STATISTICAL ANALYSIS PLAN

A Multicenter, Open-label, Uncontrolled, Long-term Trial to Demonstrate the Safety and Efficacy of 1% OPA-15406 Ointment in Adult Patients with Atopic Dermatitis and of 0.3% and 1% OPA-15406 Ointments in Pediatric Patients with Atopic Dermatitis
(Phase 3 Trial)

NCT Number: NCT03961529
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Otsuka Pharmaceutical Co., Ltd.

Investigational New Drug OPA-15406

Protocol No. 271-102-00006

A Multicenter, Open-label, Uncontrolled, Long-term Trial to Demonstrate the Safety and Efficacy of 1% OPA-15406 Ointment in Adult Patients with Atopic Dermatitis and of 0.3% and 1% OPA-15406 Ointments in Pediatric Patients with Atopic Dermatitis (Phase 3 Trial)

Statistical Analysis Plan

Version: 2.0
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Confidential

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List of Abbreviations and Definition of Terms

List of Abbreviations

Abbreviation	Expansion or Definition
BSA	Body surface area
EASI	Eczema Area and Severity Index
FAS	Full Analysis Set
IGA	Investigator's Global Assessment
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
OC	Observed Cases
POEM	Patient-Oriented Eczema Measure
SS	Safety Set
TEAE	Treatment-emergent adverse event

Definition of Terms

Term	Definition
Descriptive statistics	Number of subjects, mean, standard deviation, maximum, median, minimum
Frequency distribution	Number of subjects, percentage

1 Introduction

This statistical analysis plan details the methods for statistical analysis planned in Trial 271-102-00006. In this trial, statistical analysis will be performed at the interim visit when all subjects have completed an observation period of at least 24 weeks (or observation period up to withdrawal) and at the last visit. In most cases, the interim data cutoff date is 31 Mar 2020, and for subjects who have not completed the Week 24 visit on 31 Mar 2020, data used for analysis will be collected until the completion of the Week 24 visit.

2 Trial Objectives

Primary Objective: To evaluate the safety of OPA-15406 ointment when 1% OPA-15406 ointment is administered to adult atopic dermatitis (AD) patients and 0.3% or 1% OPA-15406 ointment is administered to pediatric AD patients twice daily for 52 weeks.

Secondary Objective: To evaluate the efficacy of OPA-15406 ointment by 1% OPA-15406 ointment administration to adult AD patients and 0.3% or 1% OPA-15406 ointment administration to pediatric AD patients twice daily for 52 weeks.

3 Trial Design

3.1 Type/Design of Trial

This trial is being conducted to evaluate the safety and efficacy of OPA-15406 ointment by 1% OPA-15406 ointment administration to adult AD patients and 0.3% or 1% OPA-15406 ointment administration to pediatric AD patients twice daily for 52 weeks. The trial design is shown in Figure 3.1-1.

1) Screening period
   After obtaining informed consent from the subject for subjects aged ≥20 years old, from both the subject and the subject's legal guardian for subjects aged ≥15 to <20 years old, and from the subject's legal guardian for subjects aged <15 years old, the investigator or subinvestigator will perform the screening examination. The screening period is defined as the period between the day of screening examination and the day of baseline examination (2 - 30 days).
2) Assessment period (treatment period)
   The assessment period is defined as the period between the day of baseline examination and the end of Week 52 examination (or the end of withdrawal examination). The subjects who meet the inclusion and do not meet exclusion criteria at the baseline examination will be allocated to the investigational medicinal product (IMP) (Adult patients will be prescribed with 1% OPA-15406 ointment. Pediatric patients will be prescribed with 0.3% OPA-15406 ointment; however, the starting dose will be 1% if necessary based on the judgment of the

investigator or subinvestigator in consideration of each subject's condition [eg, severity of rash, affected area, etc]). The allocated IMP will be administered to the treatment area from the day of baseline examination twice daily for 52 weeks. After the baseline examination, the examinations will be performed at Weeks 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52.
If a subject discontinues the IMP administration between the day of baseline examination and the day of Week 52 examination, a withdrawal examination will be performed for that subject.

3) Trial period
The trial period for individual subjects is the period from the day of obtaining the subject's or subject's legal guardian's written informed consent to the day of the Week 52 examination or withdrawal examination. For subjects who missed the Week 52 examination or withdrawal examination, the day of discontinuation will be the day when the investigator or subinvestigator determined that the subject was to be withdrawn from the trial. It does not include the follow-up period for adverse events (AEs).

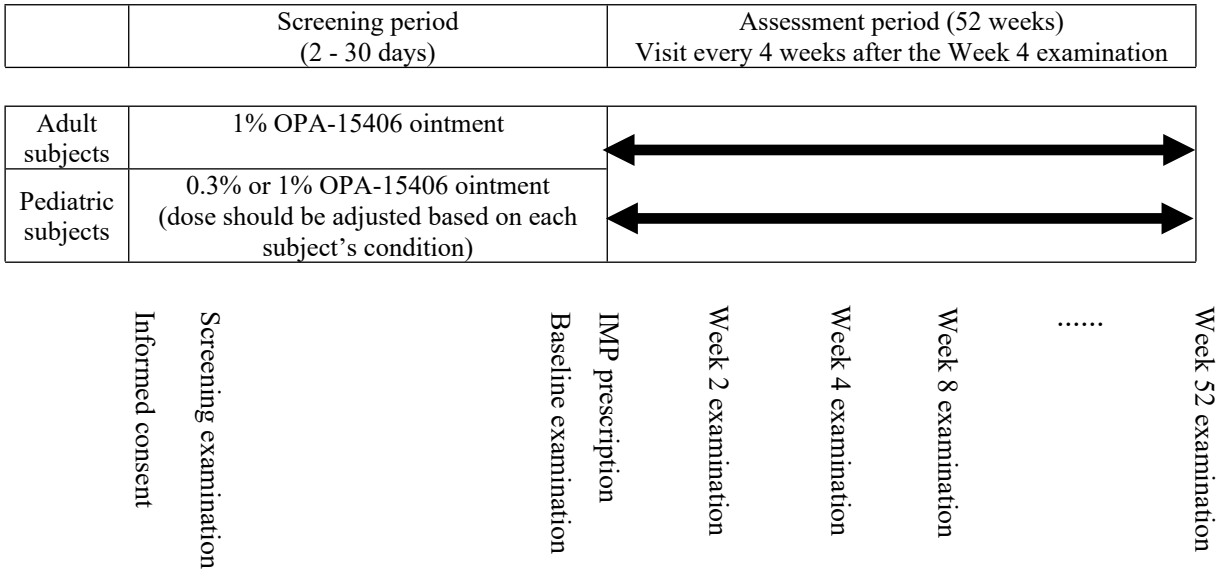

Figure 3.1-1 Trial Design

3.2 Trial Treatments

3.2.1 Dose, Regimen, and Treatment Period

[Adult subjects] The 1% formulation of OPA-15406 ointment will be administered twice daily (approximately 12 hours apart between morning and night administration) for 52 weeks. If all skin symptoms have resolved, IMP administration may be suspended based

on the judgment of the investigator or subinvestigator. If skin symptoms relapse, IMP administration will be restarted.

[Pediatric subjects] The 0.3% formulation of OPA-15406 ointment will be administered as the starting dose, twice daily (approximately 12 hours apart between morning and night administration) for 52 weeks. However, the 1% formulation of OPA-15406 ointment will be administered as the starting dose, if judged necessary by the investigator or subinvestigator in consideration of each subject's condition (eg, severity of rash, affected area, etc).

