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Statistical Analysis Plan for Interventional Studies

Sponsor Name: Galderma Research & Development, LLC

Protocol Number: RD.06.SPR.118295

Protocol Title: A Multi-Center Study to Evaluate Subject Reported Outcomes with use of Trifarotene 50 µg/g Cream in the Treatment of Moderate Facial and Truncal Acne Vulgaris

Clinical Trial Phase: IIIb

Protocol Version and Date: 2.0 (4-Jun-2019)

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Authors: PPD

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Revision History

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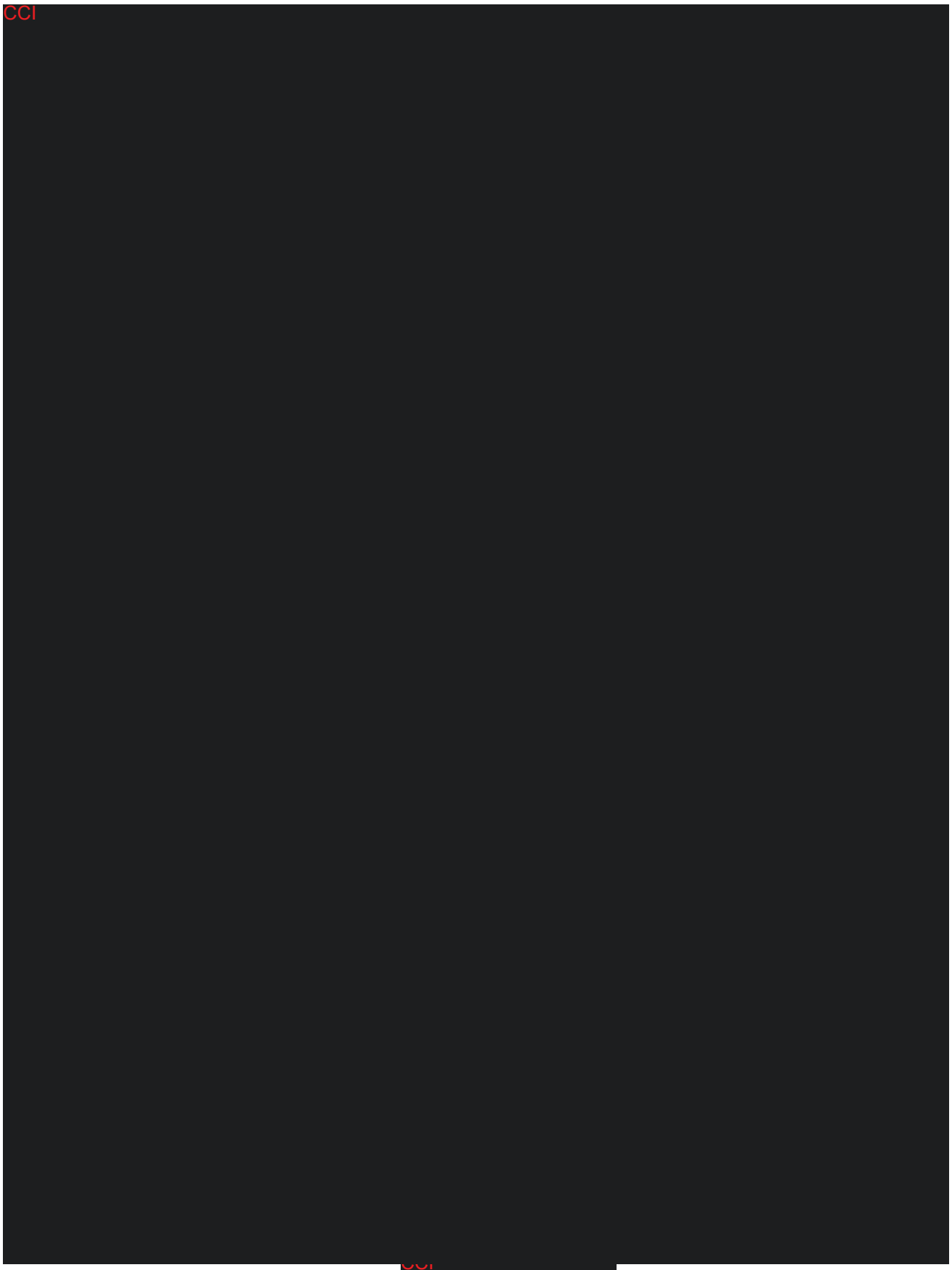
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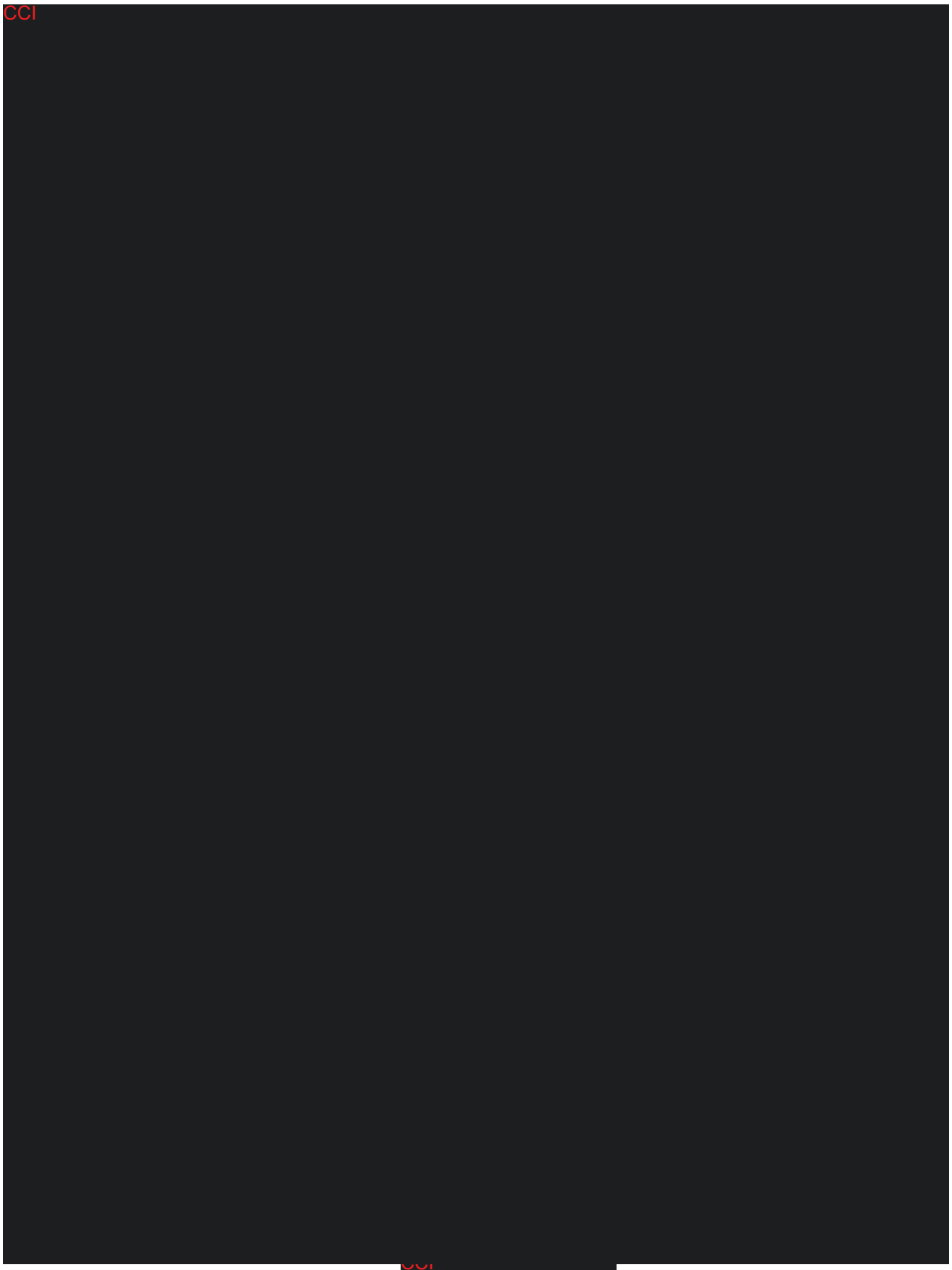
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Table of Contents

