | PP | Repeat |
| 14.2.1.1.7 | Summary of Values and Change from Baseline for WI-NRS by Race | mITT | Repeat |
| 14.2.1.1.8 | Summary of Values and Change from Baseline for WI-NRS by Race | PP | Repeat |
| 14.2.1.1.9 | Summary of Values and Change from Baseline for WI-NRS by Baseline IGA | mITT | Repeat |
| 14.2.1.1.10 | Summary of Values and Change from Baseline for WI-NRS by Baseline IGA | PP | Repeat |
| 14.2.1.1.11 | Summary of Values and Change from Baseline for WI-NRS by Baseline EASI | mITT | Repeat |
| 14.2.1.1.12 | Summary of Values and Change from Baseline for WI-NRS by Baseline EASI | PP | Repeat |
| 14.2.1.1.13 | Summary of Values and Change from Baseline for WI-NRS by Baseline BSA | mITT | Repeat |
| 14.2.1.1.14 | Summary of Values and Change from Baseline for WI-NRS by Baseline BSA | PP | Repeat |

| | | | |
|---|---|---|---|
| 14.2.1.1.15 | Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status at Baseline | mITT | Repeat |
| 14.2.1.1.16 | Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status at Baseline | PP | Repeat |
| 14.2.1.1.17 | Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status on Treatment | mITT | Repeat |
| 14.2.1.1.18 | Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status on Treatment | PP | Repeat |
| 14.2.1.1.19 | Summary of WI-NRS Diary Completion | mITT | Unique |
| 14.2.1.1.20 | Summary of WI-NRS Diary Completion | PP | Repeat |
| 14.2.1.2.1 | Summary of Values and Change from Baseline for AI-NRS | mITT | Repeat |
| 14.2.1.2.2 | Summary of Values and Change from Baseline for AI-NRS | PP | Repeat |
| 14.2.1.2.3 | Summary of Values and Change from Baseline for AI-NRS by Age Group | mITT | Repeat |
| 14.2.1.2.4 | Summary of Values and Change from Baseline for AI-NRS by Age Group | PP | Repeat |
| 14.2.1.2.5 | Summary of Values and Change from Baseline for AI-NRS by Sex | mITT | Repeat |
| 14.2.1.2.6 | Summary of Values and Change from Baseline for AI-NRS by Sex | PP | Repeat |
| 14.2.1.2.7 | Summary of Values and Change from Baseline for AI-NRS by Race | mITT | Repeat |
| 14.2.1.2.8 | Summary of Values and Change from Baseline for AI-NRS by Race | PP | Repeat |

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| 14.2.1.2.9 | Summary of Values and Change from Baseline for AI-NRS by Baseline IGA | mITT | Repeat |
| 14.2.1.2.10 | Summary of Values and Change from Baseline for AI-NRS by Baseline IGA | PP | Repeat |
| 14.2.1.2.11 | Summary of Values and Change from Baseline for AI-NRS by Baseline EASI | mITT | Repeat |
| 14.2.1.2.12 | Summary of Values and Change from Baseline for AI-NRS by Baseline EASI | PP | Repeat |
| 14.2.1.2.13 | Summary of Values and Change from Baseline for AI-NRS by Baseline BSA | mITT | Repeat |
| 14.2.1.2.14 | Summary of Values and Change from Baseline for AI-NRS by Baseline BSA | PP | Repeat |
| 14.2.1.2.15 | Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status at Baseline | mITT | Repeat |
| 14.2.1.2.16 | Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status at Baseline | PP | Repeat |
| 14.2.1.2.17 | Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status on Treatment | mITT | Repeat |
| 14.2.1.2.18 | Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status on Treatment | PP | Repeat |
| 14.2.1.2.19 | Summary of AI-NRS Diary Completion | mITT | Repeat |
| 14.2.1.2.20 | Summary of AI-NRS Diary Completion | PP | Repeat |
| 14.2.1.3.1 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score | mITT | Repeat |
| 14.2.1.3.2 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score | PP | Repeat |

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| 14.2.1.3.3 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Age Group | mITT | Repeat |
| 14.2.1.3.4 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Age Group | PP | Repeat |
| 14.2.1.3.5 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Sex | mITT | Repeat |
| 14.2.1.3.6 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Sex | PP | Repeat |
| 14.2.1.3.7 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Race | mITT | Repeat |
| 14.2.1.3.8 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Race | PP | Repeat |
| 14.2.1.3.9 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline IGA | mITT | Repeat |
| 14.2.1.3.10 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline IGA | PP | Repeat |
| 14.2.1.3.11 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline EASI | mITT | Repeat |
| 14.2.1.3.12 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline EASI | PP | Repeat |
| 14.2.1.3.13 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline BSA | mITT | Repeat |

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| 14.2.1.3.14 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline BSA | PP | Repeat |
| 14.2.1.3.15 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status at Baseline | mITT | Repeat |
| 14.2.1.3.16 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status at Baseline | PP | Repeat |
| 14.2.1.3.17 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status on Treatment | mITT | Repeat |
| 14.2.1.3.18 | Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status on Treatment | PP | Repeat |
| 14.2.1.4.1 | Summary of Values and Change from Baseline for EASI Total Score | mITT | Repeat |
| 14.2.1.4.2 | Summary of Values and Change from Baseline for EASI Total Score | PP | Repeat |
| 14.2.1.4.3 | Summary of Values and Change from Baseline for EASI Total Score by Age Group | mITT | Repeat |
| 14.2.1.4.4 | Summary of Values and Change from Baseline for EASI Total Score by Age Group | PP | Repeat |
| 14.2.1.4.5 | Summary of Values and Change from Baseline for EASI Total Score by Sex | mITT | Repeat |
| 14.2.1.4.6 | Summary of Values and Change from Baseline for EASI Total Score by Sex | PP | Repeat |

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| 14.2.1.4.7 | Summary of Values and Change from Baseline for EASI Total Score by Race | mITT | Repeat |
| 14.2.1.4.8 | Summary of Values and Change from Baseline for EASI Total Score by Race | PP | Repeat |
| 14.2.1.4.9 | Summary of Values and Change from Baseline for EASI Total Score by Baseline IGA | mITT | Repeat |
| 14.2.1.4.10 | Summary of Values and Change from Baseline for EASI Total Score by Baseline IGA | PP | Repeat |
| 14.2.1.4.11 | Summary of Values and Change from Baseline for EASI Total Score by Baseline EASI | mITT | Repeat |
| 14.2.1.4.12 | Summary of Values and Change from Baseline for EASI Total Score by Baseline EASI | PP | Repeat |
| 14.2.1.4.13 | Summary of Values and Change from Baseline for EASI Total Score by Baseline BSA | mITT | Repeat |
| 14.2.1.4.14 | Summary of Values and Change from Baseline for EASI Total Score by Baseline BSA | PP | Repeat |
| 14.2.1.4.15 | Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status at Baseline | mITT | Repeat |
| 14.2.1.4.16 | Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status at Baseline | PP | Repeat |
| 14.2.1.4.17 | Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status on Treatment | mITT | Repeat |

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| 14.2.1.4.18 | Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status on Treatment | PP | Repeat |
| 14.2.1.5.1 | Summary of Values and Change from Baseline for IGA | mITT | Repeat |
| 14.2.1.5.2 | Summary of Values and Change from Baseline for IGA | PP | Repeat |
| 14.2.1.5.3 | Summary of Values and Change from Baseline for IGA by Age Group | mITT | Repeat |
| 14.2.1.5.4 | Summary of Values and Change from Baseline for IGA by Age Group | PP | Repeat |
| 14.2.1.5.5 | Summary of Values and Change from Baseline for IGA by Sex | mITT | Repeat |
| 14.2.1.5.6 | Summary of Values and Change from Baseline for IGA by Sex | PP | Repeat |
| 14.2.1.5.7 | Summary of Values and Change from Baseline for IGA by Race | mITT | Repeat |
| 14.2.1.5.8 | Summary of Values and Change from Baseline for IGA by Race | PP | Repeat |
| 14.2.1.5.9 | Summary of Values and Change from Baseline for IGA by Baseline IGA | mITT | Repeat |
| 14.2.1.5.10 | Summary of Values and Change from Baseline for IGA by Baseline IGA | PP | Repeat |
| 14.2.1.5.11 | Summary of Values and Change from Baseline for IGA by Baseline EASI | mITT | Repeat |
| 14.2.1.5.12 | Summary of Values and Change from Baseline for IGA by Baseline EASI | PP | Repeat |
| 14.2.1.5.13 | Summary of Values and Change from Baseline for IGA by Baseline BSA | mITT | Repeat |
| 14.2.1.5.14 | Summary of Values and Change from Baseline for IGA by Baseline BSA | PP | Repeat |

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| 14.2.1.5.15 | Summary of Values and Change from Baseline for IGA by Rescue Medication Status at Baseline | mITT | Repeat |
| 14.2.1.5.16 | Summary of Values and Change from Baseline for IGA by Rescue Medication Status at Baseline | PP | Repeat |
| 14.2.1.5.17 | Summary of Values and Change from Baseline for IGA by Rescue Medication Status on Treatment | mITT | Repeat |
| 14.2.1.5.18 | Summary of Values and Change from Baseline for IGA by Rescue Medication Status on Treatment | PP | Repeat |
| 14.2.1.6.1 | Summary of Values and Change from Baseline for POEM Total Score | mITT | Repeat |
| 14.2.1.6.2 | Summary of Values and Change from Baseline for POEM Total Score | PP | Repeat |
| 14.2.1.6.3 | Summary of Values and Change from Baseline for POEM Total Score by Age Group | mITT | Repeat |
| 14.2.1.6.4 | Summary of Values and Change from Baseline for POEM Total Score by Age Group | PP | Repeat |
| 14.2.1.6.5 | Summary of Values and Change from Baseline for POEM Total Score by Sex | mITT | Repeat |
| 14.2.1.6.6 | Summary of Values and Change from Baseline for POEM Total Score by Sex | PP | Repeat |
| 14.2.1.6.7 | Summary of Values and Change from Baseline for POEM Total Score by Race | mITT | Repeat |
| 14.2.1.6.8 | Summary of Values and Change from Baseline for POEM Total Score by Race | PP | Repeat |

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| 14.2.1.6.9 | Summary of Values and Change from Baseline for POEM Total Score by Baseline IGA | mITT | Repeat |
| 14.2.1.6.10 | Summary of Values and Change from Baseline for POEM Total Score by Baseline IGA | PP | Repeat |
| 14.2.1.6.11 | Summary of Values and Change from Baseline for POEM Total Score by Baseline EASI | mITT | Repeat |
| 14.2.1.6.12 | Summary of Values and Change from Baseline for POEM Total Score by Baseline EASI | PP | Repeat |
| 14.2.1.6.13 | Summary of Values and Change from Baseline for POEM Total Score by Baseline BSA | mITT | Repeat |
| 14.2.1.6.14 | Summary of Values and Change from Baseline for POEM Total Score by Baseline BSA | PP | Repeat |
| 14.2.1.6.15 | Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status at Baseline | mITT | Repeat |
| 14.2.1.6.16 | Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status at Baseline | PP | Repeat |
| 14.2.1.6.17 | Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status on Treatment | mITT | Repeat |
| 14.2.1.6.18 | Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status on Treatment | PP | Repeat |
| 14.2.1.7.1 | Shift from Baseline for IGA | mITT | Unique |
| 14.2.1.7.2 | Shift from Baseline for IGA | PP | Repeat |
| *INFERENTIAL* | | | |

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| 14.2.2.1 | Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA | mITT | Unique |
| 14.2.2.2 | Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA | PP | Repeat |
| 14.2.2.3.1 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | mITT | Unique |
| 14.2.2.3.2 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.3.3 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.3.4 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.3.5 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | PP | Repeat |
| 14.2.2.3.6 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | PP | Repeat |
| 14.2.2.3.7 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.3.8 | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | PP | Repeat |
| 14.2.2.4.1 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | mITT | Repeat |

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| 14.2.2.4.2 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.4.3 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.4.4 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.4.5 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | PP | Repeat |
| 14.2.2.4.6 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | PP | Repeat |
| 14.2.2.4.7 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.4.8 | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | PP | Repeat |
| 14.2.2.5.1 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | mITT | Unique |
| 14.2.2.5.2 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.5.3 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.5.4 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline | mITT | Repeat |

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| | to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | | |
| 14.2.2.5.5 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.5.6 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.5.7 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | PP | Repeat |
| 14.2.2.5.8 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | PP | Repeat |
| 14.2.2.5.9 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.5.10 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | PP | Repeat |
| 14.2.2.5.11 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.5.12 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non- | PP | Repeat |

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| | Responder Imputation (NRI) Analysis – Sensitivity | | |
| 14.2.2.6.1 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.6.2 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.6.3 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.6.4 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.6.5 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.6.6 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.6.7 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | PP | Repeat |
| 14.2.2.6.8 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline | PP | Repeat |

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| | to Weeks 1 Through 8 – Primary Analysis – Sensitivity | | |
| 14.2.2.6.9 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.6.10 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | PP | Repeat |
| 14.2.2.6.11 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.6.12 | Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity | PP | Repeat |
| 14.2.2.7.1 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.7.2 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.7.3 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.7.4 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | mITT | Repeat |

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| 14.2.2.7.5 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.7.6 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.7.7 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | PP | Repeat |
| 14.2.2.7.8 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | PP | Repeat |
| 14.2.2.7.9 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.7.10 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | PP | Repeat |
| 14.2.2.7.11 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.7.12 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity | PP | Repeat |

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| 14.2.2.8.1 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.8.2 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.8.3 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.8.4 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.8.5 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.8.6 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity | mITT | Repeat |
| 14.2.2.8.7 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis | PP | Repeat |
| 14.2.2.8.8 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity | PP | Repeat |

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| 14.2.2.8.9 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.8.10 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity | PP | Repeat |
| 14.2.2.8.11 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.8.12 | Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity | PP | Repeat |
| 14.2.2.9.1 | Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.9.2 | Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.9.3 | Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.9.4 | Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.10.1 | Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |

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| 14.2.2.10.2 | Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.10.3 | Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.10.4 | Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.11.1 | Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.11.2 | Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.11.3 | Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.11.4 | Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.12.1 | Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.12.2 | Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.12.3 | Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.12.4 | Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.13.1 | Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |

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| 14.2.2.13.2 | Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.13.3 | Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.13.4 | Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.13.5 | Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.13.6 | Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.14.1 | Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.14.2 | Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.14.3 | Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |

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| 14.2.2.14.4 | Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.14.5 | Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.14.6 | Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.15.1 | Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.15.2 | Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.15.3 | Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.15.4 | Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.15.5 | Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |

| | | | |
|---|---|---|---|
| 14.2.2.15.6 | Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.16.1 | Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.16.2 | Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.16.3 | Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.16.4 | Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.16.5 | Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.16.6 | Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.17.1 | Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |

| | | | |
|---|---|---|---|
| 14.2.2.17.2 | Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.17.3 | Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.17.4 | Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.17.5 | Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |
| 14.2.2.17.6 | Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |
| 14.2.2.18.1 | Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis | mITT | Repeat |
| 14.2.2.18.2 | Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | mITT | Repeat |
| 14.2.2.18.3 | Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | mITT | Repeat |
| 14.2.2.18.4 | Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis | PP | Repeat |
| 14.2.2.18.5 | Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis | PP | Repeat |

| | | | |
|---|---|---|---|
| 14.2.2.18.6 | Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis | PP | Repeat |

Table 14.2.1.1.1
Summary of Values and Change from Baseline for WI-NRS
(mITT Population)

| Visit | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Screening | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Baseline | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Week 1 | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Week 1 CFB [1] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Week 1 PCFB [2] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| Repeat for Weeks 2 – 8 | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] CFB = Change from Baseline.
[2] PCFB = Percent Change from Baseline.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.1.1.2 Summary of Values and Change from Baseline for WI-NRS for PP Population
  - Repeat for 14.2.1.1.3 Summary of Values and Change from Baseline for WI-NRS by Age Group – mITT Population
  - Repeat for 14.2.1.1.4 Summary of Values and Change from Baseline for WI-NRS by Age Group – PP Population
  - Repeat for 14.2.1.1.5 Summary of Values and Change from Baseline for WI-NRS by Sex – mITT Population
  - Repeat for 14.2.1.1.6 Summary of Values and Change from Baseline for WI-NRS by Sex – PP Population

- Repeat for 14.2.1.1.7 Summary of Values and Change from Baseline for WI-NRS by Race – mITT Population
- Repeat for 14.2.1.1.8 Summary of Values and Change from Baseline for WI-NRS by Race – PP Population
- Repeat for 14.2.1.1.9 Summary of Values and Change from Baseline for WI-NRS by Baseline IGA – mITT Population
- Repeat for 14.2.1.1.10 Summary of Values and Change from Baseline for WI-NRS by Baseline IGA – PP Population
- Repeat for 14.2.1.1.11 Summary of Values and Change from Baseline for WI-NRS by Baseline EASI – mITT Population
- Repeat for 14.2.1.1.12 Summary of Values and Change from Baseline for WI-NRS by Baseline EASI – PP Population
- Repeat for 14.2.1.1.13 Summary of Values and Change from Baseline for WI-NRS by Baseline BSA – mITT Population
  - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Four subjects in the mITT population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and two included in the >30-40% category (117001 [BSA=65%] and 150006 [BSA=56%])."
- Repeat for 14.2.1.1.14 Summary of Values and Change from Baseline for WI-NRS by Baseline BSA – PP Population
  - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Three subjects in the PP population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and one included in the >30-40% category (150006 [BSA=56%])."
- Repeat for 14.2.1.1.15 Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status at Baseline – mITT Population
- Repeat for 14.2.1.1.16 Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status at Baseline – PP Population
- Repeat for 14.2.1.1.17 Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status on Treatment – mITT Population
- Repeat for 14.2.1.1.18 Summary of Values and Change from Baseline for WI-NRS by Rescue Medication Status on Treatment – PP Population

- Repeat for 14.2.1.2.1 Summary of Values and Change from Baseline for AI-NRS for mITT Population
- Repeat for 14.2.1.2.2 Summary of Values and Change from Baseline for AI-NRS for PP Population
  - Repeat for 14.2.1.2.3 Summary of Values and Change from Baseline for AI-NRS by Age Group – mITT Population
  - Repeat for 14.2.1.2.4 Summary of Values and Change from Baseline for AI-NRS by Age Group – PP Population
  - Repeat for 14.2.1.2.5 Summary of Values and Change from Baseline for AI-NRS by Sex – mITT Population
  - Repeat for 14.2.1.2.6 Summary of Values and Change from Baseline for AI-NRS by Sex – PP Population
  - Repeat for 14.2.1.2.7 Summary of Values and Change from Baseline for AI-NRS by Race – mITT Population
  - Repeat for 14.2.1.2.8 Summary of Values and Change from Baseline for AI-NRS by Race – PP Population
  - Repeat for 14.2.1.2.9 Summary of Values and Change from Baseline for AI-NRS by Baseline IGA – mITT Population
  - Repeat for 14.2.1.2.10 Summary of Values and Change from Baseline for AI-NRS by Baseline IGA – PP Population
  - Repeat for 14.2.1.2.11 Summary of Values and Change from Baseline for AI-NRS by Baseline EASI – mITT Population
  - Repeat for 14.2.1.2.12 Summary of Values and Change from Baseline for AI-NRS by Baseline EASI – PP Population
  - Repeat for 14.2.1.2.13 Summary of Values and Change from Baseline for AI-NRS by Baseline BSA – mITT Population
    - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Four subjects in the mITT population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and two included in the >30-40% category (117001 [BSA=65%] and 150006 [BSA=56%])."
  - Repeat for 14.2.1.2.14 Summary of Values and Change from Baseline for AI-NRS by Baseline BSA – PP Population
    - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Three subjects in the PP population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and one included in the >30-40% category (150006 [BSA=56%])."
  - Repeat for 14.2.1.2.15 Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status at Baseline – mITT Population
  - Repeat for 14.2.1.2.16 Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status at Baseline – PP Population
  - Repeat for 14.2.1.2.17 Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status on Treatment – mITT Population

- Repeat for 14.2.1.2.18 Summary of Values and Change from Baseline for AI-NRS by Rescue Medication Status on Treatment – PP Population

Table 14.2.1.1.19
Summary of WI-NRS Diary Completion
(mITT Population)

| Week | Day | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 1 | 1 [1] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 4 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 5 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 6 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 7 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total [2] | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Week 2 | 1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 4 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 5 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 6 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | 7 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| Repeat for | | Median | xx.x | xx.x | xx.x | xx.x |
| Weeks 3 – 8 | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] Percentage and all subsequent percentages based on the number treated.
[2] Descriptive statistics for the total number of diary entries completed for the corresponding week.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.1.1.20 Summary of WI-NRS Diary Completion for PP Population
- Repeat for 14.2.1.2.19 Summary of AI-NRS Diary Completion for mITT Population
- Repeat for 14.2.1.2.20 Summary of AI-NRS Diary Completion for PP Population

Table 14.2.1.3.1
Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score
(mITT Population)

| Visit | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Screening | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Baseline | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Week 2 | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Week 2 CFB [1] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Week 2 PCFB [2] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| Repeat for Weeks 4 and 8 | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] CFB = Change from Baseline.
[2] PCFB = Percent Change from Baseline.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.1.3.2 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score for PP Population
    - Repeat for 14.2.1.3.3 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Age Group – mITT Population
    - Repeat for 14.2.1.3.4 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Age Group – PP Population
    - Repeat for 14.2.1.3.5 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Sex – mITT Population
    - Repeat for 14.2.1.3.6 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Sex – PP Population
    - Repeat for 14.2.1.3.7 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Race – mITT Population

- Repeat for 14.2.1.3.8 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Race – PP Population
- Repeat for 14.2.1.3.9 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline IGA – mITT Population
- Repeat for 14.2.1.3.10 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline IGA – PP Population
- Repeat for 14.2.1.3.11 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline EASI – mITT Population
- Repeat for 14.2.1.3.12 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline EASI – PP Population
- Repeat for 14.2.1.3.13 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline BSA – mITT Population
    - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Four subjects in the mITT population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and two included in the >30-40% category (117001 [BSA=65%] and 150006 [BSA=56%])."
- Repeat for 14.2.1.3.14 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Baseline BSA – PP Population
    - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Three subjects in the PP population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and one included in the >30-40% category (150006 [BSA=56%])."
- Repeat for 14.2.1.3.15 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status at Baseline – mITT Population
- Repeat for 14.2.1.3.16 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status at Baseline – PP Population
- Repeat for 14.2.1.3.17 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status on Treatment – mITT Population
- Repeat for 14.2.1.3.18 Summary of Values and Change from Baseline for 5-D Pruritus Scale Total Score by Rescue Medication Status on Treatment – PP Population

- Repeat for 14.2.1.4.1 Summary of Values and Change from Baseline for EASI Total Score for mITT Population
- Repeat for 14.2.1.4.2 Summary of Values and Change from Baseline for EASI Total Score for PP Population
    - Repeat for 14.2.1.4.3 Summary of Values and Change from Baseline for EASI Total Score by Age Group – mITT Population
    - Repeat for 14.2.1.4.4 Summary of Values and Change from Baseline for EASI Total Score by Age Group – PP Population
    - Repeat for 14.2.1.4.5 Summary of Values and Change from Baseline for EASI Total Score by Sex – mITT Population
    - Repeat for 14.2.1.4.6 Summary of Values and Change from Baseline for EASI Total Score by Sex – PP Population
    - Repeat for 14.2.1.4.7 Summary of Values and Change from Baseline for EASI Total Score by Race – mITT Population
    - Repeat for 14.2.1.4.8 Summary of Values and Change from Baseline for EASI Total Score by Race – PP Population
    - Repeat for 14.2.1.4.9 Summary of Values and Change from Baseline for EASI Total Score by Baseline IGA – mITT Population
    - Repeat for 14.2.1.4.10 Summary of Values and Change from Baseline for EASI Total Score by Baseline IGA – PP Population
    - Repeat for 14.2.1.4.11 Summary of Values and Change from Baseline for EASI Total Score by Baseline EASI – mITT Population
    - Repeat for 14.2.1.4.12 Summary of Values and Change from Baseline for EASI Total Score by Baseline EASI – PP Population
    - Repeat for 14.2.1.4.13 Summary of Values and Change from Baseline for EASI Total Score by Baseline BSA – mITT Population
        - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Four subjects in the mITT population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and two included in the >30-40% category (117001 [BSA=65%] and 150006 [BSA=56%])."
    - Repeat for 14.2.1.4.14 Summary of Values and Change from Baseline for EASI Total Score by Baseline BSA – PP Population
        - Add footnote [3], placing the [3] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Three subjects in the PP population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and one included in the >30-40% category (150006 [BSA=56%])."

    - Repeat for 14.2.1.4.15 Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status at Baseline – mITT Population
    - Repeat for 14.2.1.4.16 Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status at Baseline – PP Population
    - Repeat for 14.2.1.4.17 Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status on Treatment – mITT Population
    - Repeat for 14.2.1.4.18 Summary of Values and Change from Baseline for EASI Total Score by Rescue Medication Status on Treatment – PP Population
- Repeat for 14.2.1.5.1 Summary of Values and Change from Baseline for IGA for mITT Population
    - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
- Repeat for 14.2.1.5.2 Summary of Values and Change from Baseline for IGA for PP Population
    - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.3 Summary of Values and Change from Baseline for IGA by Age Group – mITT Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.4 Summary of Values and Change from Baseline for IGA by Age Group – PP Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.5 Summary of Values and Change from Baseline for IGA by Sex – mITT Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.6 Summary of Values and Change from Baseline for IGA by Sex – PP Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.7 Summary of Values and Change from Baseline for IGA by Race – mITT Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.8 Summary of Values and Change from Baseline for IGA by Race – PP Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.9 Summary of Values and Change from Baseline for IGA by Baseline IGA – mITT Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.10 Summary of Values and Change from Baseline for IGA by Baseline IGA – PP Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.11 Summary of Values and Change from Baseline for IGA by Baseline EASI – mITT Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.12 Summary of Values and Change from Baseline for IGA by Baseline EASI – PP Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.13 Summary of Values and Change from Baseline for IGA by Baseline BSA – mITT Population
        - Additional footnotes to be added:
            - [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
            - [4], placing the [4] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Four subjects in the mITT population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and two included in the >30-40% category (117001 [BSA=65%] and 150006 [BSA=56%])."
    - Repeat for 14.2.1.5.14 Summary of Values and Change from Baseline for IGA by Baseline BSA – PP Population
        - Additional footnotes to be added:
            - [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
            - [4], placing the [4] next to BSA (#byval) category: "BSA: Body Surface Area. Measured at baseline. Three subjects in the PP population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and one included in the >30-40% category (150006 [BSA=56%])."
    - Repeat for 14.2.1.5.15 Summary of Values and Change from Baseline for IGA by Rescue Medication Status at Baseline – mITT Population

        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.16 Summary of Values and Change from Baseline for IGA by Rescue Medication Status at Baseline – PP Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.17 Summary of Values and Change from Baseline for IGA by Rescue Medication Status on Treatment – mITT Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
    - Repeat for 14.2.1.5.18 Summary of Values and Change from Baseline for IGA by Rescue Medication Status on Treatment – PP Population
        - Additional footnote to be added: [3] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
- Repeat for 14.2.1.6.1 Summary of Values and Change from Baseline for POEM Total Score for mITT Population
- Repeat for 14.2.1.6.2 Summary of Values and Change from Baseline for POEM Total Score for PP Population
    - Repeat for 14.2.1.6.3 Summary of Values and Change from Baseline for POEM Total Score by Age Group – mITT Population
    - Repeat for 14.2.1.6.4 Summary of Values and Change from Baseline for POEM Total Score by Age Group – PP Population
    - Repeat for 14.2.1.6.5 Summary of Values and Change from Baseline for POEM Total Score by Sex – mITT Population
    - Repeat for 14.2.1.6.6 Summary of Values and Change from Baseline for POEM Total Score by Sex – PP Population
    - Repeat for 14.2.1.6.7 Summary of Values and Change from Baseline for POEM Total Score by Race – mITT Population
    - Repeat for 14.2.1.6.8 Summary of Values and Change from Baseline for POEM Total Score by Race – PP Population
    - Repeat for 14.2.1.6.9 Summary of Values and Change from Baseline for POEM Total Score by Baseline IGA – mITT Population
    - Repeat for 14.2.1.6.10 Summary of Values and Change from Baseline for POEM Total Score by Baseline IGA – PP Population
    - Repeat for 14.2.1.6.11 Summary of Values and Change from Baseline for POEM Total Score by Baseline EASI – mITT Population
    - Repeat for 14.2.1.6.12 Summary of Values and Change from Baseline for POEM Total Score by Baseline EASI – PP Population
    - Repeat for 14.2.1.6.13 Summary of Values and Change from Baseline for POEM Total Score by Baseline BSA – mITT Population
        - Add footnote [3], placing the [3] next to BSA (#byval) category: “BSA: Body Surface Area. Measured at baseline. Four subjects in the mITT population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and two included in the >30-40% category (117001 [BSA=65%] and 150006 [BSA=56%]).”
    - Repeat for 14.2.1.6.14 Summary of Values and Change from Baseline for POEM Total Score by Baseline BSA – PP Population
        - Add footnote [3], placing the [3] next to BSA (#byval) category: “BSA: Body Surface Area. Measured at baseline. Three subjects in the PP population were allowed into the study despite having BSA out of the 10-40% range, of whom two were included in the 10-20% BSA category (148027 [BSA=4%] and 155023 [BSA=4%]) and one included in the >30-40% category (150006 [BSA=56%]).”
    - Repeat for 14.2.1.6.15 Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status at Baseline – mITT Population
    - Repeat for 14.2.1.6.16 Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status at Baseline – PP Population
    - Repeat for 14.2.1.6.17 Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status on Treatment – mITT Population
    - Repeat for 14.2.1.6.18 Summary of Values and Change from Baseline for POEM Total Score by Rescue Medication Status on Treatment – PP Population