In addition, 1% OPA-15406 ointment can be used if subjects show no improvement in skin symptoms after administration of 0.3% OPA-15406 ointment for ≥1 month (with an acceptable window of ≥21 days).

When subjects show an improvement in skin symptoms and the use of 1% OPA-15406 ointment is considered unnecessary, the dosage can be reduced to 0.3% OPA-15406 ointment.

If all skin symptoms have resolved, IMP administration may be suspended based on the judgment of the investigator or subinvestigator.

If IMP administration is continued, 0.3% OPA-15406 ointment will be used. If skin symptoms relapse, IMP administration will be restarted.

The amount of IMP (g) per dose is 10 g/m^2 body surface area (BSA), which is calculated as follows.

1) The subject's BSA (m^2) will be calculated based on height and body weight at each examination, using the following equation.

$$\text{BSA } (m^2) = \sqrt{\frac{\text{Ht (cm)} \times \text{Wt (kg)}}{3600}}$$

BSA = body surface area; Ht = height; Wt = body weight (Mosteller 1987).

2) The treatment area will be specified
3) The amount of IMP (g) per dose will be calculated as "subject's BSA (m^2)" × "treatment area (%)" × "10 g/m^2."
   Example: In case of a BSA of 0.7 m^2 and an affected BSA of 32%: 0.7 m^2 × 0.32 × 10 g/m^2 = 2.24 g

3.2.2 Treatment Area

The treatment area with the IMP is defined as follows.

- The treatment area will be the affected area determined at each examination until the time of the next examination.
- Even when the affected area is relieved after the baseline examination, the IMP administration should be continued there as the treatment area if judged necessary by the investigator or subinvestigator.

The investigator or subinvestigator will instruct the subject or the subject's legal guardian regarding the method of administration by specifying the treatment area (%) and the total amount of administration (g) for each treatment area using the human body drawing, and will give the human body drawing (copy) to the subject or the subject's legal guardian. The investigator or subinvestigator will record the treatment area (%) of the 4 body regions [face, neck, and head (excluding scalp); upper limbs; trunk; and lower limbs] in the source document and case report form (CRF).

3.3 Trial Population

The target population of this trial is AD patients with an Investigator's Global Assessment (IGA) score ≥2. Subjects will be included in the trial to reach the target number of 330 subjects (150 adult subjects, 180 pediatric subjects [2 - 6 years, 7 - 14 years, each with at least 80 subjects]) for IMP administration.

3.4 Analysis Window

The number of days after the start of IMP administration on which the endpoint measurement will be made will be calculated relative to the start day of IMP administration (Day 1). The timepoints for analysis will be determined on the basis of data collected at scheduled visits as well as data collected at unscheduled visits and at withdrawal. All data collected after the start of IMP administration will be analyzed for efficacy and safety endpoints. The timepoints for analysis and their acceptable time windows are presented in Table 3.4-1. If multiple data were collected in the window, the last data collected within the window will be used. At the last visit, the last data on efficacy and safety endpoints will be used among all data collected after the start of IMP administration.

As the baseline data for analysis, the data collected on the day closest to and before the start day of IMP administration, including screening data, will be used.

Table 3.4-1 Timepoints for Efficacy and Safety Endpoint Analysis and Their Acceptable Time Windows				
Timepoint	**Target day**	**Interval (number of days after treatment)**		
Baseline	1	-	-	1
Week 2	15	2	-	21
Week 4	29	22	-	42
Week 8	57	43	-	70
Week 12	85	71	-	98
Week 16	113	99	-	126
Week 20	141	127	-	154
Week 24	169	155	-	182
Week 28	197	183	-	210
Week 32	225	211	-	238
Week 36	253	239	-	266
Week 40	281	267	-	294
Week 44	309	295	-	322
Week 48	337	323	-	350
Week 52	365	351	-	372

4 Sample Size

330 subjects (150 adult subjects, 180 pediatric subjects [2 - 6 years, 7 - 14 years, each with at least 80 subjects])

[Rationale for sample size]

Enrollment of 150 adult and 150 pediatric subjects will enable a 1-year (52 weeks) observation of 100 adult and 100 pediatric subjects. However, 180 pediatric subjects (2 - 6 years, 7 - 14 years, each with at least 80 subjects) will be enrolled to evaluate safety in younger (2 - 6 years old) and older (7 - 14 years old) pediatric subjects.

5 Statistical Analysis Datasets

5.1 Safety Set (SS)

The SS consists of all subjects who have received the IMP at least once.

5.2 Full Analysis Set (FAS)

The FAS consists of all subjects who have received the IMP at least once.

5.3 Handling of Missing Data

Missing data will not be imputed at each timepoint and Observed Cases (OC) data will be used.

6 Primary and Secondary Outcome Variables

6.1 Safety Endpoints

1) Adverse events
- AEs occurring after the start of IMP administration (Treatment-emergent adverse event [TEAE])
- TEAEs by severity
- TEAEs resulting in death
- Serious TEAEs
- TEAEs leading to discontinuation of IMP administration
- TEAEs leading to dose reduction of the IMP
- TEAEs leading to interruption of IMP administration
- TEAEs (skin and subcutaneous tissue disorders) by grade
- TEAEs at treatment areas
- TEAEs by time of onset

2) Clinical laboratory tests
3) Vital signs and body weight

6.2 Efficacy Endpoints

- Success rate in IGA: percentage of subjects with improved IGA score of 0 or 1 with improvement of at least 2 grades
- Time to IGA response (IGA score of 0 or 1 with improvement by at least 2 grades)
- Response rate in Eczema Area and Severity Index (EASI) 90 (improvement of ≥90% in EASI), EASI 75 (improvement of ≥75% in EASI), and EASI 50 (improvement of ≥50% in EASI)
- Change from baseline in IGA score
- Change from baseline in the total score of EASI and each clinical sign score
- Change from baseline in the total score of Patient-Oriented Eczema Measure (POEM)
- Change from baseline in the total affected BSA (%)
- Change from baseline in total serum immunoglobulin E (IgE) levels
- Change from baseline in serum thymus and activation-regulated chemokine (TARC)/chemokine (C-C motif) ligand 17 (CCL17) levels

7 Disposition and Demographic Analysis

Unless otherwise specified, the data listed below will be analyzed in the following subjects: subjects in the pediatric 0.3% treatment starting group, subjects in the pediatric

1% treatment starting group, all pediatric subjects, all adult subjects, and all adult and pediatric subjects. Subjects aged ≤14 years old are regarded as pediatric subjects and those aged ≥15 years old as adult subjects. If necessary, data from pediatric subjects will be analyzed separately in younger pediatric subjects (2 - 6 years old) and older pediatric subjects (7 - 14 years old).

7.1 Subject Disposition

The number of subjects who underwent the screening examination and the number of those who received the IMP will be provided, and a frequency distribution (the number and percentage of subjects, the same shall apply hereinafter) will be calculated for subjects who completed the trial and those who discontinued the trial. The number of pediatric and/or adult subjects who received the IMP will be used as the denominator of the percentage. For subjects who discontinued the trial, a frequency distribution will be calculated by reason for withdrawal.

7.2 Demographic and Baseline Characteristics

For age, sex, duration of disease, body weight, height, body mass index (BMI), race, and severity of AD, descriptive statistics or a frequency distribution will be calculated depending on the characteristics of the respective parameters in the SS. Descriptive statistics will be presented for age, duration of disease, body weight, height, and BMI, and a frequency distribution will be presented for sex, race, and severity of AD. Prior and concomitant diseases will be coded to system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA). Prior and concomitant diseases will not be analyzed, and only a listing will be created.