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1. Glossary of Abbreviations

Abbreviation	Description
AE	Adverse event
AESI	Adverse event of special interest
ATC	Anatomical Therapeutic Chemical
cDLQI	Children's Dermatology Life Quality Index
CI	Confidence interval
CRF	Case report form
CRO	Contract research organization
CSR	Clinical study report
DLQI	Dermatology Life Quality Index
FSI	First subject in
ICF	Informed Consent Form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IGA	Investigator's Global Assessment
ITT	Intent-to-treat
ITTT	Intent-to-Treat on the trunk
IUD	Intra uterine device
LOCF	Last observation carried forward
LSO	Last subject out
MAF	Missing as failure
MedDRA	Medical Dictionary for Regulatory Activities
n	Number of subjects with an observation
N	Number of subjects in the dataset or population
OC	Observed cases
PGA	Physician Global assessment
PRO	Patient reported outcomes
PT	preferred term
QoL	Quality of Life
SAE	Serious adverse event
SAF	Safety
SAFT	Safety on the trunk
SAP	Statistical Analysis Plan
SD	Standard deviation
SOC	System organ class
SOP	Standard operating procedure
TEAE	Treatment-emergent adverse event
TFLs	Tables, figures and listings
UPT	Urine pregnancy test
UV	Ultraviolet
WHO	World Health Organization

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2. Purpose

The purpose of this statistical analysis plan (SAP) is to ensure that the data listings, summary tables and figures which will be produced, and the statistical methodologies that will be used, are complete and appropriate to allow valid conclusions regarding the study objectives. The planned analyses identified in this SAP will be included in regulatory submissions, medical communications, scientific publication/posters and for promotional material use.CCI

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2.1. Responsibilities

CCI will perform the statistical analyses and are responsible for the production and quality control of all tables, figures and listings (TFLs) outlined in this document.

2.2. Timings of Analyses

The primary analysis of safety and efficacy is planned after all enrolled subjects complete the final study visit or terminate early from the study.

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3. Study Objectives

The objective of the study is to evaluate subject reported outcomes with Trifarotene cream.

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3.1. Brief Description

This clinical trial is designed to evaluate the patient-reported outcomes (PRO) with use of Trifarotene in subjects with moderate facial and truncal acne vulgaris and also to assess the impact of such treatment instructions on overall efficacy, subject satisfaction, and safety.

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3.2. Subject Selection

At least 40 subjects meeting the eligibility requirements are expected to complete participation in the clinical trial across all sites.

