STATISTICAL ANALYSIS PLAN
PHASE II

VERSION: 1.0

DATE:

February 14, 2019

BASED ON:

Protocol Version 4.0 Date:07-Jan-19

Data Management Plan Final Version 1.0 Date: 12-Apr-18

Study Drug:

B244 Topical Application

Protocol Number:

RB244-001

Study Title:

Vehicle-Controlled, Double-Blind, Randomized Phase II Study of B244 Delivered as a Topical Spray to Determine Safety and Efficacy in Subjects with Mild to Moderate Rosacea.

Sponsor:

AOBiome, LLC

125 Cambridgepark Drive

Cambridge, MA 02140

NCT03590366

STATISTICAL ANALYSIS PLAN REVIEW AND APPROVAL

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

Prepared by:

Rahul Paul Choudhury, Lead Bio-Statistician — 19 FEB 2019 Date

Statistical Review:

Jose Nabut, Sr. Specialist Bio-Statistician — 19 Feb 2019 Date

Sponsor Review:

Judith Ng-Cashin, M.D, Chief Medical Officer — 14 Feb 2019 Date

Spiros Jamas, Sc. D., SVP of Therapeutic Development — Feb 14th 2019 Date

PROTOCOL SYNOPSIS

Study Title	A Vehicle-Controlled, Double-Blind, Randomized Phase II Study of B244 Delivered as a Topical Spray to Determine Safety and Efficacy in Subjects with Mild to Moderate Rosacea.
Protocol Number	RB244-001
Development Phase	Phase II
Type of Study	Safety Analysis and Superiority of the Study drug over Vehicle
Study Medications	1) B244 Topical Spray (Test formulation), manufactured by AOBiome Therapeutics. 2) Vehicle of test product manufactured by AOBiome Therapeutics.
Name of Active Ingredient	B244
Route of administration	Topical application
Sponsor	AOBiome, LLC,125 Cambridgepark Drive, Cambridge, MA 02140
Study Objectives	**PRIMARY** • To assess the safety and tolerability of B244 applied twice daily (BID) to the face for 8 weeks in subjects with mild to moderate rosacea. **EXPLORATORY** To assess the efficacy of B244 in subjects with mild to moderate rosacea. • Proportion of subjects with IGA improvement at Week 8 relative to baseline • Proportion of subjects with CEA improvement at Week 8 relative to baseline • Change in IGA from Baseline to Week 8 • Change in CEA from Baseline to Week 8 • Proportion of Subjects with improvement in IGA or

	CEA at Week 1, Week 4, and Week 12. • Change in Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8, and Week 12. • Proportion of subjects with change in PSA at Week 1, Week 4, Week 8 and Week 12 from Baseline. • Evaluation of Telangiectasia Score at Baseline/Day1 and Week 8
Study Design	This is a Prospective, Vehicle Controlled, Double Blind, Multicenter, Randomized Phase II trial, comparing the effect of twice daily B244 application for 8 weeks vs. vehicle application on treatment of mild to moderate rosacea. • We will enroll approximately 130 subjects and complete 104 subjects. • At Screening and Baseline: o All subjects must have diagnosis of mild to moderate Rosacea. o Subjects must have IGA score of 2-3 and CEA score of 2-3 to qualify for the study. • After screening and recruitment, participants will be randomized to active or vehicle application for 8 weeks. • Subjects will apply a total of 4 pumps of IP per application to the face twice-a-day • Randomization will be 1:1 B244 to Vehicle. • Subjects will be provided with cleanser and moisturizer to use for the duration of the study • All B244 randomized subjects will be treated at the dose of $4x10^9$ cells/ml via spray application • Screening period will occur at Days -21 to -1 • Washout will occur after Screening visit (Days - 14 to -1) • Randomization will occur during the baseline visit for the study Efficacy will be assessed using Investigator Global Assessment (IGA) score, Clinician's Erythema Assessment (CEA) score, Patient Self-Assessment (PSA) score and patient reported Skindex 16. • Clinical assessments of response to treatment will be made at Week 1(Day 7), Week 4 (Day 28), and Week 8 (Day 56) • At Baseline visit, subjects will receive a kit containing the drug product. Each bottle will be used for 2 weeks. At Week 4, subjects will return the used bottles from the kit and will be issued a new kit of drug product to be used from Week 4 through Week 8. • Subjects will stop applying investigational product at Week 8 and will return investigational product at that visit.