To calculate the duration of disease, missing data on the date will not be imputed, and if the day and month are missing, only the known year will be used and if the day is missing, the known month and year will be used.

If the “day, month, and year” are complete: (date of screening – date of diagnosis + 1) / 365.25

If only the “month and year” are known: [(year of screening × 12 + month of screening) – (year of diagnosis × 12 + month of diagnosis) + 1] / 12

If only the “year” is known: year of screening – year of diagnosis + 1

7.3 Baseline Disease Evaluation

A frequency distribution for baseline IGA score (2, 3, or 4) and descriptive statistics for baseline total EASI score will be calculated in the SS. The affected BSA at baseline will be divided into the following categories, and a frequency distribution will be calculated:

Categories of the affected BSA: ≥5% to <10%, ≥10% to <20%, ≥20% to <40%, ≥40%

7.4 Treatment Compliance

Treatment compliance based on the number of doses administered from baseline until Week 52 will be divided into the categories outlined below, and the number and percentage of subjects in each category will be calculated in the SS. The number and percentage of subjects who received the IMP will be calculated by week (Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, and any exposure). The method for calculating compliance based on the number of doses administered is defined in a separate analysis data set specification or equivalent documents.

Compliance categories based on the number of doses administered: <50%, ≥50% to <60%, ≥60% to <70%, ≥70% to <80%, ≥80% to <90%, ≥90% to <100%, ≥100% to <110%, ≥110% to <120%, ≥120%

The number and percentage of subjects who interrupted the IMP at least once will be calculated. For pediatric subjects, a frequency distribution will be calculated by reason for selecting the IMP concentration. A frequency distribution will also be presented for the reason for interruption. If there are multiple reasons for selecting the IMP concentration or interruption in a subject, the reason for the first selection or interruption will be counted.

7.5 Prior and Concomitant Medications

For medications administered before the start day of IMP administration, medications administered during the IMP treatment period, and medications administered after the end of IMP administration, the number and percentage of subjects who received these medications will be calculated in the SS. These medications will be coded using the World Health Organization (WHO) Drug Dictionary and analyzed using the Anatomical Therapeutic Chemical (ATC) classification level 2 and preferred name. Concomitant therapies will not be analyzed, and only a listing will be created.

7.6 Protocol Deviations

The number and percentage of subjects who have any major deviation from the protocol will be calculated. Additionally, the number and percentage of subjects in each major deviation category will be provided by trial site.

8 Efficacy Analysis

Data listed below will be analyzed in the FAS. Unless otherwise specified, efficacy analysis will be performed in the following subjects: subjects in the pediatric 0.3% treatment starting group, subjects in the pediatric 1% treatment starting group, all pediatric subjects, all adult subjects, and all adult and pediatric subjects.

8.1 Efficacy Endpoints

8.1.1 Success Rate in IGA

The number and percentage of subjects who showed IGA response (IGA score of 0 or 1 with improvement by at least 2 grades) at least one time after the start of IMP administration will be calculated along with the associated two-sided 95% confidence interval (based on the Clopper-Pearson method, the same shall apply hereinafter). The analysis will include all data collected after administration regardless of the timepoint of analysis. Similarly, the number and percentage of subjects who showed IGA response from the start of IMP administration to each timepoint (ie, to the upper limit of the acceptable time window of each timepoint specified in Section 3.4 Analysis Window) will be calculated along with the associated confidence interval. In this analysis, a subject who showed improvement at each timepoint will be counted as a responder whether or not subsequent data are available. The number of subjects included in the FAS will be used as the denominator of the percentage at each timepoint. The number and percentage of IGA responders at each timepoint and at the last visit (using the last observation carried forward [LOCF] method) along with the associated 95% confidence interval will be calculated using OC data.

8.1.2 Time to IGA Response

A Kaplan-Meier plot will be created for the duration of days from the start day of IMP administration until the first IGA response (IGA score of 0 or 1 with improvement by at least 2 grades). Subjects who did not have an IGA response (IGA score of 0 or 1 with improvement by at least 2 grades) will be censored on the last day of examination. The percent improvement along with its 95% confidence interval and the number at risk will be calculated at baseline and at the target day of each post-treatment timepoint (baseline,

Week 4, Week 12, Week 24, Week 36, and Week 52) specified in Section 3.4, Analysis Window.

8.1.3 EASI Response Rate

EASI 75 (improvement of ≥75% in EASI) will be analyzed in the same manner as IGA in Section 8.1.1. EASI 90 (improvement of ≥90% in EASI) and EASI 50 (improvement of ≥50% in EASI) will also be analyzed in the same manner as EASI 75.

8.1.4 Time to EASI Response

A Kaplan-Meier plot will be created for the duration of days from the start day of IMP administration until the first EASI 75 response. Subjects who did not show response (improvement of ≥75% in EASI) will be censored on the last day of examination. The percent improvement along with its 95% confidence interval and the number at risk will be calculated at baseline and at the target day of each post-treatment timepoint (baseline, Week 4, Week 12, Week 24, Week 36, and Week 52) specified in Section 3.4, Analysis Window. The time to EASI 90 (improvement of ≥90% in EASI) and EASI 50 (improvement of ≥50% in EASI) will be analyzed in the same manner as EASI 75.

8.1.5 Change from Baseline in IGA Score to Week 52 of IMP Administration

Descriptive statistics will be calculated for measured values and changes from baseline in IGA score at each timepoint (Week 2, Week 4, and thereafter every 4 weeks until Week 52) and at the last visit (LOCF) using OC data.

A graph will be created for the mean change (at each timepoint using OC data) and its standard deviations in pediatric and adult subjects.

8.1.6 Shift Table for IGA Score Through Week 52 of IMP Administration

A shift table from baseline will be created for IGA score (0, 1, 2, 3, or 4) at each timepoint and at the last visit (LOCF) using OC data.

8.1.7 Change from Baseline in the Total EASI Score and Each EASI Clinical Sign Score to Week 52 of IMP Administration

The change from baseline in the total EASI score will be analyzed in the same manner as the change in IGA score. By clinical sign and body region, these parameters will also be analyzed in the same manner. The percent change from baseline in the EASI score will also be analyzed in the same manner as above. A graph will be created for the mean change in the total EASI score (at each timepoint using OC data) and its standard deviation in pediatric and adult subjects.

8.1.8 Change from Baseline in the Total POEM Score to Week 52 of IMP Administration

The change from baseline in the total POEM score will be analyzed in the same manner as the change in IGA score. The percent change from baseline in the total POEM score will also be analyzed in the same manner.

8.1.9 Change from Baseline in the Total Affected BSA (%) to Week 52 of IMP Administration

The change from baseline in the total affected BSA (%) will be analyzed in the same manner as the change from baseline in IGA score.

8.1.10 Change from Baseline in Total Serum IgE levels to Week 52 of IMP Administration

The change from baseline in total serum IgE levels will be analyzed in the same manner as the change from baseline in IGA score.

8.1.11 Change from baseline in serum TARC/CCL17 levels to Week 52 of IMP Administration

The change from baseline in serum TARC/CCL17 levels will be analyzed in the same manner as the change from baseline in IGA score.

8.2 Subgroup Analyses

The number and percentage of subjects who showed IGA response (IGA score of 0 or 1 with improvement by at least 2 grades) at least one time after the start of IMP administration and those who achieved EASI 75, EASI 90, and EASI 50 will be calculated with their confidence intervals by subgroup as listed below. Subgroup analysis will be made in the following subjects: subjects in the pediatric 0.3% treatment starting group, subjects in the pediatric 1% treatment starting group, subjects in the pediatric modal dose 0.3% group, subjects in the pediatric modal dose 1% group, all pediatric subjects, all adult subjects, and all adult and pediatric subjects. In the subgroup analysis by modal dose, however, tabulation for subjects in the pediatric modal dose group (0.3% or 1%) will not be made.