3.2.1. Inclusion Criteria

To be eligible for study entry subjects must satisfy all of the following criteria:

1. The subject is a male or female, 9 years of age and older, at Screening visit.
2. Subject with clinical diagnosis of acne vulgaris, CCI [redacted]

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CCI [redacted]

5. The subject is a female of non-childbearing potential (pre-menarcheal or postmenopausal [absence of menstrual bleeding for 1 year prior to Screening, without any other medical reason], hysterectomy or bilateral oophorectomy).
6. The subject is a female of childbearing potential:
   6.1. With a negative urine pregnancy test (UPT) at Screening and Baseline visits,
   6.2. Who are willing to take UPTs throughout the course of the study.
   6.3. Who has been strictly abstinent for 1 month prior to Screening/Baseline and agrees to continue for the duration of the clinical trial and at least 1 month after the last study drug application, OR

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Who agrees to use an effective and approved contraceptive method(s) for the duration of the study and at least 1 month after the last study drug application. An effective method of contraception is defined as:

6.3.a. bilateral tubal ligation;

6.3.b. approved combined oral contraceptives (estrogens and progesterone), implanted or injectable contraceptives, or hormonal contraceptive vaginal rings with a stable dose for at least 1 month prior to the Screening/Baseline visit;

6.3.c. hormonal intra uterine device (IUD) inserted at least 1 month prior to the Screening/Baseline visit;

6.3.d. vasectomized partner for at least 3 months prior to the Screening/Baseline visit.

7. If a female of childbearing potential uses combined oral contraceptives approved as acne treatments (e.g., Ortho Tri-Cyclen®, Yaz®, Diane-35®), the dose should be stable for at least 6 months prior to the Screening/Baseline visit.
8. For a pre-menstrual female who begins menses during the study:
   8.1. Agrees to be strictly abstinent for the duration of the clinical trial and at least 1 month after the last study drug application,
   OR
   8.2. Agrees to use an effective and approved contraceptive method(s) for the duration of the study and at least 1 month after the last study drug application and agrees to undergo pregnancy tests. An effective method of contraception is defined as approved combined oral contraceptives (oestrogens and progesterone), implanted or injectable contraceptives, or hormonal intra-uterine device (IUD) or hormonal contraceptive vaginal rings.

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10. The subject agrees to participate in the study, verified by dating and signing an approved written Informed Consent Form (ICF) or for subjects under age of majority, an assent form signed by the subject (if required) in conjunction with an ICF signed by the parent(s)/legal representative at the Screening visit before any study procedures.

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12. Apprised of HIPAA (Health Insurance Portability and Accountability Act) and is willing to share personal information and data, as verified by signing a written authorization at the Screening/Baseline visit.

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For subjects under the age of 18:

15. Having a parent or legal guardian who is 18 years of age or older and presents proof of guardianship (eg, insurance card, certificate of residence, or copy of officially issued family registration) at screening/baseline visit.

3.2.2. Exclusion Criteria

Subjects will be excluded from the study if one or more of the following criterion are applicable:

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1. Subject with severe acne (IGA or PGA > 3).
2. The subjects has severe forms of acne (eg, acne conglobate, acne fulminans) or secondary form (eg. Chloracne, drug-induced acne, etc).
3. The subject has any acne cyst on the face at Screening and Baseline.
4. The subject has any acne cysts on the trunk at Screening and Baseline.

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3.3. Determination of Sample Size

The sample size is not based on any formal hypothesis testing. CCI

3.4. Treatment Assignment

This is an open label single arm study. All eligible subjects will be assigned to the study drug at Baseline.

3.5. Administration of Study Medication

Each subject will receive both oral and written instructions for the proper dosing and study treatment application techniques. Applications will be done by the subjects themselves at home in the evening.

The study drug will be applied to the facial (forehead, nose, chin and each cheek) and the truncal CCI. The daily drug administration diary is to be completed by the subject (if needed, with the help of the legal guardian) and returned to the site at each study visit.