Table 14.2.1.7.1
Shift from Baseline for IGA
(Safety Population)

| | | | | Baseline Value | | | | |
|---|---|---|---|---|---|---|---|---|
| Treatment Group | Visit | Visit Value | Statistic | Clear | Almost Clear | Mild | Moderate | Severe |
| B244 O.D. 5.0 (N=xx) | Week 2 | Clear [1,2] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Almost Clear | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Week 4 | Clear | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Almost Clear | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Repeat for B244 O.D. 20.0, Pooled B244, and Vehicle | Week 8 | Clear | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Almost Clear | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

[1] Percentage and all subsequent percentages based on the number treated.
[2] 0=Clear, 1=Almost Clear, 2=Mild, 3=Moderate, 4=Severe.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.1.7.2 Shift from Baseline for IGA for PP Population

Table 14.2.2.1
Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 4 CFB [1] | ANCOVA [2,3] | n | xx | xx | xx | xx |
| | | LSM (SE) [4] | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | | | | | |
| | | LSM Difference (SE) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | N/A |
| | | 90% UCL Adjusted [5] | xx.x | xx.x | xx.x | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | | | | | |
| | | LSM Difference (SE) | N/A | xx.x (xx.xxx) | N/A | N/A |
| | | 90% UCL Adjusted | N/A | xx.x | N/A | N/A |
| | | p-value | N/A | x.xxxx | N/A | N/A |

[1] CFB = Change from Baseline.
[2] ANCOVA = Analysis of Covariance model.
[3] Model contains treatment group and baseline WI-NRS as explanatory variables, where baseline WI-NRS = (Sum of daily WI-NRS scores from Day -7 to Day -1) / (Total number of WI-NRS diaries entered from Day -7 to Day -1) and at least one WI-NRS daily score is reported between Days -7 and -1. Multiplicity is adjusted for with the Dunnett Testing Method using a one-sided familywise error rate of 0.10. All subjects who meet mITT criteria are included and no data is excluded based on rescue medication use.
[4] LSM = Least Squares Mean. SE = Standard Error.
[5] UCL = Upper Confidence Limit for one-sided confidence inteval.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.2 Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA for PP Population
    - Footnote [3] will be same as in 14.2.2.1, except changing the last statement to “All subjects who meet PP criteria are included.”

Table 14.2.2.3.1
Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 1 CFB [1] | MMRM [2,3] | n | xx | xx | xx | xx |
| | | LSM (SE) [4] | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | LSM Difference (SE) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | N/A |
| | | 95% CI | xx.x | xx.x | xx.x | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | LSM Difference (SE) | N/A | x.xxxx | N/A | N/A |
| | | 95% CI | N/A | xx.x (xx.xxx) | N/A | N/A |
| Repeat for Weeks 2 – 8 | | p-value | N/A | xx.x | N/A | N/A |

[1] CFB = Change from Baseline.
[2] MMRM = Mixed Model Repeated Measures.
[3] Model uses a compound symmetry covariance structure and contains visit, treatment group, visit-by-treatment interaction, and baseline WI-NRS as explanatory variables, where baseline WI-NRS = (Sum of daily WI-NRS scores from Day -7 to Day -1) / (Total number of WI-NRS diaries entered from Day -7 to Day -1) and at least one WI-NRS daily score is reported between Days -7 and -1 and for the corresponding week. All subjects who meet mITT criteria are included and no data is excluded based on rescue medication use.
[4] LSM = Least Squares Mean. SE = Standard Error.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.3.2 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for mITT Population
  - Footnote [3] will be same as in 14.2.2.3.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are"
- Repeat for 14.2.2.3.3 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for mITT Population
  - Footnote [3] will be same as in 14.2.2.3.1, except changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
- Repeat for 14.2.2.3.4 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for mITT Population
  - Footnote [3] will be same as in 14.2.2.3.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
- Repeat for 14.2.2.3.5 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 for PP Population – Primary Analysis
  - Footnote [3] will be same as in 14.2.2.3.1, except changing the last statement to "All subjects who meet PP criteria are included."
- Repeat for 14.2.2.3.6 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8– Primary Analysis – Sensitivity for PP Population
  - Footnote [3] will be same as in 14.2.2.3.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "All subjects who meet PP criteria are included."
- Repeat for 14.2.2.3.7 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for PP Population

    - Footnote [3] will be same as in 14.2.2.3.1, except changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
- Repeat for 14.2.2.3.8 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for PP Population
    - Footnote [3] will be same as in 14.2.2.3.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
- Repeat for 14.2.2.4.1 Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for mITT Population
    - Footnote [3] will be same as in 14.2.2.3.1, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.4.2 Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for mITT Population
    - Footnote [3] will be same as in 14.2.2.3.2, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.4.3 Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for mITT Population
    - Footnote [3] will be same as in 14.2.2.3.3, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.4.4 Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for mITT Population
    - Footnote [3] will be same as in 14.2.2.3.4, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.4.5 Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for PP Population
    - Footnote [3] will be same as in 14.2.2.3.5, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.4.6 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for PP Population
    - Footnote [3] will be same as in 14.2.2.3.6, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.4.7 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for PP Population
    - Footnote [3] will be same as in 14.2.2.3.7, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.4.8 Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for PP Population
    - Footnote [3] will be same as in 14.2.2.3.8, except changing "WI-NRS" to "AI-NRS"

Table 14.2.2.5.1
Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 1 | Logistic [1,2] | n/N (Proportion %) [3] | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | Odds Ratio (95% CI) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| Repeat for Weeks 2 – 8 | 20.0 v 5.0 | Odds Ratio (95% CI) | N/A | x.xx (x.xx, x.xx) | N/A | N/A |
| | | p-value | N/A | x.xxxx | N/A | N/A |

[1] Logistic regression model contains treatment group as the explanatory variable. At least one WI-NRS daily score is reported between Days -7 and -1 and for the corresponding week. All subjects who meet mITT criteria are included and no data is excluded based on rescue medication use.
[2] Treatment response is improvement by ≥ 4 Points in WI-NRS score (i.e., decrease in WI-NRS score by at least 4 points from Baseline to Post-Baseline visit).
[3] n is the number of subjects who have improved at that visit. N is the number of subjects with data at that visit, regardless of improvement status.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.5.2 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for mITT Population
  - Footnote [1] will be same as in 14.2.2.5.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are"
  - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.3 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for mITT Population
  - Footnote [1] will be same as in 14.2.2.5.1, except changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
  - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.4 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for mITT Population
  - Footnote [1] will be same as in 14.2.2.5.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
  - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.5 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
  - Footnote [1] will be same as in 14.2.2.5.1, except changing the last statement to "Subjects who discontinue treatment early or who take on-treatment rescue medications are imputed as non-responders."
  - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.6 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for mITT Population

    - Footnote [1] will be same as in 14.2.2.5.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "Subjects who discontinue treatment early or who take on-treatment rescue medications are imputed as non-responders."
    - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.7 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for PP Population
    - Footnote [1] will be same as in 14.2.2.5.1, except changing the last statement to "All subjects who meet PP criteria are included."
    - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.8 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for PP Population
    - Footnote [1] will be same as in 14.2.2.5.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "All subjects who meet PP criteria are included."
    - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.9 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for PP Population
    - Footnote [1] will be same as in 14.2.2.5.1, except changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
    - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.10 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for PP Population
    - Footnote [1] will be same as in 14.2.2.5.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "Excludes data collected from the week of first on-treatment rescue medication use through the end of the study. Data collected prior to the week of first on-treatment rescue medication use will be included."
    - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.11 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnote [1] will be same as in 14.2.2.5.1, except changing the last statement to "Subjects who discontinue treatment early or who take on-treatment rescue medications are imputed as non-responders."
    - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.5.12 Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for PP Population
    - Footnote [1] will be same as in 14.2.2.5.1, except changing "one WI-NRS daily score is" to "four WI-NRS daily scores are" and changing the last statement to "Subjects who discontinue treatment early or who take on-treatment rescue medications are imputed as non-responders."
    - Footnotes [2,3] will be same as in 14.2.2.5.1
- Repeat for 14.2.2.6.1 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.5.1.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.2 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.5.2.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.3 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.5.3.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.4 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for mITT Population

    - Footnotes [1,3] will be same as in 14.2.2.5.4.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.5 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.5.5.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.6 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.5.6.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.7 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.5.7.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.8 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.5.8.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.9 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.5.9.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.10 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.5.10.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.11 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.5.11.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.6.12 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.5.12.
    - Update footnote [2]: "Treatment response is improvement by ≥ 1 point in WI-NRS score (i.e., decrease in WI-NRS score by at least 1 point from Baseline to Post-Baseline visit)."
- Repeat for 14.2.2.7.1 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.1, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.2 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.2, except changing "WI-NRS" to "AI-NRS"

- Repeat for 14.2.2.7.3 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.3, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.4 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.4, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.5 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.5, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.6 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.6, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.7 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.7, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.8 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.8, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.9 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.9, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.10 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.10, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.11 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.11, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.7.12 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.5.12, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.1 Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.1, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.2 Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.2, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.3 Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.3, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.4 Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.4, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.5 Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.5, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.6 Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for mITT Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.6, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.7 Proportion of Subjects with Any Improvement in AI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.7, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.8 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Primary Analysis – Sensitivity for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.8, except changing "WI-NRS" to "AI-NRS"
- Repeat for 14.2.2.8.9 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis for PP Population

    - Footnotes [1,2,3] will be same as in 14.2.2.6.9, except changing “WI-NRS” to “AI-NRS”
- Repeat for 14.2.2.8.10 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Sub-Analysis – Sensitivity for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.10, except changing “WI-NRS” to “AI-NRS”
- Repeat for 14.2.2.8.11 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.11, except changing “WI-NRS” to “AI-NRS”
- Repeat for 14.2.2.8.12 Proportion of Subjects with Any Improvement in WI-NRS from Baseline to Weeks 1 Through 8 – Non-Responder Imputation (NRI) Analysis – Sensitivity for PP Population
    - Footnotes [1,2,3] will be same as in 14.2.2.6.12, except changing “WI-NRS” to “AI-NRS”

Table 14.2.2.9.1
Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 2 CFB [1] | MMRM [2,3] | n | xx | xx | xx | xx |
| | | LSM (SE) [4] | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | LSM Difference (SE) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | N/A |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | LSM Difference (SE) | N/A | xx.x (xx.xxx) | N/A | N/A |
| | | 95% CI | N/A | (xx.x, xx.x) | N/A | N/A |
| Repeat for Weeks 4 and 8 | | p-value | N/A | x.xxxx | N/A | N/A |

[1] CFB = Change from Baseline.
[2] MMRM = Mixed Model with Repeated Measures.
[3] Model uses a compound symmetry covariance structure and contains visit, treatment group, visit-by-treatment interaction, and baseline 5-D Pruritus total score as explanatory variables. All subjects who meet mITT criteria are included and no data is excluded based on rescue medication use.
[4] LSM = Least Squares Mean. SE = Standard Error.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.9.2 Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
  - Footnote [3] will be same as in 14.2.2.9.1, except changing the last statement to "Excludes visit data collected on/after date of first on-treatment rescue medication use through the end of the study."
- Repeat for 14.2.2.9.3 Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
  - Footnote [3] will be same as in 14.2.2.9.1, except changing the last statement to "All subjects who meet PP criteria are included."
- Repeat for 14.2.2.9.4 Mean Change in 5-D Pruritus Scale Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
  - Footnote [3] will be same as in 14.2.2.9.1, except changing the last statement to "All subjects who meet PP criteria are included."
- Repeat for 14.2.2.10.1 Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis for mITT Population
  - Footnote [3] will be same as in 14.2.2.9.1, except changing "5-D Pruritus" to "EASI"
- Repeat for 14.2.2.10.2 Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
  - Footnote [3] will be same as in 14.2.2.9.2, except changing "5-D Pruritus" to "EASI"
- Repeat for 14.2.2.10.3 Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
  - Footnote [3] will be same as in 14.2.2.9.3, except changing "5-D Pruritus" to "EASI"
- Repeat for 14.2.2.10.4 Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
  - Footnote [3] will be same as in 14.2.2.9.4, except changing "5-D Pruritus" to "EASI"
- Repeat for 14.2.2.11.1 Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Primary Analysis for mITT Population
  - Footnote [3] will be same as in 14.2.2.9.1, except changing "5-D Pruritus total score" to "IGA"

- Repeat for 14.2.2.11.2 Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
    - Footnote [3] will be same as in 14.2.2.9.2, except changing "5-D Pruritus total score" to "IGA"
- Repeat for 14.2.2.11.3 Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
    - Footnote [3] will be same as in 14.2.2.9.3, except changing "5-D Pruritus total score" to "IGA"
- Repeat for 14.2.2.11.4 Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
    - Footnote [3] will be same as in 14.2.2.9.4, except changing "5-D Pruritus total score" to "IGA"
- Repeat for 14.2.2.12.1 Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis for mITT Population
    - Footnote [3] will be same as in 14.2.2.9.1, except changing "5-D Pruritus Scale" to "POEM"
- Repeat for 14.2.2.12.2 Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
    - Footnote [3] will be same as in 14.2.2.9.2, except changing "5-D Pruritus Scale" to "POEM"
- Repeat for 14.2.2.12.3 Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
    - Footnote [3] will be same as in 14.2.2.9.3, except changing "5-D Pruritus Scale" to "POEM"
- Repeat for 14.2.2.12.4 Mean Change in POEM Total Score from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
    - Footnote [3] will be same as in 14.2.2.9.4, except changing "5-D Pruritus Scale" to "POEM"