Age: ≥2 to <7 years old, ≥7 to <15 years old, ≥15 to <30 years old, ≥30 years old

Sex: male, female

Baseline IGA score: 2 (mild), 3 (moderate), 4 (severe)

Severity of AD: mild, moderate, severe, most severe

Baseline total EASI score: <15, ≥15

Baseline affected BSA: <20%, ≥20% to <40%, ≥40%

Use of anti-inflammatory agents: yes, no

Use of topical medications other than anti-inflammatory agents: yes, no

Modal dose: 0.3% OPA-15406 ointment, 1% OPA-15406 ointment

Analysis by modal dose will be performed in pediatric subjects. The modal dose is defined as the concentration administered most frequently during the IMP treatment period. When the same number of doses was administered at 0.3% and 1%, the last concentration administered is used as the modal dose. Subjects using anti-inflammatory agents are defined as those using prohibited concomitant topical medications (corticosteroids, tacrolimus) and dupilumab for medically unavoidable reasons such as worsening of symptoms during the IMP treatment period. Subjects using topical medications other than anti-inflammatory agents are defined as those using topical medications other than prohibited concomitant topical anti-inflammatory agents (corticosteroids, tacrolimus) during the IMP treatment period.

9 Safety Analyses

The following safety analyses will be made in the SS. Unless otherwise specified, safety analyses will be performed in the following subjects: subjects in the pediatric 0.3% treatment starting group, subjects in the pediatric 1% treatment starting group, all pediatric subjects, all adult subjects, and all adult and pediatric subjects.

9.1 Extent of Exposure

Descriptive statistics will be calculated for the number of treatment days (excluding interruption), the total amount of IMP administered, and the amount of IMP per dose in the SS. Allowing for the starting concentration of IMP (in the 0.3% OPA-15406 group and the 1% OPA-15406 group), descriptive statistics will also be calculated for the total amount of IMP administered and the amount of IMP per dose. If the weight of collected IMP is unknown, it will be regarded as zero to calculate the amount of IMP administered.

9.2 Adverse Events

Adverse events will be coded by SOC and PT using MedDRA.

The number and percentage of subjects experiencing the TEAEs listed below will be calculated. Treatment-emergent AEs of skin and subcutaneous tissue disorders will also be analyzed according to the grade of the Common Terminology Criteria for Adverse Events (CTCAE) v4.0, Japanese Clinical Oncology Group (JCOG) version.

- TEAEs
- TEAEs by severity
- TEAEs resulting in death
- Serious TEAEs
- TEAEs leading to discontinuation of IMP administration
- TEAEs leading to interruption of IMP administration
- TEAEs leading to dose reduction of the IMP
- TEAEs (only skin and subcutaneous tissue disorders) by CTCAE grade
- TEAEs at treatment areas
- TEAEs by time of onset

If a subject reported multiple episodes of the same event, the most severe event will be used for analysis by severity.

The number and percentage of subjects experiencing TEAEs that occurred in ≥5% of subjects in any of the treatment groups and non-serious TEAEs that occurred in ≥5% of subjects in any of the treatment groups will be calculated.

Adverse drug reactions (AEs for which a causal relationship with the IMP cannot be ruled out) will be analyzed in the same manner as AEs.

Treatment-emergent AEs excluding those that occurred during interruption will be analyzed in the same manner.

By time of onset, TEAEs, including events that occurred during interruption, will be analyzed. If a subject reported multiple episodes of the same event, the event that occurred earliest will be used for the analysis. As the denominator of the percentage in each period, the number of subjects whose treatment period (from the start day of IMP administration until the last designated day of IMP administration) is included in the relevant period will be used. The time of onset will be divided into the categories listed below.

> Categories of the time of onset: ≤Week 4, >Week 4 to ≤Week 12, >Week 12 to ≤Week 24, >Week 24 to ≤Week 36, >Week 36 to ≤Week 52, >Week 52

In the pediatric population, the same analysis as above will be performed by age (2 - 6 years old, 7 - 14 years old).

According to sex, use of anti-inflammatory agents, and use of topical medications other than anti-inflammatory agents, all AEs and AEs on the treatment area will be summarized and TEAEs will be analyzed by event. Adverse drug reactions will also be analyzed by event.

The following analyses will also be performed:

- The number and percentage of subjects who experienced TEAEs during each period or those who experienced TEAEs before each period and did not recover during the period will be calculated by period. If a subject experienced an AE and did not recover across multiple periods, the subject will be counted once during each period. As the denominator of the percentage in each period, the number of subjects whose treatment period (from the start day of IMP administration until the last designated day of IMP administration) is included in the relevant period will be used. The period will be divided into the categories listed below. In the pediatric population, the same analysis as above will be performed by age (2 - 6 years old, 7 - 14 years old).
  Categories of the period: ≤Week 4, >Week 4 to ≤Week 12, >Week 12 to ≤Week 24, >Week 24 to ≤Week 36, >Week 36 to ≤Week 52, >Week 52

9.3 Clinical Laboratory Data

For each parameter (except qualitative urinalysis), descriptive statistics will be calculated using OC data for measured values and changes from the baseline at each timepoint and at the last visit (LOCF) in pediatric subjects, adult subjects, and all subjects. For qualitative urinalysis values of clinical laboratory tests, a shift table at each timepoint against the baseline will be created. For clinical laboratory tests except qualitative urinalysis, a shift table will be created for pre- and post-treatment values classified into normal, high, or low according to the normal range in pediatric subjects, adult subjects, and all subjects.

9.4 Vital Sign and Body Weight Data

For body weight, temperature, blood pressure (systolic and diastolic), and pulse rate, descriptive statistics will be calculated using OC data for measured values and changes from baseline at each timepoint and at the last visit (LOCF) in pediatric subjects, adult subjects, and all subjects. The number and percentage of subjects with clinically abnormal changes (Appendix 1 Criteria for Vital Signs Potential Clinical Significance) in temperature, blood pressure (systolic and diastolic), pulse rate, and body weight will be calculated in pediatric subjects, adult subjects, and all subjects. A listing of subjects with abnormal changes will be created.

9.5 Physical Examination Data

Not applicable.

9.6 Electrocardiogram Data

Not applicable.

9.7 Liver Function Test

The number and percentage of potential Hy's Law Cases (Appendix 2 Criteria for Potential Hy's Law) will be calculated in pediatric subjects, adult subjects, and all subjects. A listing of potential Hy's Law Cases will also be produced. All post-treatment data, excluding baseline data and data with missing timepoint, will be used to determine if the criteria are met.

9.8 Other Safety Endpoints

Not applicable.

10 Pharmacokinetic Analyses

Not applicable.

11 Pharmacodynamic Analyses

Not applicable.

12 Pharmacogenomic Analyses

Not applicable.

13 Interim Analysis

Not applicable.

14 Changes in the Planned Analyses

The following analysis, which was specified in Section 7.5.2, Clinical Laboratory Tests, of the protocol was not performed:

- For clinical laboratory tests, the number and percentage of subjects who are in the potentially clinically significant range will be calculated.

15 References

None.