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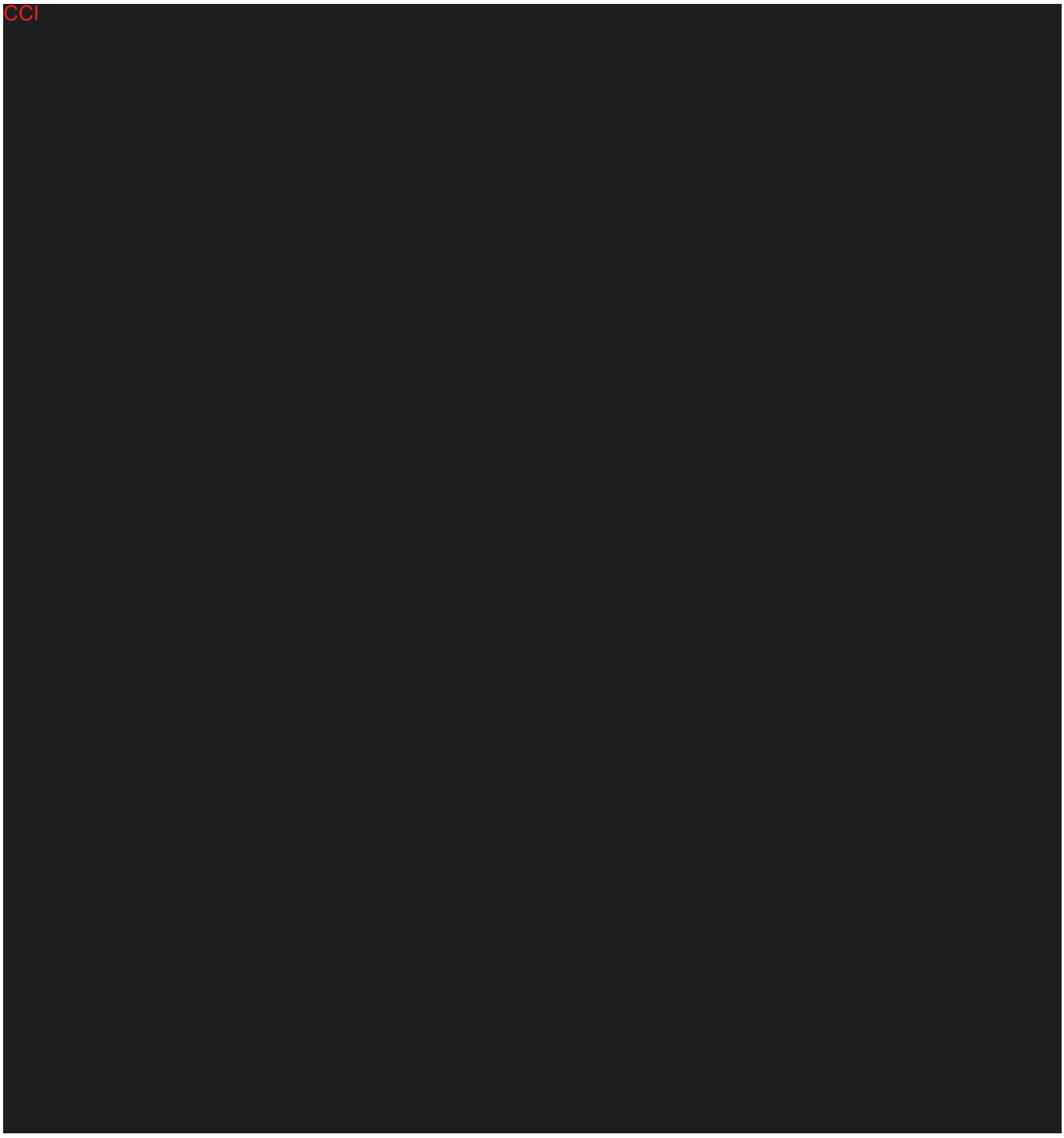
3.6. Study Procedures

The study procedures are described in Table 1.

Table 1: Schedule of Assessments



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4. Endpoints

4.1. Efficacy Endpoints

- Facial Success Rate at Week 12 and at Week 24, defined as the percentage of subjects who achieve an IGA score of 1 (Almost Clear) or 0 (Clear) AND at least a 2-grade improvement from Baseline to Week 12 and Week 24 respectively.
- CCI [redacted].
- CCI [redacted].
- Truncal Success Rate at Week 12 and at Week 24, defined as the percentage of subjects who achieve a PGA score of 1 (Almost Clear) or 0 (Clear) AND at least a 2-grade improvement from Baseline to Week 12 and Week 24 respectively.
- CCI [redacted]
- CCI [redacted]
- Percent change in facial non-inflammatory lesion counts from Baseline to week 12 and week 24.
- Percent change in facial inflammatory lesion counts from Baseline to week 12 and week 24.
- Percent change in truncal non-inflammatory lesion counts from Baseline to week 12 and week 24.
- Percent change in truncal inflammatory lesion counts from Baseline to week 12 and Week 24.

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4.3. Safety Endpoints

- Local tolerability parameters (erythema, scaling, dryness and stinging/burning) will be evaluated at each visit on a 4-point scale rangingfrom 0 (none) to 3 (severe). The assessments to be conducted separately for the face and trunk. CCI [redacted].
- Adverse Events which includes AEs, SAE, AESI and Death.

4.4. Quality of Life Questionnaires

The quality of life questionnaires endpoint consists of the following subject-reported outcomes:

- Dermatology Life Questionnaire Index (DLQI) comparing Baseline to Weeks 12 and 24 or Early termination.
- Children Dermatology Life Questionnaire Index (cDLQI) comparing Baseline to Weeks 12 and 24 or Early termination.
- CompAQ (for ≥16 years age) comparing Baseline to Weeks 12 and 24 or Early termination.
- EQ-5D-5L comparing Baseline to Weeks 12 and 24 or Early termination.
- Subject satisfaction questionnaire at Week 12 and 24 or Early termination.

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4.5. Other Assessments

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5. Analysis Populations

5.1. Intent-to-Treat population

CCI The ITT population will be used for all analyses of efficacy endpoints CCI

5.2. CCI

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5.3. CCI

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5.4. CCI

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5.5. Protocol Deviations

Protocol deviations will be captured by the clinical monitoring team on an ongoing basis throughout the study and recorded in the CRF. These deviations will be discussed in a case by case basis, classified CCI

All protocol deviations CCI will be identified, evaluated, and resolved (if applicable) before the respective database lock (interim or final analysis).

All protocol deviations will be summarized by classification CCI and category. Protocol deviations will be tabulated and listed.