	• Subjects will come back for a 4-week posttreatment follow up visit at Week 12 (Day 84). • Participant's safety will be monitored throughout the study. Safety will be assessed by monitoring reported adverse events, vital signs, clinical chemistry and hematology and overall tolerability of the investigational product. • Subjects would be required to discontinue the investigational product under the following circumstances: o Development of an intercurrent illness that would jeopardize the safety, or significantly affect assessments of clinical status of a subject o Either at the discretion of the Investigator or at the participant's request o Development of any investigational product-related SAE o Suspected or laboratory-confirmed pregnancy
Number of Subjects and Sites	Approximately 130 subjects are planned to be enrolled, and assuming a 20% drop out rate, the planned overall sample size for this clinical trial is approximately 104 adult male and female subjects, 18 years of age and older with mild to moderate rosacea. Subjects will be randomized at a 1:1 ratio (B244: vehicle) at about 8 clinical research centers in the United States.
Eligibility Criteria	INCLUSION CRITERIA • Male and female subjects ≥18. • A clinical diagnosis of mild to moderate facial rosacea. • In good general health as determined by a thorough medical history, physical examination, clinical chemistry and hematology. • A Clinician Erythema Assessment (CEA) score of 2-3 at Screening and at Baseline Visits (prior to the investigational product application). • Mild to Moderate IGA score of 2-3 at Screening and at Baseline Visits (prior to the investigational product application). • Willing to refrain from using any topical or systemic treatments for the treatment of rosacea, other than the investigational product. • Females of childbearing potential with a negative urine pregnancy test (UPT) at Screening and Baseline/Day 1 (prior to the investigational product application). • Ability to comprehend and comply with study procedures. • Agree to commit to participate in the current protocol.

	• Provide written informed consent prior to any study procedure being performed. EXCLUSION CRITERIA Any subject who meet one or more of the following criteria are excluded from this study. • Female subjects who are pregnant, lactating or who are trying to conceive will be excluded from participation in this study. • Any uncontrolled chronic or serious disease or medical condition that would normally prevent participation in a clinical trial, or, in the judgment of the Investigator, would put the subject at undue risk, or might confound the study assessments (e.g., other dermatological diseases), or might interfere with the subject's participation in the study, (e.g., planned hospitalization during the study). • Particular forms of rosacea (e.g., rosacea conglobata, rosacea fulminans, isolated rhinophyma, isolated pustulosis of the chin, Ocular rosacea Phymatous rosacea, Steroid-induced rosacea, severe rosacea including pyoderma faciale) or other concomitant facial dermatoses that are similar to rosacea such as peri-oral dermatitis, demodicidosis, facial keratosis pilaris, seborrheic dermatitis, acute lupus erythematosus, or actinic telangiectasia. • Presence of three (3) or more facial inflammatory lesions of rosacea. • Any skin condition which in the investigator's opinion may interfere with the evaluation of rosacea. • Severe papulopustular rosacea requiring systemic treatment. • Participation at the time of eligibility assessment (Screening) in any other investigational drug or device study or may have participated within 30 days prior to Screening. • Commencement of new hormonal therapy or dose change to hormonal therapy within 90 days prior to baseline. Dose and frequency of use of any hormonal therapy started more than 90 days prior to baseline must remain unchanged throughout the study. Hormonal therapies include, but are not limited to, oral, injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS) or other forms of hormonal contraception that have comparable efficacy (e.g. vaginal ring or transdermal hormone contraception).

- Presence of beard or excessive facial hair at Screening which would interfere with the study treatments or study assessments and refusal to remove for duration of study.
- Current treatment with monoamine oxidase (MAO) inhibitors, barbiturates, opiates, sedatives, systemic anesthetics, or alpha-agonists.
- Carcinoid, Pheochromocytoma or other systemic causes of flushing.
- Known sensitivity to B244 or its components.
- Refusal to submit to blood and urine sampling for laboratory analysis.
- Treatment with the following:

Prohibited Topical Treatments:

Topical Treatment	Prohibited Time Frame prior to Baseline
Astringents or abrasives	2 days
RHOFADE™ (oxymetazoline HCl) Cream,1%	1 week
Bleach baths	1 week
Mirvaso (brimonidine) topical cream	1 week
Vinegar	1 week
Topical Prescription/OTC medications for treatment of acne	1 week
Soolantra (Ivermectin 1%) topical cream	1 week
Topical Antibiotic	2 weeks
Use of over the counter antimicrobial	2 weeks
Benzoyl Peroxide	2 weeks
Immunomodulators	4 weeks
Oracea (doxycycline) topical cream	2 weeks
Corticosteroids	4 weeks
Electrocoagulation, Dermabrasion; Facial peels	4 weeks
Dermatologic/surgical procedure on the face	4 weeks
Topical Prescription medications for the treatment of rosacea (e.g. azelaic acid, metronidazole, etc.)	4 weeks
Laser, Phototherapy, Photodynamic Therapy or IPL (intense pulsed light) treatment	4 weeks

	Prescription or over the counter topical retinoid use on the face (e.g., tretinoin, tazarotene, adapalene) — 4 weeks Prohibited Systemic Treatments: Topical Treatment — Prohibited Time Frame prior to Baseline Exposed to excessive ultraviolet (UV) radiation and/or subject was unwilling to refrain from excessive exposure to UV radiation during the course of the study. — 1 week Prescription anti inflammatory — 2 weeks Prescription/OTC anti-inflammatory medications (excludes low dose aspirin) — 2 weeks Systemic Antibiotics — 4 weeks Prescription medications for the treatment of rosacea (e.g. doxycycline, tetracycline, macrolides) — 4 weeks Prescription medications for treatment of acne — 4 weeks Corticosteroids (oral or injectable) — 4 weeks Immunomodulators — 12 weeks Oral retinoid use (e.g., isotretinoin), vitamin A supplements greater than 10,000 units/day — 6 months
Withdrawal and Early Discontinuation	A subject may voluntarily withdraw from the study at any time and for any reason without prejudice to his or her future medical care. The Investigator, Sponsor, or Medical Monitor may also withdraw a subject at any time if it is medically necessary or in the interest of subject's safety. If a subject discontinues prematurely, the Investigator will perform Early Termination (ET) visit, capturing the reason for discontinuation. Further details are provided in section 5.2 & 5.3 of the Protocol RB244-001 v4.0.
Prohibited Concomitant Medication	Prohibited Therapies are those medicinal products and treatment methods that are not allowed during the study period and within the timeframes specified in the section 8.1 of the Protocol RB244-001 v4.0.
Study Drug	Study drug includes Test and Placebo drug products. The Sponsor will supply study drug as matching 30ml/bottle, labeled for a blinded study. • Test Drug: B244, 30ml/bottle (AOBiome, LLC) • Placebo: Vehicle, 30ml/bottle (AOBiome, LLC)

Duration of Patient Study Participation	Up to 84 ± 2 days
Study Endpoints	**PRIMARY** • The primary safety endpoint is to assess the safety and tolerability of B244 applied twice daily (BID) to the face for 8 weeks in subjects with mild to moderate rosacea based on the number of AE & SAE. **EXPLORATORY** To assess the efficacy of B244 in subjects with mild to moderate rosacea. • Change of IGA score at Baseline to Week 1, Week 4, Week 8 and Week 12 • Change of CEA score at Baseline to Week 1, Week 4, Week 8 and Week 12. • Change of PSA score at Baseline to Week 1, Week 4, Week 8 and Week 12. • Change of Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8 and Week 12 • IGA treatment success, defined as "clear" or "almost clear" with a 2-grade improvement in IGA score from baseline to the end of treatment. • CEA treatment success, defined as "clear" or "almost clear" with a 2-grade improvement in CEA score from baseline to the end of treatment
Statistical Analysis	**SAFETY ANALYSIS** The reporting of safety data is descriptive (arithmetic mean, standard deviation (SD), coefficient of variation (CV), median, minimum, and maximum) will be calculated for quantitative safety data as well as for the difference from baseline, when appropriate. The analysis will include all subjects who receive at least one dose of investigational product. The variables for safety endpoints are AEs, Local Application Site Reactions, vital signs measurements, clinical chemistry and hematology. AEs will be summarized based on the frequency of AEs and their severity for all treated subjects. All AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA) and summarized by treatment group. Data will be summarized using preferred term and primary system organ class, including verbatim term, dose level, severity, and relationship to treatment, will be provided.

	Concomitant medications will be listed by treatment and coded using the most recent version of the World Health Organization (WHO) Drug Dictionary (DD). **EFFICACY ANALYSIS** The Evaluable Period for the outcome variables will be weeks 1, 4, 8 and 12. The superiority of the drug over the vehicle will be tested at week 8 based on the probability of improvement from baseline with a continuity-corrected Z-tests comparing the change from baseline of treatments vs Placebo. For all other evaluable periods, descriptive statistics for the change from baseline will be shown. The change from baseline score of Skindex-16 will be compared among treatments at Week 12 using an ANOVA.