16 Revision History

Version	Date of revision	Section No./ heading	Before revision	After revision	Reason for revision
Ver.2.0	23 Dec 2020	8.1.2 Time to IGA Response		The following analysis was added: The percent improvement along with its 95% confidence interval and the number at risk will be calculated at baseline and at the target day of each post-treatment timepoint (baseline, Week 4, Week 12, Week 24, Week 36, and Week 52) specified in Section 3.4, Trial Visit Window.	To provide the statistics required for assessment.
		8.1.4 Time to EASI Response		The following analysis was added: The percent improvement along with its 95% confidence interval and the number at risk will be calculated at baseline and at the target day of each post-treatment timepoint (baseline, Week 4, Week 12, Week 24, Week 36, and Week 52) specified in Section 3.4, Trial Visit Window.	To provide the statistics required for assessment.
		8.2 Subgroup Analyses		The following analysis was added: Subgroup analysis will be made in the following subjects: subjects in the pediatric 0.3% treatment starting group, subjects in the pediatric 1% treatment starting group, subjects in the pediatric modal dose 0.3% group, subjects	To provide the statistics required for assessment.

Version	Date of revision	Section No./ heading	Before revision	After revision	Reason for revision
				in the pediatric modal dose 1% group, all pediatric subjects, all adult subjects, and all adult and pediatric subjects. In the subgroup analysis by modal dose, however, tabulation for subjects in the pediatric modal dose group (0.3% or 1%) will not be made.	
		9.2 Adverse Events		The following analysis was added: The number and percentage of subjects who experienced TEAEs during each period or those who experienced TEAEs before each period and did not recover during the period will be calculated by period. In line with the addition above, the method for counting events in the analysis by time of onset was added: By time of onset, TEAEs, including events that occurred during interruption, will be analyzed. If a subject reported multiple episodes of the same event, the event that occurred earliest will be used for the analysis. As the denominator of the percentage in each period, the number of subjects whose treatment period (from the start day of IMP administration until the last designated day of	To provide the statistics required for assessment.

Version	Date of revision	Section No./ heading	Before revision	After revision	Reason for revision
				IMP administration) is included in the relevant period will be used.	
		9.2 Adverse Events		The following text was deleted: “In the analysis by time of onset, the event that occurred earlier”	The description was duplicated.

Appendix 1 Criteria for Vital Signs Potential Clinical Significance

Variable	CRITERIA 1	CRITERIA 2
DIASTOLIC BLOOD PRESSURE (mmHg)	DIASTOLIC BLOOD PRESSURE (mmHg) < 50 AND DECREASE > = 15	DIASTOLIC BLOOD PRESSURE (mmHg) > 105 AND INCREASE > = 15
PULSE RATE (beats/min)	PULSE RATE (BPM) < 50 AND DECREASE > = 15	PULSE RATE (BPM) > 120 AND INCREASE > = 15
SYSTOLIC BLOOD PRESSURE (mmHg)	SYSTOLIC BLOOD PRESSURE (mmHg) < 90 AND DECREASE > = 20	SYSTOLIC BLOOD PRESSURE (mmHg) > 180 AND INCREASE > = 20
TEMPERATURE (C)		TEMPERATURE (C) > = 37.8 AND INCREASE > = 1.1C
WEIGHT (kg)	WEIGHT (kg) DECREASE > = 7%	WEIGHT (kg) INCREASE > = 7%

Appendix 2 Criteria for Potential Hy's Law

The potential Hy's Law Cases are defined as subjects with the following criteria: ALT > = 3xULN (OR SCREENING VALUE) OR AST > = 3xULN (OR SCREENING VALUE) AND BILIRUBIN > = 2xULN (OR SCREENING VALUE)

Appendix 3 List of Summary Tables

CT-1	Subject Disposition
CT-2	Reasons for Discontinuation
CT-3	Demographic Characteristics
CT-4.1	Concomitant Medications: Medications Taken Prior to Start of Study Therapy
CT-4.2	Concomitant Medications: Medications Taken During Study Therapy
CT-4.3	Concomitant Medications: Medications Taken After Study Therapy
CT-5.1.1	Analysis of Responder Rate for Overall IGA Score - Overall
CT-5.1.2	Analysis of Responder Rate for Overall IGA Score by Visit - OC
CT-5.1.3	Analysis of Responder Rate for Overall IGA Score by Visit - Cumulative
CT-5.2.1	Analysis of 75% Over Responder Rate for Overall EASI Score - Overall
CT-5.2.2	Analysis of 75% Over Responder Rate for Overall EASI Score by Visit - OC
CT-5.2.3	Analysis of 75% Over Responder Rate for Overall EASI Score by Visit - Cumulative
CT-5.3.1	Analysis of 90% Over Responder Rate for Overall EASI Score - Overall
CT-5.3.2	Analysis of 90% Over Responder Rate for Overall EASI Score by Visit - OC
CT-5.3.3	Analysis of 90% Over Responder Rate for Overall EASI Score by Visit - Cumulative
CT-5.4.1	Analysis of 50% Over Responder Rate for Overall EASI Score - Overall
CT-5.4.2	Analysis of 50% Over Responder Rate for Overall EASI Score by Visit - OC
CT-5.4.3	Analysis of 50% Over Responder Rate for Overall EASI Score by Visit - Cumulative
CT-5.5.1	Analysis of Baseline and Change from Baseline in Overall IGA Score
CT-5.5.2	Shift Tables of Overall IGA Score - OC
CT-5.6.1	Analysis of Baseline and Change from Baseline in Overall EASI Score

CT-5.6.2 Analysis of Baseline and Percent Change from Baseline in Overall EASI Score

CT-5.6.3 Analysis of Baseline and Change from Baseline in Overall EASI Score, Erythema

CT-5.6.4 Analysis of Baseline and Percent Change from Baseline in Overall EASI Score, Erythema

CT-5.6.5 Analysis of Baseline and Change from Baseline in Overall EASI Score, Induration/Papulation

CT-5.6.6 Analysis of Baseline and Percent Change from Baseline in Overall EASI Score, Induration/Papulation

CT-5.6.7 Analysis of Baseline and Change from Baseline in Overall EASI Score, Excoriation

CT-5.6.8 Analysis of Baseline and Percent Change from Baseline in Overall EASI Score, Excoriation

CT-5.6.9 Analysis of Baseline and Change from Baseline in Overall EASI Score, Lichenification

CT-5.6.10 Analysis of Baseline and Percent Change from Baseline in Overall EASI Score, Lichenification

CT-5.6.11 Analysis of Baseline and Change from Baseline in Overall EASI Score, HEAD/NECK

CT-5.6.12 Analysis of Baseline and Percent Change from Baseline in Overall EASI Score, HEAD/NECK

CT-5.6.13 Analysis of Baseline and Change from Baseline in Overall EASI Score, UPPER LIMBS

CT-5.6.14 Analysis of Baseline and Percent Change from Baseline in Overall EASI Score, UPPER LIMBS

CT-5.6.15 Analysis of Baseline and Change from Baseline in Overall EASI Score, TRUNK

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CT-5.6.17 Analysis of Baseline and Change from Baseline in Overall EASI Score, LOWER LIMBS

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CT-5.7.1 Analysis of Baseline and Change from Baseline in POEM Score

CT-5.7.2 Analysis of Baseline and Percent Change from Baseline in POEM Score

CT-5.8 Analysis of Baseline and Change from Baseline in Overall Percentage Affected Body Surface Area

CT-5.9 Analysis of Baseline and Change from Baseline in Serum IgE

CT-5.10 Analysis of Baseline and Change from Baseline in TARC

CT-6.1.1 Subgroup Analysis of Responder Rate for Overall IGA Score - by Age

CT-6.1.2 Subgroup Analysis of Responder Rate for Overall IGA Score - by Sex

CT-6.1.3 Subgroup Analysis of Responder Rate for Overall IGA Score - by IGA Score at Baseline