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6. General Aspects for Statistical Analysis

6.1. General Methods

This section describes analytical analysis issues that relate to all or some of the analytic analysis sections that follow. It describes general guidelines for analysis as well as the following items:

- SAS version 9.4 or higher will be used.
- CCI will be responsible for reporting the demographic, safety, and efficacy.
- ITT population will be used for data listings (if not differently stated).
- Unless otherwise specified, summaries will be presented by time points CCI
- For summaries tables foreseen at "Week 24/ET" the label "Week 24/ET" to be presented, however for individual data listings only “Week 24" or "ET" - according to the visit that actually occurred - to be presented.
- The total number of subjects (N) will be used as the denominator for percentage calculations, unless stated otherwise in the table shell.
- Continuous variables will be summarized using the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized using number of observations (n), frequency and percentages of subjects.
- In general, the listings will be sorted by subject number, and assessment date (and time) if applicable.
- Multiple assessments at a given time point (repeat, and unscheduled) will not be included in summary tables unless specified otherwise, but will be included in the listings. For example if there are multiple laboratory results at a given visit, the latest non-missing value within the visit window will be used.

6.2. Key Definitions

The date of first treatment is defined as the date of first application of Trifarotene cream 50 µg/g.

The date of last treatment is defined as the date of last application of Trifarotene cream 50 µg/g.

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A subject’s date of last participation in the trial is the last date of contact. Date of completion/withdrawal is recorded as the date of completion/withdrawal on the exit form of the CRF.

Baseline is defined as the last measurement prior to or on the date of first treatment or as the screening/baseline measurement in case of no treatment.

6.3. Imputation of Missing Data

The last observation carried forward (LOCF) will be used to impute efficacy endpoints, where applicable. If no post-baseline observations are available, baseline observation will be carried forward.

Non-responder analysis will also be carried out for binary endpoints by imputing missing data using the missing as failure (MAF) method.

No imputations will be performed for safety analyses.

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6.4. Pooling of Centers

No pooling of centers is planned.

6.5. Subgroups

Subgroup analyses were deemed not appropriate and thus no subgroup analysis will be performed, neither for efficacy endpoints nor for safety endpoints.

6.6. Analysis Visit Window

Efficacy by-visit summaries will use the analysis visit. CCI

Early termination visit will be managed as a stand-alone visit. CCI

Safety data will not be windowed for by-visit summary. i.e., scheduled visit data will be used for analysis and the assessments of early termination visit will be summarized together with the assessments of Week 24.

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7. Demographic, Other Baseline Characteristics and Medication

7.1. Subject Disposition and Withdrawals

All subjects who provide informed consent will be accounted in this study.

Subject disposition will be summarized overall and by site for the ITT, CCI [redacted] population.

The treatment and study discontinuation along with the reasons for discontinuation as recorded in the CRF, and the study day of discontinuation will be listed.

The disposition summary tables will include the number of screened subjects and the number and percentage of screen failure subjects and the reason for screen failure, enrolled subjects, subjects in each of the analysis populations, completed/discontinued subjects and the reason for study discontinuation.

Subject attendance will be summarized by scheduled visit CCI [redacted]

7.2. Demographic and Other Baseline Characteristics

Age (years) at screening, baseline face inflammatory lesions CCI [redacted] baseline face non-inflammatory lesions CCI [redacted] baseline IGA, baseline trunk inflammatory lesions CCI [redacted] baseline PGA and baseline trunk non-inflammatory lesions CCI [redacted] will be summarized using summary statistics for continuous variables.

Sex, ethnicity, race, Fitzpatrick skin type (classified as 'Type I-II-III' and 'Type IV-V-VI') and age categories (<18 years old, sub-classified as 9-11 years old and 12-17 years old, and ≥ 18 years old; ≤16 years old and >16 years old; <16 years old and ≥16 years old) will be summarized using the summary statistics for categorical variables. CCI [redacted]

All demographic data will be listed.

7.3. Medical History

Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA, Version 21.1).

Medical History as recorded at screening will be summarized using the number and percent of subjects reporting each system organ class (SOC) and preferred term (PT) and sorted by descending overall total of SOC and PT. Summary tables will be presented for ITT.

Medical history data listings will be sorted by subject number, onset date, end date, SOC, and PT.

7.4. Medical and Surgical Procedures

Medical and surgical procedures will be classified and presented as follows:

- Prior medical and surgical procedures: CCI [redacted]
- Concomitant medical and surgical procedures: CCI [redacted]

If the start date and/or stop date and 'ongoing' are missing then the medical and surgical procedure will be considered CCI [redacted].

Medical and surgical procedures be coded using MedDRA, Version 21.1.

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CCI [redacted]

Medical and surgical procedures (prior and concomitant) will be summarized using the number and percent of subjects reporting each SOC and PT and sorted by descending overall total of SOC and PT. Summary tables will be presented for ITT population.

Medical and surgical procedures listings will be sorted by subject number, onset date, end date, SOC, and PT.

7.5. Medications

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All medications will be listed.

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8. Efficacy

All efficacy assessments will be summarized by visit using descriptive statistics. A two-sided 95% Clopper-Pearson confidence interval (CI) for success rate and a two-sided 95% Student's t-distribution CI for mean values will be included in the efficacy summary tables, if applicable.

Efficacy analyses will be performed with the observed cases (OC) and with last observation carried forward (LOCF) for data imputation for Investigator's Global Assessment (IGA), Physician's Global Assessment (PGA) and acne lesions counts on the face and trunk. Non-responder analysis will also be carried out for binary endpoints by with missing as failure (MAF) for data imputation.