Table 14.2.2.13.1
Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Primary Analysis
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 2 | Logistic [1,2] | n/N (Proportion %) [3] | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | Odds Ratio (95% CI) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| Repeat for Weeks 4, 8 | 20.0 v 5.0 | Odds Ratio (95% CI) | N/A | x.xx (x.xx, x.xx) | N/A | N/A |
| | | p-value | N/A | x.xxxx | N/A | N/A |

[1] Logistic regression model contains treatment group as the explanatory variable. All subjects who meet mITT criteria are included and no data is excluded based on rescue medication use.
[2] Treatment response is improvement by ≥ 50% in EASI score.
[3] n is the number of subjects who have improved at that visit. N is the number of subjects with data at that visit, regardless of improvement status.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.13.2 Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
  - Footnote [1] will be same as in 14.2.2.13.1, except changing the last statement to "Excludes visit data collected on/after date of first on-treatment rescue medication use through the end of the study."
  - Footnotes [2,3] will be same as in 14.2.2.13.1
- Repeat for 14.2.2.13.3 Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
  - Footnote [1] will be same as in 14.2.2.13.1, except changing the last statement to "Subjects who discontinue treatment early or who take on-treatment rescue medications are imputed as non-responders."
  - Footnotes [2,3] will be same as in 14.2.2.13.1
- Repeat for 14.2.2.13.4 Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
  - Footnote [1] will be same as in 14.2.2.13.1, except changing the last statement to "All subjects who meet PP criteria are included."
  - Footnotes [2,3] will be same as in 14.2.2.13.1
- Repeat for 14.2.2.13.5 Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
  - Footnote [1] will be same as in 14.2.2.13.1, except changing the last statement to "All subjects who meet PP criteria are included."
  - Footnotes [2,3] will be same as in 14.2.2.13.1
- Repeat for 14.2.2.13.6 Proportion of Subjects with ≥50% Improvement in EASI (EASI-50) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for PP Population
  - Footnote [1] will be same as in 14.2.2.13.1, except changing the last statement to "Subjects who discontinue treatment early or who take on-treatment rescue medications are imputed as non-responders."
  - Footnotes [2,3] will be same as in 14.2.2.13.1
- Repeat for 14.2.2.14.1 Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Primary Analysis for mITT Population

    - Footnotes [1,3] will be same as in 14.2.2.13.1.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “75%”
- Repeat for 14.2.2.14.2 Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.2.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “75%”
- Repeat for 14.2.2.14.3 Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.3.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “75%”
- Repeat for 14.2.2.14.4 Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.4.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “75%”
- Repeat for 14.2.2.14.5 Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.5.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “75%”
- Repeat for 14.2.2.14.6 Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.6.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “75%”
- Repeat for 14.2.2.15.1 Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Primary Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.1.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “90%”
- Repeat for 14.2.2.15.2 Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.2.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “90%”
- Repeat for 14.2.2.15.3 Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.3.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “90%”
- Repeat for 14.2.2.15.4 Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.4.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “90%”
- Repeat for 14.2.2.15.5 Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.5.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “90%”
- Repeat for 14.2.2.15.6 Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.6.
    - Footnote [2] will be same as in 14.2.2.13.1, except changing “50%” to “90%”
- Repeat for 14.2.2.16.1 Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.1.
    - Footnote [2]: Treatment response is improvement by ≥ 2 Points in IGA score to Clear or Almost Clear.

- Repeat for 14.2.2.16.2 Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.2.
    - Footnote [2] will be same as in 14.2.2.16.1.
- Repeat for 14.2.2.16.3 Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.3.
    - Footnote [2] will be same as in 14.2.2.16.1.
- Repeat for 14.2.2.16.4 Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.4.
    - Footnote [2] will be same as in 14.2.2.16.1.
- Repeat for 14.2.2.16.5 Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.5.
    - Footnote [2] will be same as in 14.2.2.16.1.
- Repeat for 14.2.2.16.6 Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.6.
    - Footnote [2] will be same as in 14.2.2.16.1.
- Repeat for 14.2.2.17.1 Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Primary Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.1.
    - Footnote [2]: Treatment response is improvement by ≥ 2 Points in IGA score.
- Repeat for 14.2.2.17.2 Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.2.
    - Footnote [2] will be same as in 14.2.2.17.1.
- Repeat for 14.2.2.17.3 Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.3.
    - Footnote [2] will be same as in 14.2.2.17.1.
- Repeat for 14.2.2.17.4 Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Primary Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.4.
    - Footnote [2] will be same as in 14.2.2.17.1.
- Repeat for 14.2.2.17.5 Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Sub-Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.5.
    - Footnote [2] will be same as in 14.2.2.17.1.
- Repeat for 14.2.2.17.6 Proportion of Subjects with IGA of Clear or Almost Clear at Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.6.
    - Footnote [2] will be same as in 14.2.2.17.1.
- Repeat for 14.2.2.18.1 Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.1.
    - Footnote [2]: Treatment response is any improvement in IGA score. Any improvement is defined as ≥ 1 point improvement from Baseline.
- Repeat for 14.2.2.18.2 Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.2.
    - Footnote [2] will be same as in 14.2.2.18.1.

- Repeat for 14.2.2.18.3 Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for mITT Population
    - Footnotes [1,3] will be same as in 14.2.2.13.3.
    - Footnote [2] will be same as in 14.2.2.18.1.
- Repeat for 14.2.2.18.4 Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Primary Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.4.
    - Footnote [2] will be same as in 14.2.2.18.1.
- Repeat for 14.2.2.18.5 Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Sub-Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.5.
    - Footnote [2] will be same as in 14.2.2.18.1.
- Repeat for 14.2.2.18.6 Proportion of Subjects with Any IGA Improvement from Baseline to Weeks 2, 4, and 8 – Non-Responder Imputation (NRI) Analysis for PP Population
    - Footnotes [1,3] will be same as in 14.2.2.13.6.
    - Footnote [2] will be same as in 14.2.2.18.1.

### 1.1.3 Safety

| Display Number | Title | Population | Unique/Repeat |
|---|---|---|---|
| 14.3.1 | Overall Summary of Treatment Emergent Adverse Events | Safety | Unique |
| 14.3.1.1 | Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term | Safety | Unique |
| 14.3.1.2 | Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity | Safety | Repeat |
| 14.3.1.3 | Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug | Safety | Repeat |
| 14.3.1.4 | Summary of Severe (Grade 3) Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug | Safety | Repeat |
| 14.3.1.5 | Summary of Treatment Emergent Adverse Events Leading to Discontinuation from Study by System Organ Class, Preferred Term | Safety | Repeat |
| 14.3.1.6 | Summary of Treatment Emergent Adverse Events with ≥ 2% Frequency by System Organ Class, Preferred Term | Safety | Repeat |
| 14.3.2.1 | Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term | Safety | Repeat |
| 14.3.2.2 | Summary of Treatment Emergent Serious Adverse Events by System | Safety | Repeat |

| | | | |
|---|---|---|---|
| | Organ Class, Preferred Term and Relationship to Study Drug | | |
| 14.3.2.3 | Summary of Deaths | Safety | Unique |
| 14.3.4.1.1 | Summary of Values and Change from Baseline for Hematology Parameters | Safety | Unique |
| 14.3.4.1.2 | Shift from Baseline for Hematology Parameters | Safety | Unique |
| 14.3.4.2.1 | Summary of Values and Change from Baseline for Chemistry Parameters | Safety | Repeat |
| 14.3.4.2.2 | Shift from Baseline for Chemistry Parameters | Safety | Repeat |
| 14.3.4.3.1 | Summary of Values and Change from Baseline for Urinalysis Parameters | Safety | Repeat |
| 14.3.4.3.2 | Shift from Baseline for Urinalysis Parameters | Safety | Repeat |
| 14.3.5 | Summary of Study Drug Accountability and Compliance | Safety | Unique |
| 14.3.6.1 | Summary of Values and Change from Previous Day for Patient Reported Local Tolerability | Safety | Unique |
| 14.3.6.2 | Shift from Previous Day for Patient Reported Local Tolerability | Safety | Unique |
| 14.3.7 | Summary of Values and Change from Baseline for Vital Signs | Safety | Repeat |
| 14.3.8.1 | Summary of Prior Medications by ATC Class Level 1 and Preferred Term | Safety | Unique |
| 14.3.8.2 | Summary of Concomitant Medications by ATC Class Level 1 and Preferred Term | Safety | Repeat |
| 14.3.8.3 | Summary of Rescue Medications by Class | Safety | Unique |

| | | | |
|---|---|---|---|
| 14.3.9.1 | Summary of Values and Change from Baseline for Rescue Medication Days for All Subjects | Safety | Unique |
| 14.3.9.2 | Summary of Values and Change from Baseline for Rescue Medication Days for Subjects Who Took At Least One Rescue Medication | Safety | Unique |
| 14.3.10 | Summary of Medical History by System Organ Class and Preferred Term | Safety | Unique |

Table 14.3.1
Overall Summary of Treatment Emergent Adverse Events
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Total Number of TEAEs [1] | n | xx | xx | xx | xx |
| Total Number of TESAEs | n | xx | xx | xx | xx |
| Number of Subjects with: | | | | | |
| At Least One TEAE [2] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| At Least One Treatment-Related TEAE [3] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| At Least One Severe (Grade 3) TEAE | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| At Least One Treatment-Related Severe (Grade 3) TEAE | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| At Least One TEAE Leading to Study Discontinuation | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| At Least One TEAE Leading to Death | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| At Least One TESAE [4] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| At Least One Treatment-Related TESAE [3] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

[1] TEAE: Treatment-Emergent Adverse Event – defined as any AE with onset after the first dose of study medication through 28 days after the last dose of study medication.
[2] Percentage and all subsequent percentages based on the number treated.
[3] Treatment-Related TE(S)AE – defined as TE(S)AE that was considered by the Investigator to be at least possibly related to the study medication.
[4] TESAE: Treatment-Emergent Serious Adverse Event.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.1.1
Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Total Number of TEAEs [1] | n | xx | xx | xx | xx |
| Number of Subjects with at Least One TEAE [2] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| System Organ Class #1 [3,4] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |
| System Organ Class #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |

[1] TEAE: Treatment-Emergent Adverse Event – defined as any AE with onset after the first dose of study medication through 28 days after the last dose of study medication.
[2] Percentage and all subsequent percentages based on the number treated.
[3] Subjects will be counted once per System Organ Class/Preferred Term.
[4] MedDRA Dictionary version XX.X was used to code adverse events.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.3.1.6 Summary of Treatment Emergent Adverse Events with ≥ 2% Frequency by System Organ Class and Preferred Term for Safety Population
    - Add footnote: TEAEs are presented if they occur in ≥ 2% of subjects in any treatment arm.

Table 14.3.1.2
Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term and Severity
(Safety Population)

| | Severity | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Total Number of TEAEs [1] | | n | xx | xx | xx | xx |
| Number of Subjects with at Least One TEAE [2] | | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| System Organ Class #1 [3,4] | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | | |

[1] TEAE: Treatment-Emergent Adverse Event – defined as any AE with onset after the first dose of study medication through 28 days after the last dose of study medication.
[2] Percentage and all subsequent percentages based on the number treated.
[3] Subjects will be counted once per System Organ Class/Preferred Term at the highest level of severity.
[4] MedDRA Dictionary version XX.X was used to code adverse events.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.1.3
Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term and Relationship to Study Drug
(Safety Population)

| | Relationship | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Total Number of TEAEs [1] | | n | xx | xx | xx | xx |
| Number of Subjects with at Least One TEAE [2] | | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| System Organ Class #1 [3,4,5] | Definitely Not | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Unlikely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Possibly | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Probably | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Definitely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | Definitely Not | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Unlikely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Possibly | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Probably | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Definitely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | Definitely Not | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Unlikely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Possibly | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Probably | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Definitely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | Definitely Not | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Unlikely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Possibly | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Probably | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Definitely | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | | |

[1] TEAE: Treatment-Emergent Adverse Event – defined as any AE with onset after the first dose of study medication through 28 days after the last dose of study medication.
[2] Percentage and all subsequent percentages based on the number treated.
[3] Treatment-Related TEAE – defined as TEAE that was considered by the Investigator to be at least possibly related to the study medication.
[4] Subjects will be counted once per System Organ Class/Preferred Term at the highest level of relatedness.
[5] MedDRA Dictionary version XX.X was used to code adverse events.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.3.1.4 Summary of Severe (Grade 3) Treatment Emergent Adverse Events by System Organ Class and Preferred Term and Relationship to Study Drug for Safety Population
- Repeat for 14.3.2.2 Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term and Relationship to Study Drug for Safety Population

Table 14.3.1.5
Summary of Treatment Emergent Adverse Events Leading to Discontinuation from Study by System Organ Class and Preferred Term
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Total Number of TEAEs [1] | n | xx | xx | xx | xx |
| Number of Subjects with at Least One TEAE [2] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| System Organ Class #1 [3,4] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |
| System Organ Class #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |

[1] TEAE: Treatment-Emergent Adverse Event – defined as any AE with onset after the first dose of study medication through 28 days after the last dose of study medication.
[2] Percentage and all subsequent percentages based on the number treated.
[3] Subjects will be counted once per System Organ Class/Preferred Term.
[4] MedDRA Dictionary version XX.X was used to code adverse events.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.2.1
Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Total Number of TESAEs [1] | n | xx | xx | xx | xx |
| Number of Subjects with at Least One TESAE [2] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| System Organ Class #1 [3,4] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |
| System Organ Class #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |

[1] TESAE: Treatment-Emergent Serious Adverse Event.
[2] Percentage and all subsequent percentages based on the number treated.
[3] Subjects will be counted once per System Organ Class/Preferred Term.
[4] MedDRA Dictionary version XX.X was used to code adverse events.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.2.3
Summary of Deaths
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Total Number of Deaths | n | xx | xx | xx | xx |
| Related to Disease Under Study [1] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| AE Outcome = Death [2] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Related to Disease Under Study and AE Outcome = Death | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