CT-6.1.4 Subgroup Analysis of Responder Rate for Overall IGA Score - by Severity of Atopic Dermatitis

CT-6.1.5 Subgroup Analysis of Responder Rate for Overall IGA Score - by Total EASI Score at Baseline (<15, 15< =)

CT-6.1.6 Subgroup Analysis of Responder Rate for Overall IGA Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =)

CT-6.1.7 Subgroup Analysis of Responder Rate for Overall IGA Score - by Topical Anti-Inflammatory Agents

CT-6.1.8 Subgroup Analysis of Responder Rate for Overall IGA Score - by Topical Medications Excluding Anti-Inflammatory Agents

CT-6.1.9 Subgroup Analysis of Responder Rate for Overall IGA Score - by Modal Dose

CT-6.2.1 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Age

CT-6.2.2 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Sex

CT-6.2.3 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by IGA Score at Baseline

CT-6.2.4 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Severity of Atopic Dermatitis

CT-6.2.5 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Total EASI Score at Baseline (<15, 15< =)

CT-6.2.6 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =)

CT-6.2.7 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Topical Anti-Inflammatory Agents

CT-6.2.8 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Topical Medications Excluding Anti-Inflammatory Agents

CT-6.2.9 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Modal Dose

CT-6.3.1 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Age

CT-6.3.2 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Sex

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CT-6.3.4 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Severity of Atopic Dermatitis

CT-6.3.5 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Total EASI Score at Baseline (<15, 15< =)

CT-6.3.6 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =)

CT-6.3.7 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Topical Anti-Inflammatory Agents

CT-6.3.8 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Topical Medications Excluding Anti-Inflammatory Agents

CT-6.3.9 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Modal Dose

CT-6.4.1 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Age

CT-6.4.2 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Sex

CT-6.4.3 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by IGA Score at Baseline

CT-6.4.4 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Severity of Atopic Dermatitis

CT-6.4.5 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Total EASI Score at Baseline (<15, 15< =)

CT-6.4.6 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =)

CT-6.4.7 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Topical Anti-Inflammatory Agents

CT-6.4.8 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Topical Medications Excluding Anti-Inflammatory Agents

CT-6.4.9 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Modal Dose

CT-6.5.1 Subgroup Analysis of Responder Rate for Overall IGA Score - by Age and Modal Dose [Pediatric]

CT-6.5.2 Subgroup Analysis of Responder Rate for Overall IGA Score - by Sex and Modal Dose [Pediatric]

CT-6.5.3 Subgroup Analysis of Responder Rate for Overall IGA Score - by IGA Score at Baseline and Modal Dose [Pediatric]

CT-6.5.4 Subgroup Analysis of Responder Rate for Overall IGA Score - by Severity of Atopic Dermatitis and Modal Dose [Pediatric]

CT-6.5.5 Subgroup Analysis of Responder Rate for Overall IGA Score - by Total EASI Score at Baseline (<15, 15< =) and Modal Dose [Pediatric]

CT-6.5.6 Subgroup Analysis of Responder Rate for Overall IGA Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =) and Modal Dose [Pediatric]

CT-6.5.7 Subgroup Analysis of Responder Rate for Overall IGA Score - by Topical Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.5.8 Subgroup Analysis of Responder Rate for Overall IGA Score - by Topical Medications Excluding Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.6.1 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Age and Modal Dose [Pediatric]

CT-6.6.2 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Sex and Modal Dose [Pediatric]

CT-6.6.3 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by IGA Score at Baseline and Modal Dose [Pediatric]

CT-6.6.4 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Severity of Atopic Dermatitis and Modal Dose [Pediatric]

CT-6.6.5 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Total EASI Score at Baseline (<15, 15< =) and Modal Dose [Pediatric]

CT-6.6.6 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =) and Modal Dose [Pediatric]

CT-6.6.7 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Topical Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.6.8 Subgroup Analysis of 75% Over Responder Rate for Overall EASI Score - by Topical Medications Excluding Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.7.1 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Age and Modal Dose [Pediatric]

CT-6.7.2 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Sex and Modal Dose [Pediatric]

CT-6.7.3 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by IGA Score at Baseline and Modal Dose [Pediatric]

CT-6.7.4 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Severity of Atopic Dermatitis and Modal Dose [Pediatric]

CT-6.7.5 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Total EASI Score at Baseline (<15, 15< =) and Modal Dose [Pediatric]

CT-6.7.6 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =) and Modal Dose [Pediatric]

CT-6.7.7 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Topical Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.7.8 Subgroup Analysis of 90% Over Responder Rate for Overall EASI Score - by Topical Medications Excluding Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.8.1 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Age and Modal Dose [Pediatric]

CT-6.8.2 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Sex and Modal Dose [Pediatric]

CT-6.8.3 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by IGA Score at Baseline and Modal Dose [Pediatric]

CT-6.8.4 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Severity of Atopic Dermatitis and Modal Dose [Pediatric]

CT-6.8.5 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Total EASI Score at Baseline (<15, 15< =) and Modal Dose [Pediatric]

CT-6.8.6 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Affected Body Surface Area (<20%, 20%< = - <40%, 40< =) and Modal Dose [Pediatric]

CT-6.8.7 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Topical Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.8.8 Subgroup Analysis of 50% Over Responder Rate for Overall EASI Score - by Topical Medications Excluding Anti-Inflammatory Agents and Modal Dose [Pediatric]

CT-6.9.1 Analysis of Time to Response for Overall IGA Score

CT-6.9.2 Analysis of Time to 75% Over Response Rate for Overall EASI Score

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CT-6.9.4 Analysis of Time to 50% Over Response Rate for Overall EASI Score

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CT-7.3.1 Summary of Reason for Interruption of IMP

CT-7.3.2 Summary of Reason for Use of 1% OPA-15406 ointment

CT-7.4 Summary of Treatment Period

CT-7.5 Summary of Exposure to Trial Medication

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CT-8.1.1.2 Adverse Events (All Causalities) Pediatric (Age: Less Than 7)

CT-8.1.1.3 Adverse Events (All Causalities) Pediatric (Age: Greater Than or Equal to 7)

CT-8.1.1.4 Adverse Events (All Causalities) - Sex: Male

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CT-8.1.1.6 Adverse Events (All Causalities) - With Topical Anti-Inflammatory Agents

CT-8.1.1.7 Adverse Events (All Causalities) - Without Topical Anti-Inflammatory Agents

CT-8.1.1.8 Adverse Events (All Causalities) - With Topical Medications Excluding Anti-Inflammatory Agents

CT-8.1.1.9 Adverse Events (All Causalities) - Without Topical Medications Excluding Anti-Inflammatory Agents

CT-8.1.2.1 Adverse Events According to Application Site (All Causalities)

CT-8.1.2.2 Adverse Events According to Application Site (All Causalities) Pediatric (Age: Less Than 7)

CT-8.1.2.3 Adverse Events According to Application Site (All Causalities) Pediatric (Age: Greater Than or Equal to 7)

CT-8.1.2.4 Adverse Events According to Application Site (All Causalities) - Sex: Male

CT-8.1.2.5 Adverse Events According to Application Site (All Causalities) - Sex: Female

CT-8.1.2.6 Adverse Events According to Application Site (All Causalities) - With Topical Anti-Inflammatory Agents

CT-8.1.2.7 Adverse Events According to Application Site (All Causalities) - Without Topical Anti-Inflammatory Agents

CT-8.1.2.8 Adverse Events According to Application Site (All Causalities) - With Topical Medications Excluding Anti-Inflammatory Agents

CT-8.1.2.9 Adverse Events According to Application Site (All Causalities) - Without Topical Medications Excluding Anti-Inflammatory Agents