8.1. Efficacy Endpoints and Analysis

8.1.1. CCI

The Investigator's Global Assessment (IGA) is an instrument to evaluate the facial acne severity CCI IGA will be recorded in the CRF CCI using a 5-point scale, as described in Table 3.

Table 3: Scale for acne assessment

0	Clear	Clear skin with no inflammatory or non-inflammatory lesions.
1	Almost Clear	A few scattered comedones and a few small papules.
2	Mild	Easily recognizable; less than half the surface is involved. Some comedones and some papules and pustules.
3	Moderate	More than half of the surface is involved. Many comedones, papules and pustules. One nodule may be present.
4	Severe	Entire surface is involved. Covered with comedones, numerous papules and pustules. Few nodules may be present.

IGA will be summarized by visit CCI as categorical variables. All IGA data will be listed.

IGA treatment success is defined as 0 (clear) or 1 (almost clear) and at least a 2-grade improvement from baseline. The IGA treatment success rate will be will be summarized by visit CCI

Analyses will be performed with LOCF and MAF for data imputation and with the observed cases (OC).

For the LOCF analysis, the imputation will be performed based on the recorded IGA per visit, and the imputed IGA treatment success rate will be based on the imputed values. For the MAF analysis, non-evaluable subjects will be considered as IGA treatment failures. For both LOCF and MAF analyses, the IGA treatment success rate will be calculated as the ratio between the number of subjects achieving IGA treatment success CCI and the number of subjects included in the ITT population.

For the OC analysis, the IGA treatment success rate will be calculated as the ratio between the number of subjects achieving IGA treatment success CCI and the number of subjects evaluable at each visit (i.e. the ones with data available at that visit).

IGA treatment success rate (LOCF) will be presented using line plots over time.

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8.1.2. Physician's Global Assessment of truncal acne

The Physician's Global Assessment (PGA) is an instrument to evaluate the truncal acne severity CCI [redacted] PGA will be recorded in the CRF and assessed CCI [redacted] using the 5-point scale as described in Table 3.

PGA will be summarized by visit CCI [redacted] as categorical variables. All PGA data will be listed.

PGA treatment success is defined as 0 (clear) or 1 (almost clear) and at least a 2-grade improvement from baseline. The PGA treatment success rate will be will be summarized by visit CCI [redacted]

Analyses will be performed with LOCF and MAF for data imputation and with the observed cases (OC).

For the LOCF analysis, the imputation will be performed based on the recorded PGA per visit, and the imputed PGA treatment success rate will be based on the imputed values. For the MAF analysis, non-evaluable subjects will be considered as PGA treatment failures. For both LOCF and MAF analyses, the PGA treatment success rate will be calculated as the ratio between the number of subjects achieving PGA treatment success CCI [redacted] and the number of subjects included in the ITTT population.

For the OC analysis, the PGA treatment success rate will be calculated as the ratio between the number of subjects achieving PGA treatment success CCI [redacted] and the number of subjects evaluable at each visit (i.e. the ones with data available at that visit).

PGA treatment success rate (LOCF) will be presented using line plots over time.

8.1.3. Acne lesions counts on the face and trunk

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8.2. Subject Reported Efficacy Assessments

8.2.1. Dermatology Life Quality Index (DLQI):

DLQI is a validated 10-item questionnaire for subjects aged > 16 years, covering domains including symptoms/feelings, daily activities, leisure, work/school, personal relationships and treatment. DLQI data will be recorded in the CRF.

The total DLQI score is calculated by summing the scores of each question, resulting in a maximum of 30 and a minimum of 0. A lower score on the DLQI indicates increased QOL; therefore, negative changes

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from Baseline indicate improvement. The DLQI total scores (which measure the impact of skin disease on the quality of life of an affected person) can be interpreted as: no effect (0-1), small effect (2-5), moderate effect (6-10), very large effect (11-20), or extremely large effect (21-30).

DLQI will be summarized by visit (Baseline, Week 12 and Week 24/ET) and as continuous variables. Absolute change from baseline will also be included in the descriptive analysis. All DLQI data will be listed.

8.2.2. Children's Dermatology Life Quality Index (cDLQI):

cDLQI is a comparable validated 10-item questionnaire designed for pediatric subjects aged 16 years or less. cDLQI will be reported at Baseline, Week 12 and Week 24/ET.

The total cDLQI score is calculated by summing the scores of each question, resulting in a maximum of 30 and a minimum of 0. A lower score on the cDLQI indicates increased QOL; therefore, negative changes from Baseline indicate improvement. The cDLQI total scores (which measure the impact of skin disease on the quality of life of an affected person) can be interpreted as: no effect (0-1), small effect (2-6), moderate effect (7-12), very large effect (13-18),or extremely large effect (19-30).

cDLQI will be summarized by visit (Baseline, Week 12 and Week 24/ET) as continuous variables. Absolute change from baseline will also be included in the descriptive analysis. All cDLQI data will be listed.

8.2.3. CompAQ for Facial and Truncal Acne

Subjects (16 years of age and older) are provided with the comprehensive QoL measure inclusive of facial and truncal form and instructed to read and answer all 20 quality of life questions. The questionnaire measures the impact of facial and torso acne on health-related quality of life.

The 20 questions consist of 5 domains that assess a variety of psychosocial and physical impacts of acne: Psychological/Emotional, Social (Judgement from Others), Social Interactions, Treatment Concerns, Physical Symptoms. The higher the score, the more quality of life is impaired. Each question is assessed with a numeric score between 0 (Never) and 8 (All the time).