[1] Percentage and all subsequent percentages based on the number treated.
[2] Corresponds to TEAEs Leading to Death.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.4.1.1
Summary of Values and Change from Baseline for Hematology Parameters
(Safety Population)

| Hematology Parameters | Visit | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Basophils (10^6/L) | Screening | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Week 4 | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Week 4 CFB [1] | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Early Termination | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Early Termination CFB | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| Repeat for all Hematology parameters | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] CFB = Change from Baseline. For this analysis, Screening value is used as Baseline.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.3.4.2.1 Summary of Values and Change from Baseline for Chemistry Parameters for Safety Population
- Repeat for 14.3.4.3.1 Summary of Values and Change from Baseline for Urinalysis Parameters for Safety Population

Table 14.3.4.1.2
Shift from Baseline for Hematology Parameters
(Safety Population)

| Hematology Parameters | Treatment Group | Visit | Visit Value [2] | Statistic | Baseline Value | |
|---|---|---|---|---|---|---|
| | | | | | Normal | Abnormal |
| Basophils (10^6/L) [1] | B244 O.D. 5.0 (N=xx) | Week 4 | Normal | n (%) | xx (xx.x) | xx (xx.x) |
| | | | Abnormal | n (%) | xx (xx.x) | xx (xx.x) |
| | | Early Termination | Normal | n (%) | xx (xx.x) | xx (xx.x) |
| | | | Abnormal | n (%) | xx (xx.x) | xx (xx.x) |
| | B244 O.D. 20.0 (N=xx) | Week 4 | Normal | n (%) | xx (xx.x) | xx (xx.x) |
| | | | Abnormal | n (%) | xx (xx.x) | xx (xx.x) |
| | | Early Termination | Normal | n (%) | xx (xx.x) | xx (xx.x) |
| | | | Abnormal | n (%) | xx (xx.x) | xx (xx.x) |
| | Pooled B244 | Week 4 | Normal | n (%) | xx (xx.x) | xx (xx.x) |
| | | | Abnormal | n (%) | xx (xx.x) | xx (xx.x) |
| | | Early Termination | | | | |
| Repeat for all Hematology parameters | Repeat for Vehicle | | | | | |

[1] Percentage and all subsequent percentages based on the number treated.
[2] Parameters with reference range indicators equal to High or Low are counted as Abnormal.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.3.4.2.2 Shift from Baseline for Chemistry Parameters for Safety Population
- Repeat for 14.3.4.3.2 Shift from Baseline for Urinalysis Parameters for Safety Population

Table 14.3.5
Summary of Drug Accountability and Compliance at End of Week 4
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Total Weight Dispensed (g) | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Total Weight Returned (g) | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Net Weight of Study Drug (g) [1] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Compliance (%) based on IP Weight [2] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| 50% IP Applied [3] | | | | | |
| Yes | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| No | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Number of Dosing Diaries Entered [4] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Compliance (%) based on Diary Entries [5] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] Net Weight of Study Drug (g) = (Total Weight Dispensed (g)) – (Total Weight Returned (g)).
[2] Compliance (%) based on IP Weight = (Net Weight of Study Drug (g)) / (Planned Study Drug Use per Day (g) * Number of Days Expected Use of Study Drug) where Planned Study Drug Used per Day = 2.8g and Number of Days Expected Use of Study Drug = 28 days.

[3] Subjects who administered at least 50% of IP (where Net Weight of Study Drug (g) is at least 50% of the initial product weight (g) (i.e., 0.14 g per pump * 20 pumps per day * 28 days = 78.4 g).
[4] Number of Dosing Diaries Entered = Number of dosing diaries entered with a YES confirming study drug dosing.
[5] Compliance (%) based on Diary Entries = (Number of Dosing Diaries Entered) / (Number of Dosing Diaries Available) where Number of Dosing Diaries Available is the total number of dosing diaries expected from a 28 day treatment (56 diaries).
Source: Listing XXXX

Table 14.3.6.1
Summary of Values and Change from Previous Day for Patient Reported Local Tolerability
(Safety Population)

| Local Tolerability Symptom | Day | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Skin Redness and/or Color Change | Day 1 | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Day 2 | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Day 2 CFPD | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Day 3 | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Day 3 CFPD | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Day 4 | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Day 4 CFPD | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| Repeat for all Patient Reported | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Local Tolerability Symptoms | Repeat for Days 5 – 7 | | | | | |

[1] CFPD = Change from Previous Day.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.6.2
Shift from Previous Day for Patient Reported Local Tolerability
(Safety Population)

| Local Tolerability Symptom | Treatment Group | Day | Day 2 – 7 Value | Statistic | Previous Day Value: None | Mild | Moderate | Severe |
|---|---|---|---|---|---|---|---|---|
| Skin Redness and/or Color Change [1] | B244 O.D. 5.0 (N=xx) | Day 2 | None | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Day 3 | None | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Day 4 | None | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Repeat for all Patient Reported Local Tolerability Symptoms | Repeat for B244 O.D. 20.0, Pooled B244, and Vehicle | Day 5 | None | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Mild | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | Repeat for Days 6, 7 | Moderate | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | | | Severe | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

[1] Percentage and all subsequent percentages based on the number treated.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.7
Summary of Values and Change from Baseline for Vital Signs
(Safety Population)

| Vital Signs | Visit | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Diastolic Blood Pressure (mmHg) | Screening | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Baseline | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Week 2 | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Week 2 CFB [1] | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Week 4 | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| | Week 4 CFB | n | xx | xx | xx | xx |
| | | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| Repeat for Systolic Blood Pressure, Heart Rate, Respiratory Rate, and Temperature | Repeat for Week 8 and Early Termination | Median | xx.x | xx.x | xx.x | xx.x |
| | | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] CFB = Change from Baseline.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Height, Weight, BMI, and BSA are reported in table 14.1.3.1 and should not be included here.

Table 14.3.8.1
Summary of Prior Medications by ATC Class Level 1 and Preferred Term
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Number of Subjects with at Least One Prior Medication [1] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| ATC Class Level 1 #1 [2,3] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |
| ATC Class Level 1 #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |

[1] Percentage and all subsequent percentages based on the number treated.
[2] Subjects will be counted once per ATC Class/Preferred Term.
[3] WHO Drug Dictionary version YYYYMMM was used to code medication names.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.3.8.2 Summary of Concomitant Medications by ATC Class Level 1 and Preferred Term for Safety Population

Table 14.3.8.3
Summary of Rescue Medications by Class
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Number of Subjects with at Least One Rescue Medication [1] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Class 4: Mid-Strength [2] | | | | | |
| Clocortolone pivalate (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Mometasone furoate (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Triamcinolone acetonide (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Betamethasone valerate (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Fluocinolone acetonide (0.025%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Class 5: Lower Mid-Strength | | | | | |
| Fluticasone propionate (0.05%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Prednicarbate (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Hydrocortisone probutate (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Triamcinolone acetonide (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Fluocinolone acetonide (0.025%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Class 6: Mild | | | | | |
| Alclometasone dipropionate (0.05%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Desonide (0.05%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Triamcinolone acetonide (0.025%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Hydrocortisone butyrate (0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Fluocinolone acetonide (0.01%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Class 7: Least Potent | | | | | |
| Hydrocortisone (2%/2.5%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Hydrocortisone (0.5 to 0.1%) | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Other [3] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

[1] Percentage and all subsequent percentages based on the number treated.
[2] Subjects will be counted once per Rescue Medication term.
[3] Rescue medications reported as “Other” in the ERT will be cross referenced with allowed rescue medications, prohibited medications, and concomitant medications (e.g., emollients, antihistamines, etc.) and only “Other” resuce medications that are on the allowed rescue medication list are included here.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.9.1
Summary of Values and Change from Baseline for Rescue Medication Days for All Subjects
(Safety Population)

| Visit [1,2] | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Baseline | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 1 – 2 | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 1 – 2 CFB [3] | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 3 – 4 | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 3 – 4 CFB | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 1 – 4 Total | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 5 – 6 | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 5 – 6 CFB | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

| | | | | | |
|---|---|---|---|---|---|
| Weeks 7 – 8 | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 7 – 8 CFB | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 5 – 8 Total | n | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] Baseline rescue medication days = number of rescue medication days from Day -14 to Day -1.
Weeks 1 – 2 rescue medication days = number of rescue medication days from Day 1 to Day of Visit 3 – 1.
Weeks 3 – 4 rescue medication days = number of rescue medication days from Day of Visit 3 to Day of Visit 4 – 1.
Weeks 1 – 4 total rescue medication days = number of rescue medication days from Day 1 to Day of Visit 4 – 1.
Weeks 5 – 6 rescue medication days = number of rescue medication days from Day of Visit 4 to Day of Visit 4 + 13.
Weeks 7 – 8 rescue medication days = number of rescue medication days from Day of Visit 4 + 14 to Day of Visit 5 – 1.
Weeks 5 – 8 total rescue medication days = number of rescue medication days from Day of Visit 4 to Day of Visit 5 – 1.
[2] Each time interval is normalized as a rate where (# Rescue Medication Days) = [ (# Days Rescue Medications Used in Interval) / (# Actual Days in Interval) ] * (# Expected Days in Interval).
[3] CFB = Change from Baseline.

Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.9.2
Summary of Values and Change from Baseline for Rescue Medication Days for Subjects Who Took At Least One Rescue Medication
(Safety Population)

| Visit [1,2] | Statistic [4] | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Baseline | n/N (%) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 1 – 2 | n/N (%) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 1 – 2 CFB [3] | N | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 3 – 4 | n/N (%) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 3 – 4 CFB | N | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 1 – 4 Total | n/N (%) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 5 – 6 | n/N (%) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 5 – 6 CFB | N | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

| | | | | | |
|---|---|---|---|---|---|
| Weeks 7 – 8 | n/N (%) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 7 – 8 CFB | N | xx | xx | xx | xx |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |
| Weeks 5 – 8 Total | n/N (%) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | Mean (SD) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) | xx.x (xx.xx) |
| | Median | xx.x | xx.x | xx.x | xx.x |
| | Min, Max | xx, xx | xx, xx | xx, xx | xx, xx |

[1] Baseline rescue medication days = number of rescue medication days from Day -14 to Day -1.
Weeks 1 – 2 rescue medication days = number of rescue medication days from Day 1 to Day of Visit 3 – 1.
Weeks 3 – 4 rescue medication days = number of rescue medication days from Day of Visit 3 to Day of Visit 4 – 1.
Weeks 1 – 4 total rescue medication days = number of rescue medication days from Day 1 to Day of Visit 4 – 1.
Weeks 5 – 6 rescue medication days = number of rescue medication days from Day of Visit 4 to Day of Visit 4 + 13.
Weeks 7 – 8 rescue medication days = number of rescue medication days from Day of Visit 4 + 14 to Day of Visit 5 – 1.
Weeks 5 – 8 total rescue medication days = number of rescue medication days from Day of Visit 4 to Day of Visit 5 – 1.
[2] Each time interval is normalized as a rate where (# Rescue Medication Days) = [ (# Days Rescue Medications Used in Interval) / (# Actual Days in Interval) ] * (# Expected Days in Interval).
[3] CFB = Change from Baseline.
[4] n = Number of subjects who have taken at least one rescue medication during that time point. N = Number of subjects with data at that time point. Statistics for Mean, SD, Median, Min, and Max are computed for subjects who have taken at least one rescue medication during that time point.

Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Table 14.3.10
Summary of Medical History by System Organ Class and Preferred Term
(Safety Population)

| | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|
| Number of Subjects with at Least One MH Event [1] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| System Organ Class #1 [2,3] | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |
| System Organ Class #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #1 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #2 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Preferred Term #3 | n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| etc. | | | | | |

[1] Percentage and all subsequent percentages based on the number treated.
[2] Subjects will be counted once per System Organ Class/Preferred Term.
[3] MedDRA Dictionary version XX.X was used to code medical history events.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

## 1.2 APPENDIX B: Listings

| Display Number | Title | Population |
|---|---|---|
| Listing 16.2.1 | Subject Enrollment and Disposition | All Subjects |
| Listing 16.2.2 | Protocol Deviations (PD)/Violations (PV) | Randomized |
| Listing 16.2.3 | Subjects Excluded from the Efficacy Analysis | Randomized |
| Listing 16.2.4 | Demographic and Baseline Characteristics | Randomized |
| Listing 16.2.5.1 | Study Drug Accountability | Safety |
| Listing 16.2.5.2 | Study Drug Exposure and Treatment Compliance | Safety |
| Listing 16.2.5.3 | Study Drug Dosing and Secondary Treatment Compliance | Safety |
| Listing 16.2.6.1 | WI-NRS Daily Ratings and Weekly Averages | Randomized |
| Listing 16.2.6.2 | AI-NRS Daily Ratings and Weekly Averages | Randomized |
| Listing 16.2.6.3 | POEM Items and Score | Randomized |
| Listing 16.2.6.4 | 5-D Pruritus Scale Items and Score | Randomized |
| Listing 16.2.6.5 | IGA | Randomized |
| Listing 16.2.6.6 | EASI Items and Score | Randomized |
| Listing 16.2.7.1 | Adverse Events | Safety |
| Listing 16.2.7.2 | Adverse Event Details | Safety |
| Listing 16.2.7.3 | Adverse Events for COVID-19 | Safety |
| Listing 16.2.7.4 | Deaths | Safety |
| Listing 16.2.8.1 | Hematology Parameters | Safety |
| Listing 16.2.8.2 | Clinical Chemistry Parameters | Safety |
| Listing 16.2.8.3 | Urinalysis Parameters | Safety |
| Listing 16.2.8.4 | Urine Pregnancy Test | Safety |
| Listing 16.2.8.5 | Serology Parameters | Safety |
| Listing 16.2.9 | Patient Reported Local Tolerability | Safety |
| Listing 16.2.10 | Vitals Signs | Safety |
| Listing 16.2.11 | Physical Examination | Safety |
| Listing 16.2.12 | Smoking History | Safety |
| Listing 16.2.13.1 | Prior and Concomitant Medications | Safety |
| Listing 16.2.13.2 | Rescue Medications | Safety |

| | | |
|---|---|---|
| Listing 16.2.13.3 | Rescue Medication Days | Safety |
| Listing 16.2.14 | Medical History | Safety |
| Listing 16.2.15.1 | COVID-19 Test Results | Safety |
| Listing 16.2.15.2 | COVID-19 Missed Assessments | Safety |