CT-8.1.3.1 Adverse Events Occurring on Treatment (All Causalities)

CT-8.1.3.2 Adverse Events Occurring on Treatment (All Causalities) Pediatric (Age: Less Than 7)

CT-8.1.3.3 Adverse Events Occurring on Treatment (All Causalities) Pediatric (Age: Greater Than or Equal to 7)

CT-8.1.4.1 Adverse Events (All Causalities) on Treatment by SOC, PT and Period of Onset

CT-8.1.4.2 Adverse Events (All Causalities) on Treatment by SOC, PT and Period of Onset Pediatric (Age: Less Than 7)

CT-8.1.4.3 Adverse Events (All Causalities) on Treatment by SOC, PT and Period of Onset Pediatric (Age: Greater Than or Equal to 7)

CT-8.1.5.1 Incidence of Treatment-emergent Adverse Events on Treatment by Visit

CT-8.1.5.2 Incidence of Treatment-emergent Adverse Events on Treatment by Visit Pediatric (Age: Less Than 7)

CT-8.1.5.3 Incidence of Treatment-emergent Adverse Events on Treatment by Visit Pediatric (Age: Greater Than or Equal to 7)

CT-8.2.1.1 Incidence of Treatment-emergent Adverse Events by System Organ Class

CT-8.2.1.2 Incidence of Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Less Than 7)

CT-8.2.1.3 Incidence of Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Greater Than or Equal to 7)

CT-8.2.2.1 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term

CT-8.2.2.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.2.2.3 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.2.2.4 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Sex: Male

CT-8.2.2.5 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Sex: Female

CT-8.2.2.6 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term - With Topical Anti-Inflammatory Agents

CT-8.2.2.7 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Without Topical Anti-Inflammatory Agents

CT-8.2.2.8 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term - With Topical Medications Excluding Anti-Inflammatory Agents

CT-8.2.2.9 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Without Topical Medications Excluding Anti-Inflammatory Agents

CT-8.2.3.1 Incidence of Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity

CT-8.2.3.2 Incidence of Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity Pediatric (Age: Less Than 7)

CT-8.2.3.3 Incidence of Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity Pediatric (Age: Greater Than or Equal to 7)

CT-8.2.4.1 Incidence of Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade

CT-8.2.4.2 Incidence of Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Less Than 7)

CT-8.2.4.3 Incidence of Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Greater Than or Equal to 7)

CT-8.3.1.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class

CT-8.3.1.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Less Than 7)

CT-8.3.1.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Greater Than or Equal to 7)

CT-8.3.2.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term

CT-8.3.2.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.3.2.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.3.2.4 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Sex: Male

CT-8.3.2.5 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Sex: Female

CT-8.3.2.6 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term - With Topical Anti-Inflammatory Agents

CT-8.3.2.7 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Without Topical Anti-Inflammatory Agents

CT-8.3.2.8 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term - With Topical Medications Excluding Anti-Inflammatory Agents

CT-8.3.2.9 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term - Without Topical Medications Excluding Anti-Inflammatory Agents

CT-8.3.3.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity

CT-8.3.3.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity Pediatric (Age: Less Than 7)

CT-8.3.3.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity Pediatric (Age: Greater Than or Equal to 7)

CT-8.3.4.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade

CT-8.3.4.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Less Than 7)

CT-8.3.4.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Greater Than or Equal to 7)

CT-8.4.1.1 Incidence of Deaths due to Treatment-emergent Adverse Events by System Organ Class

CT-8.4.1.2 Incidence of Deaths due to Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Less Than 7)

CT-8.4.1.3 Incidence of Deaths due to Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Greater Than or Equal to 7)

CT-8.4.2.1 Incidence of Deaths due to Treatment-emergent Adverse Events by System Organ Class and Preferred Term

CT-8.4.2.2 Incidence of Deaths due to Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.4.2.3 Incidence of Deaths due to Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.5.1.1 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class

CT-8.5.1.2 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Less Than 7)

CT-8.5.1.3 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class Pediatric (Age: Greater Than or Equal to 7)

CT-8.5.2.1 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term

CT-8.5.2.2 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.5.2.3 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.5.3.1 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity

CT-8.5.3.2 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity Pediatric (Age: Less Than 7)

CT-8.5.3.3 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Severity Pediatric (Age: Greater Than or Equal to 7)

CT-8.5.4.1 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade

CT-8.5.4.2 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Less Than 7)

CT-8.5.4.3 Incidence of Serious Treatment-emergent Adverse Events by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Greater Than or Equal to 7)

CT-8.6.1.1 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class

CT-8.6.1.2 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class Pediatric (Age: Less Than 7)

CT-8.6.1.3 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class Pediatric (Age: Greater Than or Equal to 7)

CT-8.6.2.1 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class and Preferred Term

CT-8.6.2.2 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.6.2.3 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.6.3.1 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class, Preferred Term and Severity

CT-8.6.3.2 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class, Preferred Term and Severity Pediatric (Age: Less Than 7)

CT-8.6.3.3 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class, Preferred Term and Severity Pediatric (Age: Greater Than or Equal to 7)

CT-8.6.4.1 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class, Preferred Term and CTCAE Grade

CT-8.6.4.2 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Less Than 7)

CT-8.6.4.3 Incidence of Treatment-emergent Adverse Events Resulting in Discontinuation from Study by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Greater Than or Equal to 7)

CT-8.7.1.1 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class

CT-8.7.1.2 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class Pediatric (Age: Less Than 7)

CT-8.7.1.3 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class Pediatric (Age: Greater Than or Equal to 7)

CT-8.7.2.1 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class and Preferred Term

CT-8.7.2.2 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.7.2.3 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.7.3.1 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class, Preferred Term and Severity

CT-8.7.3.2 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class, Preferred Term and Severity Pediatric (Age: Less Than 7)

CT-8.7.3.3 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class, Preferred Term and Severity Pediatric (Age: Greater Than or Equal to 7)

CT-8.7.4.1 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class, Preferred Term and CTCAE Grade

CT-8.7.4.2 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Less Than 7)

CT-8.7.4.3 Incidence of Treatment-emergent Adverse Events Resulting in Reduction of IMP by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Greater Than or Equal to 7)

CT-8.8.1.1 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class

CT-8.8.1.2 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class Pediatric (Age: Less Than 7)

CT-8.8.1.3 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class Pediatric (Age: Greater Than or Equal to 7)

CT-8.8.2.1 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class and Preferred Term

CT-8.8.2.2 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.8.2.3 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.8.3.1 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class, Preferred Term and Severity

CT-8.8.3.2 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class, Preferred Term and Severity Pediatric (Age: Less Than 7)

CT-8.8.3.3 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class, Preferred Term and Severity Pediatric (Age: Greater Than or Equal to 7)

CT-8.8.4.1 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class, Preferred Term and CTCAE Grade

CT-8.8.4.2 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Less Than 7)

CT-8.8.4.3 Incidence of Treatment-emergent Adverse Events Resulting in Interruption of IMP by System Organ Class, Preferred Term and CTCAE Grade Pediatric (Age: Greater Than or Equal to 7)

CT-8.9.1.1 Incidence of Treatment-emergent Adverse Events Greater Than or Equal to 5% in Any Group by System Organ Class and Preferred Term

CT-8.9.1.2 Incidence of Treatment-emergent Adverse Events Greater Than or Equal to 5% in Any Group by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.9.1.3 Incidence of Treatment-emergent Adverse Events Greater Than or Equal to 5% in Any Group by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.9.2.1 Incidence of Non-Serious Treatment-emergent Adverse Events Greater Than or Equal to 5% in Any Group by System Organ Class and Preferred Term