Higher scores indicate greater adverse impact.

- The response range for each question is from 0–8 with higher numbers indicating greater adverse impact.
- For each domain, response range is from 0–32.
- For the long form questionnaire, response range is from 0–160
- For the short form questionnaire, response range is from 0–40

A final question will also assess the change in overall QoL since baseline with a numeric score between -7 (a great deal worse) and 7 (a great deal better), with 0 denoting no change in QoL.

CompAQ for Facial and Truncal Acne will be summarized by visit (Baseline, Week 12 and Week 24/ET) as continuous variables. Absolute change from baseline will also be included in the descriptive analysis. All CompAQ for Facial and Truncal Acne data will be listed.

8.2.4. EuroQoL 5-Dimension (EQ-5D-5L)

At Baseline, Week 12 and Week 24/ET, subject will complete the EQ-5D-5L questionnaire for the assessment of the general health state, which contains two parts: a descriptive system and a VAS.

The descriptive system is made up of five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The VAS consists of a vertical line where the subject can assess his or her own

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health status with a numerical value between 100 (Best imaginable health state) and 0 (Worst imaginable health state).

Each of the 5 dimensions comprising the EQ-5D descriptive system is divided into 5 levels of perceived problems:

- Level 1: indicating no problem.
- Level 2: indicating slight problems.
- Level 3: indicating moderate problems.
- Level 4: indicating severe problems.
- Level 5: indicating extreme problems.

A unique Health State is defined by combining 1 level from each of the 5 dimensions.

A total of 3125 possible Health States is defined in this way. Each state is referred to in terms of a 5 digit code. For example, state 11111 indicates no problems on any of the 5 dimensions, while state 12345 indicates no problems with mobility, slight problems withwashing or dressing, moderate problems with doingusual activities, severe pain or discomfort and extreme anxiety or depression.

EQ-5D-5L Health States, defined by the EQ-5D-5L descriptive system, have to be converted into EQ-5D-5L Index Scores using country specific value sets.

For the US, the EQ-5D-5L Index Score ranges from -0.109 (corresponding to the Health State 55555) to 1.000 (corresponding to the Health State 11111).

EQ-5D-5L Index Score and VAS will be summarized by visit (Baseline, Week 12 and Week 24/ET) as continuous variables. Absolute change from baseline will also be included in the descriptive analysis.

EuroQoL 5-Dimension health profiles (i.e. the levels for mobility, self-care, usual activities, pain/discomfort and anxiety/depression) will be summarized by visit (Baseline, Week 12 and Week 24/ET) using frequency tables.

EuroQoL 5-Dimension levels, index score and VAS will be listed.

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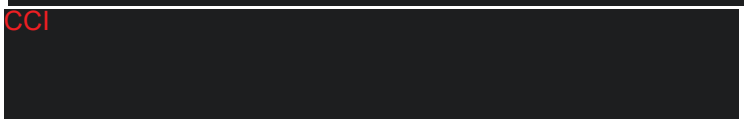

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9. Analysis Of Pharmacokinetics

Not applicable in this study.

10. Analysis Of Pharmacodynamics

Not applicable in this study.

11. Safety

The population used for safety analyses will be the SAF. All data for all safety assessments will be presented in data listings.

11.1. Extent of Exposure and Study Duration

The extent of exposure and the number of subjects exposed to study drug will be summarized.

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11.2. Missing Applications and Dose Reductions

The occurrence of missed applications since last scheduled visit, the occurrence of prescribed dose reductions and the reasons for dose reduction since last scheduled visit will be summarized separately for Face and Trunk by visit CCI using the summary statistics for categorical variables.

The number of missed application since last scheduled visit and the number of missed application since last scheduled visit due to dose reductions will be summarized separately for Face and Trunk by visit CCI using summary statistics for continuous variables.

11.3. Treatment Compliance

Treatment compliance will be calculated as the ratio (expressed as percentage) between the number of actual applications and the number of expected applications.

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11.4. Adverse Events

Adverse events (AEs) will be coded using MedDRA Version 21.1. Summaries of AEs will include only treatment-emergent AEs (TEAEs) defined as AEs with an onset date on or after the date of first treatment. AEs with missing onset dates will be considered as TEAEs.

TEAEs will be summarized using the number and percent of subjects reporting each SOC and PT and sorted by descending overall total of SOC and PT. Subjects who experienced multiple events within the

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same SOC will be counted once in the SOC summary. Subjects who experienced multiple occurrences of events with the same PT will be counted once in the PT summary. Percentages will be calculated using the total number of subjects in the SAF.

If a subject experiences more than 1 occurrence of the same AE, the occurrence with the greatest severity and the closest association with the study drug will be used in summary tables. TEAEs related to study drug are those for which a 'Reasonable Possibility' of relationship is reported in the CRF, or with missing relationship.

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11.5. Other Safety

11.5.1. Local Tolerability

Local tolerability (irritation) parameters (erythema, scaling, dryness and stinging/burning) will be evaluated at each visit on a 4-point scale between 0 (none), 1 (mild), 2 (moderate) and 3 (severe). The assessments will be conducted separately for the face and trunk.

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Summary tables will be presented separately for face CCI and trunk CCI , using both frequency tables and descriptive statistics.

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Mean values of erythema, scaling, dryness and stinging/burning on face and trunk will be presented using line plots over time.