Listing 16.2.1
Subject Enrollment and Disposition
(All Subjects)

| Subject ID | Treatment | Study Population | Disposition | Date of Study Completion or Discontinuation | Reason for Discontinuation |
|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | Screen Failure,<br>Enrolled,<br>Completed,<br>Discontinued | DDMMMYYYY | xxxxxxxx |

Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.2
Protocol Deviations (PD) / Violations (PV)
(Randomized Subjects)

| Subject ID | Treatment | Date of Deviation | Deviation Grade | Deviation Category | Deviation Description |
|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | DDMMMYYYY | Major,<br>Minor | xxxxxxxx | xxxxxxxx |

Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX

DATE: HH:MM/DDMMMYYYY

Listing 16.2.3
Subjects Excluded from the Efficacy Analysis
(Randomized Subjects)

| Subject ID | Treatment | Safety Population | mITT Population | PP Population | Reason for Exclusion |
|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Yes,<br>No | Yes,<br>No | Yes,<br>No | No IP Applied,<br>No Post-Baseline Evaluation Visit,<br>Major Protocol Deviation,<br>Did Not Complete Week 4 Visit,<br>Applied <50% IP |

Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.4
Demographic and Baseline Characteristics
(Randomized Subjects)

| Subject ID | Treatment | Age (Years) | Sex | Ethnicity | Race | Smoking Status | Rescue Medication Days [1] |
|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xx | Male,<br>Female | Hispanic or Latino,<br>Not Hispanic or Latino | American Indian or Alaska Native,<br>Asian,<br>Black or African American,<br>Native Hawaiian or Other Pacific Islander,<br>White,<br>Other (Specify) | Yes,<br>No | xx |

[1] Number of days during the washout period (Days -14 to -1) that rescue medications were taken.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.5.1
Study Drug Accountability
(Safety Population)

| Subject ID | Treatment | Kit Number | Kit Label | Lot Number | Visit/ Date Dispensed | Visit/ Date Returned | Weight Dispensed (g) | Weight Returned (g) |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A, | 1 | xxxxx | xxxxx | Baseline / DDMMMYYYY | Week X / DDMMMYYYY | xx.x | xx.x |
| | B244 O.D. 5.0, | 2 | xxxxx | xxxxx | Baseline / DDMMMYYYY | Week X / DDMMMYYYY | xx.x | xx.x |
| | B244 O.D. 20.0, Vehicle | 3 | xxxxx | xxxxx | Week 2 / DDMMMYYYY | Week X / DDMMMYYYY | xx.x | xx.x |

Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.5.2
Study Drug Exposure and Treatment Compliance
(Safety Population)

| Subject ID | Treatment | Total Weight Dispensed (g) | Total Weight Returned (g) | Net Weight (g) [1] | 50% IP Applied [2] | Compliance (%) based on Weight [3] |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xx.x | xx.x | xx.x | Yes, No | xx.x |

[1] Net Weight of Study Drug (g) = (Total Weight Dispensed (g)) – (Total Weight Returned (g)).
[2] Subjects who administered at least 50% of IP (where Net Weight of Study Drug (g) is at least 50% of the initial product weight (g) (i.e., 0.14 g per pump * 20 pumps per day * 28 days = 78.4 g).
[3] Compliance (%) based on IP Weight = (Net Weight of Study Drug (g)) / (Planned Study Drug Use per Day (g) * Number of Days Expected Use of Study Drug) where Planned Study Drug Used per Day = 2.8g and Number of Days Expected Use of Study Drug = 28 days.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.5.3
Study Drug Dosing and Secondary Treatment Compliance
(Safety Population)

| Subject ID | Treatment | Date/Time of AM Dose [1] | Date/Time of PM Dose [1] | Record Used for Secondary Compliance [2] | Number of Dosing Diaries Entered [1] | Compliance (%) based on Diary Entries [3] |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | DDMMMYYYY/<br>HH:MM | DDMMMYYYY/<br>HH:MM | Yes, No | xxx | xx.x |

[1] Date/Time of AM/PM Dose is taken from the Dosing Diaries Entered, which is the number of dosing diaries with a YES confirming study drug dosing.
[2] Only dosing diary records from date of first dose through date of Visit 4-1 will be considered for calculating secondary compliance to maintain the 28-day treatment period.
[3] Compliance (%) based on Diary Entries = (Number of Dosing Diaries Entered) / (Number of Dosing Diaries Available) where Number of Dosing Diaries Available is the total number of dosing diaries expected from a 28-day treatment (56 diaries).
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.6.1
WI-NRS Daily Ratings and Weekly Averages
(Randomized Subjects)

| Subject ID | Treatment | Study Population | Week | Date (Study Day) of Rating | Daily Rating | Weekly Average | ≥4-Point Improvement | Any Improvement [1] |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | 1, 2…8 | DDMMMYYYY (xx) | xx | xx | Yes, No | Yes, No |

[1] Any improvement is defined as ≥ 1 point improvement from Baseline.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.6.2
AI-NRS Daily Ratings and Weekly Averages
(Randomized Subjects)

| Subject ID | Treatment | Study Population | Week | Date (Study Day) of Rating | Daily Rating | Weekly Average | ≥4-Point Improvement | Any Improvement [1] |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | 1, 2…8 | DDMMMYYYY (xx) | xx | xx | Yes, No | Yes, No |

[1] Any improvement is defined as ≥ 1 point improvement from Baseline.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.6.3
POEM Items and Score
(Randomized Subjects)

| Subject ID | Treatment | Study Population | Visit | Date of Rating | POEM Item | Rating [1,2] |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | Screening,<br>Baseline,<br>Week 2,<br>Week 4,<br>Week 8 | DDMMMYYYY | Days Skin was Itchy,<br>Nights Sleep was Disturbed,<br>Days Skin was Bleeding,<br>Days Skin was Weeping or Oozing,<br>Days Skin was Cracked,<br>Days Skin was Flaking Off,<br>Days Skin Felt Dry or Rough,<br>Total Score | No days,<br>1-2 days,<br>3-4 days,<br>5-6 days,<br>Every day,<br>xxx (total score) |

[1] Numeric item conversion: No days=0; 1-2 days=1; 3-4 days=2; 5-6 days=3; Every day=4.
[2] Total score conversion: 0-2=Clear or almost clear; 3-7=Mild eczema; 8-16=Moderate eczema; 17-24=Severe eczema; 25-28=Very severe eczema.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.6.4
5-D Pruritus Scale Items and Score
(Randomized Subjects)

| Subject ID | Treatment | Study Population | Visit | Date of Rating | 5-D Pruritus Scale Item [1] | Rating [1] |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | Screening,<br>Baseline,<br>Week 2,<br>Week 4,<br>Week 8 | DDMMMYYYY | Duration: Hours per day Itching, | <6, 6-12, 12-18, 18-23, All Day |
| | | | | | Degree: Intensity of Itching, | Not Present, Mild, Moderate, Severe, Unbearable |
| | | | | | Direction: Itching Better or Worse, | Resolved, Much Better, Little Better, Unchanged, Worse |
| | | | | | Disability: Impact of Itching on Sleep, | Never, Occasionally, Frequent Delayed Sleep, Delayed Sleep and Occasional Night Waking, Delayed Sleep and Frequent Night Waking |
| | | | | | Disability: Impact of Itching on Leisure/School, | N/A, Never, Rarely, Occasionally, Frequently, Always |
| | | | | | Disability: Impact of Itching on Housework/Errands, | N/A, Never, Rarely, Occasionally, Frequently, Always |
| | | | | | Disability: Impact of Itching on Work/School, | N/A, Never, Rarely, Occasionally, Frequently, Always |
| | | | | | Distribution: Itching Present on Body Parts | Head/Scalp, Face, Chest, Abdomen, Back, Buttocks, Thighs, Lower Legs, Tops of Feet/Toes, Soles, Palms, Tops of Hands/Fingers, Forearms, Upper Arms, Points of Contact with Clothing, Groin |
| | | | | | Total Score | xxx |

[1] Duration, Degree, Direction, and Disability ratings use a 5-point Likert scale with responses rated from 1 (Low) to 5 (High). N/A ratings and Distribution ratings do not have a numeric equivalent.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.6.5
IGA
(Randomized Subjects)

| Subject ID | Treatment | Study Population | Visit | Date of Rating | Rating [1] | Clear or Almost Clear | Any Improvement [2] | ≥2-Point Improvement to Clear or Almost Clear |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | Screening,<br>Baseline,<br>Week 2,<br>Week 4,<br>Week 8 | DDMMMYYYY | Clear,<br>Almost Clear,<br>Mild,<br>Moderate,<br>Severe | Yes, No | Yes, No | Yes, No |

[1] Numeric item conversion: Clear=0; Almost Clear=1; Mild=2; Moderate=3; Severe=4.
[2] Any improvement is defined as ≥ 1 point improvement from Baseline.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.6.6
EASI Items and Score
(Randomized Subjects)

| Subject ID | Treatment | Study Population | Visit | Date of Rating | Body Area | EASI Item | Rating [1] | Improvement |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | Screening,<br>Baseline,<br>Week 2,<br>Week 4,<br>Week 8 | DDMMMYYYY | Head/Neck,<br>Trunk,<br>Upper Extremities,<br>Lower Extremities,<br><br>Total | Erythema<br>Edema/Papulation<br>Excoriation<br>Lichenification,<br>Area Score (%) [2],<br>Total Score | None,<br>Mild,<br>Moderate,<br>Severe,<br>xx-xx%,<br>xxx | Null if < 50%,<br>≥50%,<br>≥75%<br>≥90% |

[1] Numeric item conversion: None=0; Mild=1; Moderate=2; Severe=3.
[2] Numeric area score conversion: 1-9%=0; 10-29%=2; 30-49%=3; 50-69%=4; 70-89%=5; 90-100%=6.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Notes:

- Body Area=Total corresponds to EASI Item=Total Score.

Listing 16.2.7.1
Adverse Events
(Safety Population)

| Subject ID | Treatment | System Organ Class/ Preferred Term [1] | AE # | Start Date | End Date/Ongoing | Serious | SAE Criteria | Treatment Emergent |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xxxxxxx/<br>xxxxxxxx | xxx | DDMMMYYYY | DDMMMYYYY,<br>Ongoing | Yes, No | xxxxx | Yes. No |

[1] MedDRA Dictionary version XX.X was used to code adverse events.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX

DATE: HH:MM/DDMMMYYYY

Listing 16.2.7.2
Adverse Event Details
(Safety Population)

| Subject ID | Treatment | System Organ Class/ Preferred Term [1] | AE # | Severity | Relationship | Outcome | Led to Study Discontinuation |
|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xxxxxxx/<br>xxxxxxxx | xxx | Mild,<br>Moderate,<br>Severe | Definitely Not,<br>Unlikely,<br>Possibly,<br>Probably,<br>Definitely | Recovered,<br>Not Recovered,<br>Recovered with Sequelae,<br>Fatal,<br>Unknown | Yes, No |

[1] MedDRA Dictionary version XX.X was used to code adverse events.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.7.3
Adverse Events for COVID-19
(Safety Population)

| Subject ID | Treatment | System Organ Class/ Preferred Term [1] | AE # | Start Date | End Date/Ongoing | Severity | Outcome | Led to Study Discontinuation |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xxxxxxx/<br>xxxxxxxx | xxx | DDMMMYYYY | DDMMMYYYY,<br>Ongoing | Mild,<br>Moderate,<br>Severe | Recovered,<br>Not Recovered,<br>Recovered with Sequelae,<br>Fatal,<br>Unknown | Yes. No |

[1] MedDRA Dictionary version XX.X was used to code adverse events.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.7.4
Deaths
(Safety Population)

| Subject ID | Treatment | Date/Time of Last Dose | Date of Death | Related to Disease Under Study | AE Outcome=Fatal | AE # |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | DDMMMYYYY/HH:MM | DDMMMYYYY | Yes, No | Yes, No | |

Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX

DATE: HH:MM/DDMMMYYYY

Listing 16.2.8.1
Hematology Parameters
(Safety Population)

| Subject ID | Treatment | Visit | Date/Time of Lab Test | Lab Test | Result | Unit | Normality | Alert Flag [1] |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening,<br>Week 4,<br>Week 8 | DDMMMYYYY/HH:MM | Basophils,<br>Basophils/Leukocytes,<br>Eosinophils,<br>Etc. | xxx | xxx | Normal,<br>Abnormal,<br>High,<br>Low | LP, LN, N, HN,<br>HP, AB, [Null] |

[1] LP=Low Panic. LN=Low Normal. N=Normal. HN=High Normal. HP=High Panic. AB=Abnormal. [Null] when not used.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.8.2
Clinical Chemistry Parameters
(Safety Population)

| Subject ID | Treatment | Visit | Date/Time of Lab Test | Lab Test | Result | Unit | Normality | Alert Flag [1] |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening,<br>Week 4,<br>Week 8 | DDMMMYYYY/HH:MM | Albumin,<br>Alkaline Phosphatase,<br>Alanine Aminotransferase,<br>Etc. | xxx | xxx | Normal,<br>Abnormal,<br>High,<br>Low | LP, LN, N, HN, HP, AB, [Null] |

[1] LP=Low Panic. LN=Low Normal. N=Normal. HN=High Normal. HP=High Panic. AB=Abnormal. [Null] when not used.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.8.3
Urinalysis Parameters
(Safety Population)

| Subject ID | Treatment | Visit | Date/Time of Lab Test | Lab Test | Result | Unit | Normality | Alert Flag [1] |
|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening,<br>Week 4,<br>Week 8 | DDMMMYYYY/HH:MM | Bilirubin,<br>Clarity,<br>Color,<br>Etc. | xxx | xxx | Normal,<br>Abnormal,<br>High,<br>Low | LP, LN, N, HN,<br>HP, AB, [Null] |

[1] LP=Low Panic. LN=Low Normal. N=Normal. HN=High Normal. HP=High Panic. AB=Abnormal. [Null] when not used.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.8.4
Urine Pregnancy Test
(Safety Population)

| Subject ID | Treatment | Visit | Date/Time of Pregnancy Test | Result | Reason Not Done |
|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening,<br>Week 4,<br>Week 8 | DDMMMYYYY/HH:MM | Not Done,<br>Positive,<br>Negative | Subject is of non-childbearing potential,<br>Subject is surgically sterile (for at-least one year),<br>Subject is post-menopausal (for at-least one year),<br>Other (specify) |

Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX

DATE: HH:MM/DDMMMYYYY

Listing 16.2.8.5
Serology Parameters
(Safety Population)

| Subject ID | Treatment | Visit | Date/Time of Lab Test | Lab Test | Result | Alert Flag [1] |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening | DDMMMYYYY/HH:MM | Hepatitis B Virus Surface Antigen,<br>Hepatitis C Virus Antibody,<br>HIV-1/2 Antibody | Positive,<br>Negative,<br>Borderline | LP, LN, N, HN,<br>HP, AB, [Null] |

[1] LP=Low Panic. LN=Low Normal. N=Normal. HN=High Normal. HP=High Panic. AB=Abnormal. [Null] when not used.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.9
Patient Reported Local Tolerability
(Safety Population)

| Subject ID | Treatment | Day | Date of Rating | Symptom | Rating [1] |
|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | 1, 2…7 | DDMMMYYYY | Skin redness and/or color change,<br>Itching,<br>Burning and/or stinging,<br>Pain and/or tenderness,<br>New or changing rash | None,<br>Mild,<br>Moderate,<br>Severe |

[1] Numeric item conversion: None=0; Mild=1; Moderate=2; Severe=3.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.10
Vital Signs
(Safety Population)

| Subject ID | Treatment | Visit | Date/Time of Vital Signs | Vital Signs | Result | Unit | Normality [1] |
|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening,<br>Baseline,<br>Week 2,<br>Week 4,<br>Week 8 | DDMMMYYYY/HH:MM | Height,<br>Weight,<br>Body Mass Index (BMI),<br>Body Surface Area (BSA),<br>Systolic Blood Pressure,<br>Diastolic Blood Pressure,<br>Heart Rate,<br>Respiratory Rate,<br>Temperature | xxx | xxx | Normal,<br>Abnormal NCS,<br>Abnormal CS |

[1] NCS: Not Clinically Significant. CS: Clinically Significant.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.11
Physical Examination
(Safety Population)

| Subject ID | Treatment | Visit | Date of Physical Exam | Body System | Result [1] | Description of Abnormality |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening,<br>Week 8 | DDMMMYYYY | Cardiovascular,<br>Dermatological,<br>Ears,<br>Extremities,<br>Eyes,<br>Gastrointestinal,<br>General Appearance,<br>Head,<br>Lymph Nodes,<br>Mouth/Throat/Neck,<br>Musculoskeletal,<br>Neurological,<br>Nose,<br>Respiratory,<br>Thyroid | Normal,<br>Abnormal NCS,<br>Abnormal CS | xxxxxxxx |

[1] NCS: Not Clinically Significant. CS: Clinically Significant.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.12
Smoking History
(Safety Population)

| Subject ID | Treatment | Product | Smoking Start Date | Smoking End Date/ Ongoing | Packs per Day | Smoking Sessions per Week [1] |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Tobacco Products,<br>Non-Tobacco Products | DDMMMYYYY | DDMMMYYYY,<br>Ongoing | xxx | xxx |

[1] A subject can have 4 smoking sessions per day (morning, afternoon, evening, and night). The number of smoking sessions per week = number of smoking sessions per day * 7. Thus, the maximum value for smoking sessions per week is 28.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.13.1
Prior and Concomitant Medications
(Safety Population)

| Subject ID | Treatment | ATC Class Level 1/ Preferred Term [1] | CM # | Start Date | End Date/Ongoing | Indication | Dose | Unit | Frequency | Route | Prior Med [2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xxxxxxx/<br>xxxxxxxx | xxx | DDMMMYYYY | DDMMMYYYY,<br>Ongoing | xxx | xxx | xxx | xxx | xxx | Yes,<br>No |

[1] WHO Drug Dictionary version YYYYMMM was used to code medication names.
[2] Prior medication is defined as any medication with a stop date prior to the date of first dose of study drug.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.13.2
Rescue Medications
(Safety Population)

| Subject ID | Treatment | Rescue Medication [1] | Date/ Time (Study Day) | Dose (Unit) | Route | Class |
|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xxxxxxxx | DDMMMYYYY/<br>HH:MM (xx) | xxx (xxx) | xxx | 4, 5, 6, 7 |

[1] Rescue medications reported as "Other" in the ERT will be cross referenced with allowed rescue medications, prohibited medications, and concomitant medications (e.g., emollients, antihistamines, etc.) and only "Other" resuce medications that are on the allowed rescue medication list are included here.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.13.3
Rescue Medication Days
(Safety Population)

| Subject ID | Treatment | Study Population | Study Period | Rescue Medication Days [1,2] | More than Threshold [3] |
|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | N/A,<br>Safety,<br>mITT,<br>PP | Baseline,<br>Weeks 1 – 2,<br>Weeks 3 – 4,<br>Weeks 1 – 4,<br>Weeks 5 – 6,<br>Weeks 7 – 8,<br>Weeks 5 – 8 | xxx | Yes, No |

[1] Baseline rescue medication days = number of rescue medication days from Day -14 to Day -1.
Weeks 1 – 2 rescue medication days = number of rescue medication days from Day 1 to Day of Visit 3 – 1.
Weeks 3 – 4 rescue medication days = number of rescue medication days from Day of Visit 3 to Day of Visit 4 – 1.
Weeks 1 – 4 total rescue medication days = number of rescue medication days from Day 1 to Day of Visit 4 – 1.
Weeks 5 – 6 rescue medication days = number of rescue medication days from Day of Visit 4 to Day of Visit 4 + 13.
Weeks 7 – 8 rescue medication days = number of rescue medication days from Day of Visit 4 + 14 to Day of Visit 5 – 1.
Weeks 5 – 8 total rescue medication days = number of rescue medication days from Day of Visit 4 to Day of Visit 5 – 1.
[2] Each time interval is normalized as a rate where (# Rescue Medication Days) = [ (# Days Rescue Medications Used in Interval) / (# Actual Days in Interval) ] * (# Expected Days in Interval).
[3] Rescue medication thresholds: ≤3 days in washout period (baseline), ≤7 days during Weeks 1 – 4, ≤7 days during Weeks 5 – 8.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Notes:

- More than Threshold column should be populated for Study Periods: Baseline, Weeks 1 – 4, and Weeks 5 – 8.

Listing 16.2.14
Medical History
(Safety Population)

| Subject ID | Treatment | System Organ Class/ Preferred Term [1] | MH # | Start Date | End Date/Ongoing | Current Treatment | CM # |
|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | xxxxxxx/<br>xxxxxxxx | xxx | DDMMMYYYY | DDMMMYYYY,<br>Ongoing | Yes, No | xxx |

[1] MedDRA Dictionary version XX.X was used to code medical history events.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.15.1
COVID-19 Test Results
(Safety Population)

| Subject ID | Treatment | Test Date | COVID-19 Test | Test Type [1] | Result Type [2] | Result | Medically Confirmed |
|---|---|---|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | DDMMMYYYY | Antibody,<br>Viral,<br>Other (specify) | Antigen,<br>RNA | IgM,<br>IgG | Positive,<br>Negative | Yes, No |

[1] Test type should only be populated for the Viral COVID-19 test.
[2] Result type should only be populated for the Antibody COVID-19 test.
Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Listing 16.2.15.2
COVID-19 Missed Assessments
(Safety Population)

| Subject ID | Treatment | Affected Visit | Assessments Not Done | Reason Not Done |
|---|---|---|---|---|
| xxxxxx | N/A,<br>B244 O.D. 5.0,<br>B244 O.D. 20.0,<br>Vehicle | Screening,<br>Baseline,<br>Week 2,<br>Week 4,<br>Week 8 | eDiary Review,<br>IP Compliance,<br>IP Dispensation,<br>Application of Study Drug,<br>Etc. | Site Closure,<br>Subject Decision (specify),<br>Subject Decision – Over 60,<br>Subject Decision – Underlying Health Issues,<br>Etc. |

Source: SDTM.XXXX or ADaM.XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

## 1.3 APPENDIX C: Figures

| Display Number | Title | Population | Unique/Repeat |
|---|---|---|---|
| Figure 14.2.1.1 | Daily WI-NRS Scores v Time | mITT | Unique |
| Figure 14.2.1.2 | Daily WI-NRS Scores v Time | PP | Repeat |
| Figure 14.2.1.3 | Weekly WI-NRS Scores v Time | mITT | Repeat |
| Figure 14.2.1.4 | Weekly WI-NRS Scores v Time | PP | Repeat |
| Figure 14.2.1.5 | WI-NRS Responder (4-Point Improvement) v Time | mITT | Unique |
| Figure 14.2.1.6 | WI-NRS Responder (4-Point Improvement) v Time | PP | Repeat |
| Figure 14.2.1.7 | WI-NRS Responder (Any Improvement) v Time | mITT | Unique |
| Figure 14.2.1.8 | WI-NRS Responder (Any Improvement) v Time | PP | Repeat |
| Figure 14.2.2.1 | Daily AI-NRS Scores v Time | mITT | Repeat |
| Figure 14.2.2.2 | Daily AI-NRS Scores v Time | PP | Repeat |
| Figure 14.2.2.3 | Weekly AI-NRS Scores v Time | mITT | Repeat |
| Figure 14.2.2.4 | Weekly AI-NRS Scores v Time | PP | Repeat |
| Figure 14.2.2.5 | AI-NRS Responder (4-Point Improvement) v Time | mITT | Repeat |
| Figure 14.2.2.6 | AI-NRS Responder (4-Point Improvement) v Time | PP | Repeat |
| Figure 14.2.2.7 | AI-NRS Responder (Any Improvement) v Time | mITT | Repeat |
| Figure 14.2.2.8 | AI-NRS Responder (Any Improvement) v Time | PP | Repeat |
| Figure 14.2.3.1 | IGA Score v Time | mITT | Unique |
| Figure 14.2.3.2 | IGA Score v Time | PP | Repeat |
| Figure 14.2.3.3 | IGA Responder (0 or 1 with 2-Point Improvement) v Time | mITT | Unique |
| Figure 14.2.3.4 | IGA Responder (0 or 1 with 2-Point Improvement) v Time | PP | Repeat |

| | | | |
|---|---|---|---|
| Figure 14.2.3.5 | IGA Responder (0 or 1) v Time | mITT | Repeat |
| Figure 14.2.3.6 | IGA Responder (0 or 1) v Time | PP | Repeat |
| Figure 14.2.3.7 | IGA Responder (Any Improvement) v Time | mITT | Repeat |
| Figure 14.2.3.8 | IGA Responder (Any Improvement) v Time | PP | Repeat |
| Figure 14.2.4.1 | EASI Score v Time | mITT | Unique |
| Figure 14.2.4.2 | EASI Score v Time | PP | Repeat |
| Figure 14.2.4.3 | EASI-50 v Time | mITT | Unique |
| Figure 14.2.4.4 | EASI-50 v Time | PP | Repeat |
| Figure 14.2.4.5 | EASI-75 v Time | mITT | Repeat |
| Figure 14.2.4.6 | EASI-75 v Time | PP | Repeat |
| Figure 14.2.4.7 | EASI-90 v Time | mITT | Repeat |
| Figure 14.2.4.8 | EASI-90 v Time | PP | Repeat |
| Figure 14.2.5.1 | 5-D Score v Time | mITT | Unique |
| Figure 14.2.5.2 | 5-D Score v Time | PP | Repeat |
| Figure 14.2.6.1 | POEM Score v Time | mITT | Unique |
| Figure 14.2.6.2 | POEM Score v Time | PP | Repeat |

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# ADDENDUM TO STATISTICAL ANALYSIS PLAN PHASE II

**VERSION: 1.0**

**DATE:**

**April 22, 2022**

## BASED ON:

*Statistical Analysis Plan v3.0 Date: 12-JAN-2022*

*Protocol Version Amendment 3 Date: 28-FEB-2020*

## Study Drug:

*B244 Topical application*

## Protocol Number:

*PRB244-01*

## Study Title:

*A Phase II, Randomized, Double-Blind, Vehicle Controlled Study of the Efficacy, Safety, and Tolerability of B244 Topical Spray for the Treatment of Pruritus in Adults with a History of Atopic Dermatitis*

## Sponsor:

*AOBiome, LLC*
*125 Cambridgepark Drive*
*Cambridge, MA 02140*

# ADDENDUM TO SAP REVIEW AND APPROVAL

This Addendum to Statistical Analysis Plan v3.0 (12Jan2022) has been prepared in accordance with team reviewers' specifications.

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05 May 2022

Hyun Kim, VP of Clinical Operations — Date

# Table of Contents

# 1 Background and Purpose

The purpose of this addendum to the final Statistical Analysis Plan (SAP) for the PRB244-01 study (v3.0 dated 12Jan2022) is to describe additional statistical analyses that will be performed in order to address requests by the FDA made on 27Mar2022. These requests are detailed in the sections below.

# 2 Request 1: Worst Case Analysis

FDA Request: *You proposed the non-responder imputation analysis in which subjects who discontinue treatment early or who take on-treatment rescue medications will be imputed as a non-responder. Similar to the non-responder imputation analysis, we recommend that you provide additional analyses on the primary efficacy endpoint and relevant efficacy endpoints in which the underlying score-based variable values (e.g., WI-NRS, AI-NRS, IGA, etc.), are imputed with the worst score on/after date of first rescue medication use through the end of the study.*

As a parallel to the non-responder imputation analysis, for score-based endpoints of WI-NRS, AI-NRS, IGA, and EASI, we will perform worst-value imputation on/after the date of first on-treatment rescue medication or date of subject early discontinuation through the end of the study. For this sensitivity analysis, all values on/after the date of first on-treatment rescue medication use or all values missing due to subject early discontinuation will be replaced with the worst value observed for each subject between first post-baseline assessment and first use of on-treatment rescue medication (WOCF). In the event there is no observation after baseline recorded, WOCF will be Baseline values.

Subjects who discontinue early should have (1) at least one treatment-emergent adverse event (TEAE) leading to discontinuation and (2) discontinuation occurring prior to their Week 4 visit in order to have their data imputed for WOCF analysis.

In cases where subjects completed the treatment period, but did not complete all of the follow-up period, the following logic will be used in order to fully parallel the NRI analysis. If subjects use rescue medications while on treatment and discontinue after the Week 4 visit, then only values from first on-treatment rescue medication use through last attended visit will be imputed with WOCF (i.e., missing data from visits that did not occur after Week 4 would not be imputed in this case).

The mITT population will be used for this analysis. For WOCF imputation of WI-NRS and AI-NRS values, the worst-observation would be the highest weekly average (not highest daily score) reported after baseline and before first on-treatment rescue medication use or before subject early discontinuation.