CT-8.9.2.2 Incidence of Non-Serious Treatment-emergent Adverse Events Greater Than or Equal to 5% in Any Group by System Organ Class and Preferred Term Pediatric (Age: Less Than 7)

CT-8.9.2.3 Incidence of Non-Serious Treatment-emergent Adverse Events Greater Than or Equal to 5% in Any Group by System Organ Class and Preferred Term Pediatric (Age: Greater Than or Equal to 7)

CT-8.9.3.1. Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term According to Application Site

CT-8.9.3.2 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term According to Application Site Pediatric (Age: Less Than 7)

CT-8.9.3.3 Incidence of Treatment-emergent Adverse Events by System Organ Class and Preferred Term According to Application Site Pediatric (Age: Greater Than or Equal to 7)

CT-8.9.4.1 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term According to Application Site

CT-8.9.4.2 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term According to Application Site Pediatric (Age: Less Than 7)

CT-8.9.4.3 Incidence of Potentially Drug-related Treatment-emergent Adverse Events by System Organ Class and Preferred Term According to Application Site Pediatric (Age: Greater Than or Equal to 7)

CT-9.1 Listing of Deaths

CT-9.2 Listing of Serious Adverse Events

CT-9.3 Listing of Study Drug Discontinuations Due to Adverse Events

CT-9.4 Incidence of Potential Hy's Law Cases

CT-9.5 Listing of Potential Hy's Law Cases - by Subject

CT-10.1.1 Mean Change From Baseline in Laboratory Test Values: Serum Chemistry

CT-10.1.2 Mean Change From Baseline in Laboratory Test Values: Hematology

CT-10.2.1 Shift Tables of Clinical Laboratory Test Results: Serum Chemistry

CT-10.2.2 Shift Tables of Clinical Laboratory Test Results: Hematology

CT-10.2.3 Shift Tables of Clinical Laboratory Test Results: Urinalysis

CT-11.1 Mean Change From Baseline in Vital Sign Parameters

CT-11.2 Listing of Vital Signs Abnormalities

CT-11.3 Incidence of Potential Clinical Significance in Vital Signs

CT-11.4 Criteria for Vital Signs Potential Clinical Significance

CF-1.1 Incidence of Responder Rate for Overall IGA Score - Overall

CF-1.2.1 Incidence of Responder Rate for Overall IGA Score by Visit - Cumulative

CF-1.2.2 Incidence of Responder Rate for Overall IGA Score by Visit - Cumulative (Pediatric)

CF-1.3.1 Kaplan-Meier Plot of Time to Response for Overall IGA Score

CF-1.3.2 Kaplan-Meier Plot of Time to Response for Overall IGA Score (Pediatric)

CF-2.1 Incidence of 75% Over Response Rate for Overall EASI Score - Overall

CF-2.2.1 Incidence of 75% Over Response Rate for Overall EASI Score by Visit - Cumulative

CF-2.2.2 Incidence of 75% Over Response Rate for Overall EASI Score by Visit - Cumulative (Pediatric)

CF-2.3.1 Kaplan-Meier Plot of Time to 75% Over Response Rate for Overall EASI Score

CF-2.3.2 Kaplan-Meier Plot of Time to 75% Over Response Rate for Overall EASI Score (Pediatric)

CF-3.1 Incidence of 90% Over Response Rate for Overall EASI Score - Overall

CF-3.2.1 Incidence of 90% Over Response Rate for Overall EASI Score by Visit - Cumulative

CF-3.2.2 Incidence of 90% Over Response Rate for Overall EASI Score by Visit - Cumulative (Pediatric)

CF-3.3.1 Kaplan-Meier Plot of Time to 90% Over Response Rate for Overall EASI Score

CF-3.3.2 Kaplan-Meier Plot of Time to 90% Over Response Rate for Overall EASI Score (Pediatric)

CF-4.1 Incidence of 50% Over Response Rate for Overall EASI Score - Overall

CF-4.2.1 Incidence of 50% Over Response Rate for Overall EASI Score by Visit - Cumulative

CF-4.2.2 Incidence of 50% Over Response Rate for Overall EASI Score by Visit - Cumulative (Pediatric)

CF-4.3.1 Kaplan-Meier Plot of Time to 50% Over Response Rate for Overall EASI Score

CF-4.3.2 Kaplan-Meier Plot of Time to 50% Over Response Rate for Overall EASI Score (Pediatric)

CF-5.1 Means of Change from Baseline in Overall IGA Score by Visit

CF-5.2 Means of Change from Baseline in Overall IGA Score by Visit (Pediatric)

CF-6.1 Means of Change from Baseline in Overall EASI Score by Visit

CF-6.2 Means of Change from Baseline in Overall EASI Score by Visit (Pediatric)

Appendix 4 List of Subject Data Listings

PDATA-1.1 Inclusion and Exclusion Criteria Not Met

PDATA-1.2 Subject Disposition

PDATA-2.1 Medical History

PDATA-2.2 History of Atopic Dermatitis

PDATA-3.1 Concomitant Medications: Medications Taken Prior to Start of Study Therapy

PDATA-3.2 Concomitant Medications: Medications Taken During Study Therapy

PDATA-3.3 Concomitant Medications: Medications Taken After Study Therapy

PDATA-4.1 Exposure to Trial Medication

PDATA-4.2 Listing of Trial Medication by Subject

PDATA-5.1 Physical Examination

PDATA-6 Adverse Events

PDATA-7 Vital Signs

PDATA-8 Screening Failures

PDATA-9 Protocol Deviations (Major) - CRF

PDATA-10 Eczema Area and Severity Index

PDATA-11 Overall Investigator's Global Assessment of Disease Severity

PDATA-12 Patient-Oriented Eczema Measure

PDATA-13 Affected Body Surface Area

PDATA-14 Treatment Area

PDATA-15 Patch Application and Removal

PDATA-16 Reason for Use of 1% OPA-15406 ointment and Treatment Interruption

DREAS-1 Discontinued Subjects and Reasons for Discontinuations

DEMOG-1 Demographic Characteristics

DEMOG-2 Informed Consent

AE-1 Adverse Events

SMED-1 Actual Exposure to Study Medication

SMED-2 Investigational Medicinal Product Compliance for Number of Administrations

EFF-1 Change from Baseline in IGA Score and Response with Overall IGA Score

EFF-2 Change from Baseline in Total EASI Score

EFF-3 Change from Baseline in EASI Score, Erythema

EFF-4 Change from Baseline in EASI Score, Induration/Papulation

EFF-5 Change from Baseline in EASI Score, Excoriation

EFF-6 Change from Baseline in EASI Score, Lichenification

EFF-7 Change from Baseline in EASI Score, HEAD/NECK

EFF-8 Change from Baseline in EASI Score, UPPER LIMBS

EFF-9 Change from Baseline in EASI Score, TRUNK

EFF-10 Change from Baseline in EASI Score, LOWER LIMBS

EFF-11 Change from Baseline in Overall Percentage Affected Body Surface Area

EFF-12 Change from Baseline in POEM Score

EFF-13 Change from Baseline in Serum IgE

EFF-14 Change from Baseline in TARC

LAB-1 Laboratory Test Results: Serum Chemistry

LAB-2 Laboratory Test Results: Hematology

LAB-3 Laboratory Test Results: Urinalysis

LAB-4 Laboratory Test Results: Immunohematology

PDEV-1 Summary of Subjects with Major Protocol Deviations by Type of Deviation

SUBEX-1 Subjects Excluded From Analysis Set