CCI

[redacted]

11.5.2. Pregnancy Testing

All women of childbearing potential will have a urine pregnancy test (UPT) at the screening visit and UPTs at subsequent visits.

All pregnancy testing information will be presented in a listing.

11.5.3. Photographs

CCI

[redacted]

12. Health Economics

Not applicable.

13. Interim Analyses

CCI

CCI

CCI

14. Changes from Analysis Planned in Protocol

Subgroup analyses were deemed not appropriate and thus were removed.

15. Reference List

Not applicable.

16. Programming Considerations

All TFLs and statistical analyses will be generated using SAS® 9.4 or higher (SAS® Institute Inc., Cary, NC, USA). Computer-generated TFL output will adhere to the following specifications.

16.1. General Considerations

- One SAS program will be created for each output.
- Each output will be stored in a separate file.
- Output files will be delivered in Word rtf format.
- The final TFLs will be provided in a combined pdf document including a table of contents which are hyperlinked to each output.
- Numbering of TFLs will follow International Conference on Harmonization (ICH) E3 guidance

16.2. Tables, Figures, and Listings Format

16.2.1. General

CCI [redacted]

16.2.2. Headers

CCI [redacted]

16.2.3. Display Titles

CCI [redacted]

CCI [redacted]

CCI [redacted]

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16.2.4. Column Headers

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16.2.5.1. General Conventions

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16.2.5.2. Table Conventions

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16.2.5.3. Listing Conventions

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16.2.5.4. Figure Conventions

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16.2.6. Footnotes

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17. Quality Control

SAS programs are developed to produce output such as analysis data sets, summary tables, data listings, figures or statistical analyses. CCI

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18. Index of Tables

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19. Index of Figures

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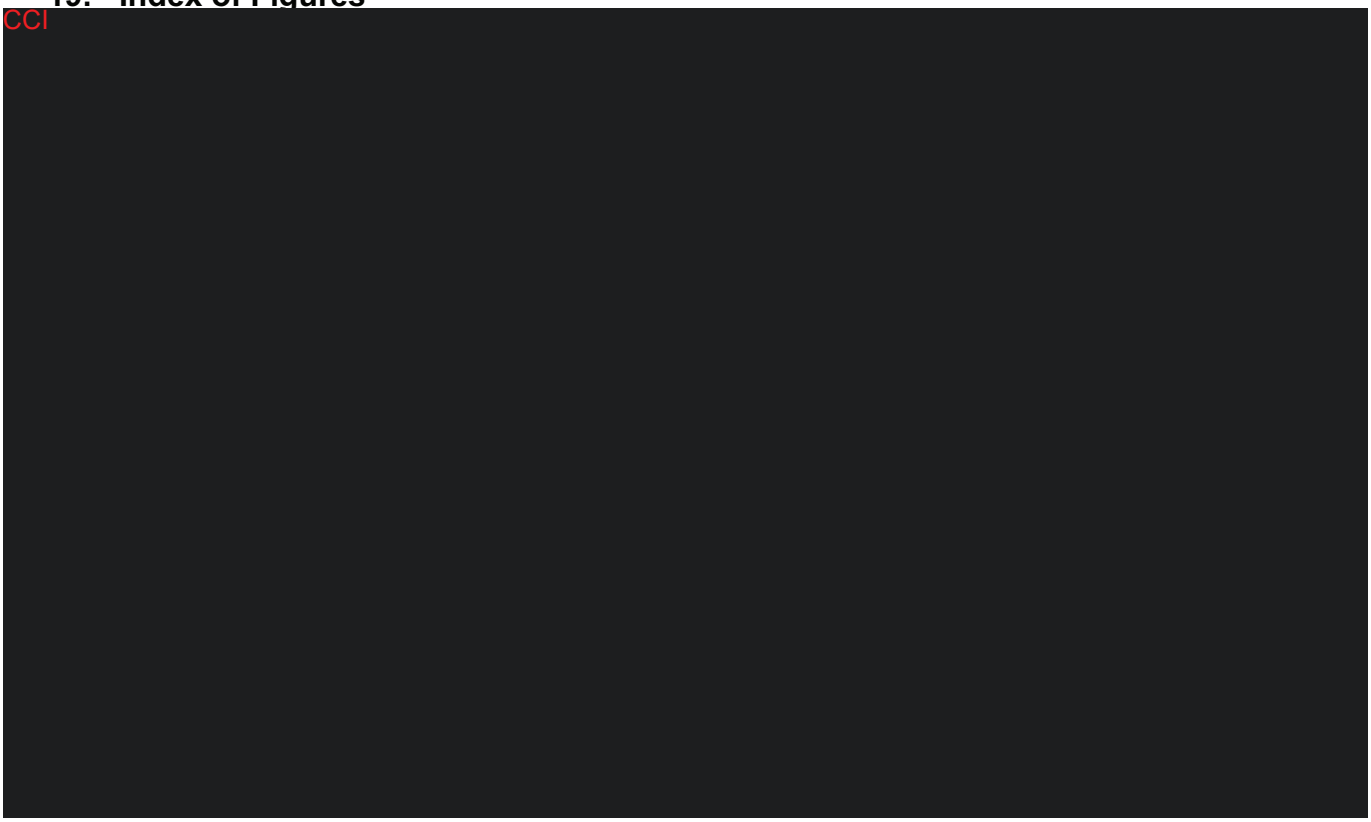

20. Index of Listings

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