If a situation occurs where a visit is missed but a subsequent visit takes place for the same subject, then the missing data for that interim visit will not be imputed unless that visit occurs on/after the date of first on-treatment medication use.

# 3 Request 2: Intention-to-Treat Analysis

FDA Request: *We recommend that you perform additional sensitivity analyses to include dropouts for whom no single score is collected and thus missing data handling strategies are to be considered. In this analysis, the analysis population will be the intent-to-treat (ITT) population.*

To approximate an intent-to-treat population, LOCF methods will be applied for all randomized subjects missing Week 4 responses for endpoints (WI-NRS, AI-NRS, IGA, EASI, and responder analyses). Subjects missing Week 4 values will have their measurement imputed to be the LOCF value on treatment or baseline, whichever is later. Sensitivity analysis of WI-NRS, AI-NRS, IGA, EASI, and related responder analyses will be performed.

Intention-to-Treat Population (ITT): All subjects who were randomized, regardless of exposure to treatment.

For subjects who were randomized, but did not receive treatment, the baseline WI-NRS and AI-NRS scores will be calculated using the same approach that is used for treated subjects (as described in section 6.4 of the SAP), except that the reference date will be the date of the baseline visit instead of the date of first dose.

# 4 List of Tables

| Display Number | Title | Population | Unique/ Repeat | Request # |
|---|---|---|---|---|
| 14.2.2.2a | Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA - WOCF | mITT | Repeat | 1 |
| 14.2.2.2b | Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA – WOCF Sensitivity | mITT | Repeat | 1 |
| 14.2.2.2c | Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA - LOCF | ITT | Repeat | 2 |
| 14.2.2.3.4a | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 - WOCF | mITT | Repeat | 1 |
| 14.2.2.3.4b | Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 - WOCF Sensitivity | mITT | Repeat | 1 |
| 14.2.2.4.4a | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 - WOCF | mITT | Repeat | 1 |
| 14.2.2.4.4b | Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 - WOCF Sensitivity | mITT | Repeat | 1 |
| 14.2.2.4.9 | Mean Change in AI-NRS from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.5.13 | Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.7.13 | Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.10.2a | Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 - WOCF | mITT | Repeat | 1 |
| 14.2.2.10.5 | Mean Change in EASI Total Score from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.11.2a | Mean Change in IGA from Baseline to Weeks 2, 4, and 8 - WOCF | mITT | Repeat | 1 |

| | | | | |
|---|---|---|---|---|
| 14.2.2.11.5 | Mean Change in IGA from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.14.7 | Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.15.7 | Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.16.7 | Proportion of Subjects with IGA of Clear or Almost Clear and ≥2 Point Improvement from Baseline to Week 4 - LOCF | ITT | Repeat | 2 |
| 14.2.2.17.7 | Proportion of Subjects with IGA of Clear or Almost Clear at Week 4 - LOCF | ITT | Repeat | 2 |

# 5 Table Shells

Table 14.2.2.2a
Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA – WOCF
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 4 CFB [1] | ANCOVA [2,3] | n | xx | xx | xx | xx |
| | | LSM (SE) [4] | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | | | | | |
| | | LSM Difference (SE) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | N/A |
| | | 90% UCL Adjusted [5] | xx.x | xx.x | xx.x | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | | | | | |
| | | LSM Difference (SE) | N/A | xx.x (xx.xxx) | N/A | N/A |
| | | 90% UCL Adjusted | N/A | xx.x | N/A | N/A |
| | | p-value | N/A | x.xxxx | N/A | N/A |

Note: WOCF = Worst Observation Carried Forward.
[1] CFB = Change from Baseline.
[2] ANCOVA = Analysis of Covariance model.
[3] Model contains treatment group and baseline WI-NRS as explanatory variables, where baseline WI-NRS = (Sum of daily WI-NRS scores from Day -7 to Day -1) / (Total number of WI-NRS diaries entered from Day -7 to Day -1) and at least one WI-NRS daily score is reported between Days -7 and -1. Multiplicity is adjusted for with the Dunnett Testing Method using a one-sided familywise error rate of 0.10. All subjects who meet mITT criteria are included. Data collected from the week of first on-treatment rescue medication use through the end of the study and missing data due to subject dropout will be imputed using WOCF. Data collected prior to the week of first on-treatment rescue medication use or dropout will be included.
[4] LSM = Least Squares Mean. SE = Standard Error.
[5] UCL = Upper Confidence Limit for one-sided confidence interval.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.2b Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA – WOCF Sensitivity for mITT Population
  - Footnote [3] will be same as in 14.2.2.2a, except changing “one WI-NRS daily score is” to “four WI-NRS daily scores are”

- Repeat for 14.2.2.2e Mean Change in WI-NRS from Baseline to Week 4 – ANCOVA – LOCF for ITT Population
  - Add new footnote "Note: LOCF = Last Observation Carried Forward." as the first footnote.
  - Footnote [3] will be "Model contains treatment group and baseline WI-NRS as explanatory variables, where baseline WI-NRS = (Sum of daily WI-NRS scores from Day -7 to Day -1) / (Total number of WI-NRS diaries entered from Day -7 to Day -1) and at least one WI-NRS daily score is reported between Days -7 and -1. Multiplicity is adjusted for with the Dunnett Testing Method using a one-sided familywise error rate of 0.10. All subjects who meet ITT criteria are included and no data is excluded based on rescue medication use. Any values missing at Week 4 will be imputed using LOCF."

Table 14.2.2.3.4a
Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – WOCF
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 1 CFB [1] | MMRM [2,3] | n | xx | xx | xx | xx |
| | | LSM (SE) [4] | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | LSM Difference (SE) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | N/A |
| | | 95% CI | xx.x | xx.x | xx.x | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | LSM Difference (SE) | N/A | x.xxxx | N/A | N/A |
| | | 95% CI | N/A | xx.x (xx.xxx) | N/A | N/A |
| Repeat for Weeks 2 – 8 | | p-value | N/A | xx.x | N/A | N/A |

Note: WOCF = Worst Observation Carried Forward.
[1] CFB = Change from Baseline.
[2] MMRM = Mixed Model Repeated Measures.
[3] Model uses a compound symmetry covariance structure and contains visit, treatment group, visit-by-treatment interaction, and baseline WI-NRS as explanatory variables, where baseline WI-NRS = (Sum of daily WI-NRS scores from Day -7 to Day -1) / (Total number of WI-NRS diaries entered from Day -7 to Day -1) and at least one WI-NRS daily score is reported between Days -7 and -1 and for the corresponding week. All subjects who meet mITT criteria are included. Data collected from the week of first on-treatment rescue medication use through the end of the study and missing data due to subject dropout will be imputed using WOCF. Data collected prior to the week of first on-treatment rescue medication use or dropout will be included.
[4] LSM = Least Squares Mean. SE = Standard Error.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.3.4b Mean Change in WI-NRS from Baseline to Weeks 1 Through 8 – WOCF Sensitivity for mITT Population
  - Footnote [3] will be same as in 14.2.2.3.4a, except changing “one WI-NRS daily score is” to “four WI-NRS daily scores are”
- Repeat for 14.2.2.4.4a Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – WOCF for mITT Population
  - Footnote [3] will be same as in 14.2.2.3.4a, except changing “WI-NRS” to “AI-NRS”
- Repeat for 14.2.2.4.4b Mean Change in AI-NRS from Baseline to Weeks 1 Through 8 – WOCF Sensitivity for mITT Population

  - Footnote [3] will be same as in 14.2.2.3.4b, except changing “WI-NRS” to “AI-NRS”
- Repeat for 14.2.2.4.9 Mean Change in AI-NRS from Baseline to Week 4 – LOCF for ITT Population
  - First column will contain only “Week 4 CFB [1]”
  - Add new footnote “Note: LOCF = Last Observation Carried Forward.” as the first footnote.
  - Footnote [3] will be “Model uses a compound symmetry covariance structure and contains treatment group and baseline AI-NRS as explanatory variables, where baseline AI-NRS = (Sum of daily AI-NRS scores from Day -7 to Day -1) / (Total number of AI-NRS diaries entered from Day -7 to Day -1) and at least one AI-NRS daily score is reported between Days -7 and -1 and for the corresponding week. All subjects who meet ITT criteria are included and no data is excluded based on rescue medication use. Any values missing at Week 4 will be imputed using LOCF.”

Table 14.2.2.5.13
Proportion of Subjects with ≥4 Point Improvement in WI-NRS from Baseline to Week 4 – LOCF
(ITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 4 | Logistic [1,2] | n/N (Proportion %) [3] | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | Odds Ratio (95% CI) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | Odds Ratio (95% CI) | N/A | x.xx (x.xx, x.xx) | N/A | N/A |
| | | p-value | N/A | x.xxxx | N/A | N/A |

Note: LOCF = Last Observation Carried Forward.
[1] Logistic regression model contains treatment group as the explanatory variable. At least one WI-NRS daily score is reported between Days -7 and -1 and for the corresponding week. All subjects who meet ITT criteria are included and no data is excluded based on rescue medication use. Any values missing at Week 4 will be imputed using LOCF.
[2] Treatment response is improvement by ≥ 4 Points in WI-NRS score (i.e., decrease in WI-NRS score by at least 4 points from Baseline to Post-Baseline visit).
[3] n is the number of subjects who have improved at that visit. N is the number of subjects with data at that visit, regardless of improvement status.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.7.13 Proportion of Subjects with ≥4 Point Improvement in AI-NRS from Baseline to Week 4 – LOCF for mITT Population
  - Add new footnote “Note: LOCF = Last Observation Carried Forward.” as the first footnote.
  - Footnote [1] will be same as in 14.2.2.5.13, except changing “WI-NRS” to “AI-NRS”

Table 14.2.2.10.2a
Mean Change in EASI Total Score from Baseline to Weeks 2, 4, and 8 – WOCF
(mITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 2 CFB [1] | MMRM [2,3] | n | xx | xx | xx | xx |
| | | LSM (SE) [4] | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | LSM Difference (SE) | xx.x (xx.xxx) | xx.x (xx.xxx) | xx.x (xx.xxx) | N/A |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | LSM Difference (SE) | N/A | xx.x (xx.xxx) | N/A | N/A |
| | | 95% CI | N/A | (xx.x, xx.x) | N/A | N/A |
| Repeat for Weeks 4 and 8 | | p-value | N/A | x.xxxx | N/A | N/A |

Note: WOCF = Worst Observation Carried Forward.
[1] CFB = Change from Baseline.
[2] MMRM = Mixed Model with Repeated Measures.
[3] Model uses a compound symmetry covariance structure and contains visit, treatment group, visit-by-treatment interaction, and baseline EASI total score as explanatory variables. All subjects who meet mITT criteria are included. Data collected from the week of first on-treatment rescue medication use through the end of the study and missing data due to subject dropout will be imputed using WOCF. Data collected prior to the week of first on-treatment rescue medication use or dropout will be included.
[4] LSM = Least Squares Mean. SE = Standard Error.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.10.5 Mean Change in EASI Total Score from Baseline to Week 4 – LOCF for ITT Population
  - First column will contain only “Week 4 CFB [1]”
  - Add new footnote “Note: LOCF = Last Observation Carried Forward.” as the first footnote.
  - Footnote [3] will be “Model uses a compound symmetry covariance structure and contains treatment group and baseline EASI total score as explanatory variables. All subjects who meet ITT criteria are included and no data is excluded based on rescue medication use. Any values missing at Week 4 will be imputed using LOCF.”
- Repeat for 14.2.2.11.2a Mean Change in IGA from Baseline to Weeks 2, 4, and 8 – WOCF for mITT Population
  - Footnote [3] will be same as in 14.2.2.10.2a, except changing “EASI” to “IGA”

- Repeat for 14.2.2.10.5 Mean Change in IGA from Baseline to Week 4 – LOCF for ITT Population
  - First column will contain only “Week 4 CFB [1]”
  - Add new footnote “Note: LOCF = Last Observation Carried Forward.” as the first footnote.
  - Footnote [3] will be same as in 14.2.2.10.5, except changing “EASI” to “IGA”

Table 14.2.2.14.7
Proportion of Subjects with ≥75% Improvement in EASI (EASI-75) from Baseline to Week 4 – LOCF
(ITT Population)

| Visit | Statistic Type | Statistic | B244 O.D. 5.0 (N=xx) | B244 O.D. 20.0 (N=xx) | Pooled B244 (N=xx) | Vehicle (N=xx) |
|---|---|---|---|---|---|---|
| Week 4 | Logistic [1,2] | n/N (Proportion %) [3] | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) | xx/xx (xx.x) |
| | | 95% CI | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) | (xx.x, xx.x) |
| | v. Vehicle | Odds Ratio (95% CI) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | x.xx (x.xx, x.xx) | N/A |
| | | p-value | x.xxxx | x.xxxx | x.xxxx | N/A |
| | 20.0 v 5.0 | Odds Ratio (95% CI) | N/A | x.xx (x.xx, x.xx) | N/A | N/A |
| | | p-value | N/A | x.xxxx | N/A | N/A |

Note: LOCF = Last Observation Carried Forward.
[1] Logistic regression model contains treatment group as the explanatory variable. All subjects who meet ITT criteria are included and no data is excluded based on rescue medication use. Any values missing at Week 4 will be imputed using LOCF.
[2] Treatment response is improvement by ≥ 75% in EASI score.
[3] n is the number of subjects who have improved at that visit. N is the number of subjects with data at that visit, regardless of improvement status.
Source: Listing XXXX
PROGRAM NAME: XXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note:

- Repeat for 14.2.2.15.7 Proportion of Subjects with ≥90% Improvement in EASI (EASI-90) from Baseline to Week 4 – LOCF for ITT Population
  - Footnote [2] will be same as in 14.2.2.14.7, except changing "75%" to "90%"
- Repeat for 14.2.2.16.7 Proportion of Subjects with IGA of Clear or Almost Clear and ≥2-Point Improvement from Baseline to Week 4 – LOCF for ITT Population
  - Footnote [2] will be "Treatment response is improvement by ≥ 2 Points in IGA score to Clear or Almost Clear."
- Repeat for 14.2.2.17.7 Proportion of Subjects with IGA of Clear or Almost Clear at Week 4 – LOCF for ITT Population
  - Footnote [2] will be "Treatment response is IGA score of 0 (Clear) or 1 (Almost Clear)."

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