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1 LIST OF ABBREVIATION

Abbreviation	Full Form
AE	Adverse Event
AOB	Ammonia-Oxidizing Bacteria
BID	Bis in Die (twice a day)
BP	Blood Pressure
CEA	Clinician Erythema Assessment
CRA	Clinical Research Associate
CI	Confidence Interval
CRF	Case Report Form
CTMF	Clinical Trial Master File
CTP	Clinical Trial Protocol
eCRF	Electronic Case Report Form
EOS	End of Study
ET	Early Termination
ETR	Erythematotelangiectatic rosacea
GCP	Good Clinical Practice
IB	Investigator's Brochure
ICH	International Conference On Harmonization
IEC	Independent Ethics Committee
IGA	Investigator Global Assessment
IGE	Investigator's Global Evaluation
IP	Investigational Product
IPL	Intense Pulsed Light
IRB	Institutional Review Board
ISF	Investigator Site File
IUD	Intrauterine Device
IUS	Intrauterine system
IWRS	Interactive Web Response System
LOCF	Last Observation Carried Forward
mITT	Modified Intent-To-Treat
NSAID	Nonsteroidal Anti-inflammatory Drug
OTC	Over the Counter
PP	Per-Protocol
PRN	Pro Re Nada (as needed)
PRN	Pro Re Nada (as needed)
PSA	Patient Self-Assessment
RR	Relative Risk
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SI	Simple Imputation
SOP	Standard Operating Procedures
SUSAR	Suspected Unexpected Serious Adverse Reactions
TEAE	Treatment Emergent Adverse Event

ULN	Upper Limit of Normal Range
UPT	Urine Pregnancy Test
UV	Ultraviolet
WBC	White Blood Cell Count

2 INTRODUCTION

This document describes the statistical methods and data presentations to be used in the summary and analysis of data from Protocol RB244-001. Background information is provided for the overall study design and objectives. The reader is referred to the study protocol and electronic case report forms (eCRFs) for details of study conduct and data collection.

2.1 Study Overview

The proposed study is aimed to evaluate the safety and efficacy of B244 topical spray. A Vehicle-Controlled, Double-Blind, Multicenter, Randomized Study Design has been Selected to Evaluate the Safety and Efficacy of the B244 Investigational product in the Treatment of Mild-to-Moderate Rosacea.

There is no cure for rosacea and treatment is aimed at alleviating the symptoms. Topical or oral medications are generally prescribed for mild to moderate papulopustular rosacea. These topical medications include: metronidazole, azelaic acid, sodium sulfacetamide and sulfur, erythromycin, and tretinoin8. Currently these approved topical medications may cause local irritation to the skin. The oral medications prescribed for severe disease include tetracycline, doxycycline, minocycline, erythromycin and metronidazole. The systemic therapies may result in systemic adverse events such as gastrointestinal upset and photosensitivity.

It is believed, that topical application of Ammonia-Oxidizing Bacteria (AOB) will reduce survival of pathogenic bacteria present on the skin and thus improve rosacea symptoms in those affected by it. B244 is being developed as a ‘live topical’ to provide a natural source of AOB and NO/NO2 to the human skin.

This is a Prospective, Vehicle Controlled, Double Blind, Multicenter, Randomized Phase II trial, Comparing the effect of twice daily B244 application for 8 weeks vs. vehicle application on treatment of mild to moderate rosacea. At Screening and Baseline all subjects must have clinical diagnosis of mild to moderate rosacea and subjects must have IGA score of 2-3 and CEA score of 2-3 to qualify for the study.

After screening and recruitment, participants will be randomized to active or vehicle application for 8 weeks. Subjects will apply a total of 4 pumps of IP per application to the face twice-a-day. Subjects will be provided with cleanser and moisturizer to use for the duration of the study. All B244 randomized subjects will be treated at the dose of $4x10^9$ cells/ml via spray application.

Efficacy will be assessed using Investigator Global Assessment (IGA) score, Clinician’s Erythema Assessment (CEA) score, Patient Self-Assessment (PSA) score and patient reported Skindex 16. Participant's safety will be monitored throughout the study. Safety

will be assessed by monitoring reported adverse events, vital signs, clinical chemistry and hematology and overall tolerability of the investigational product.

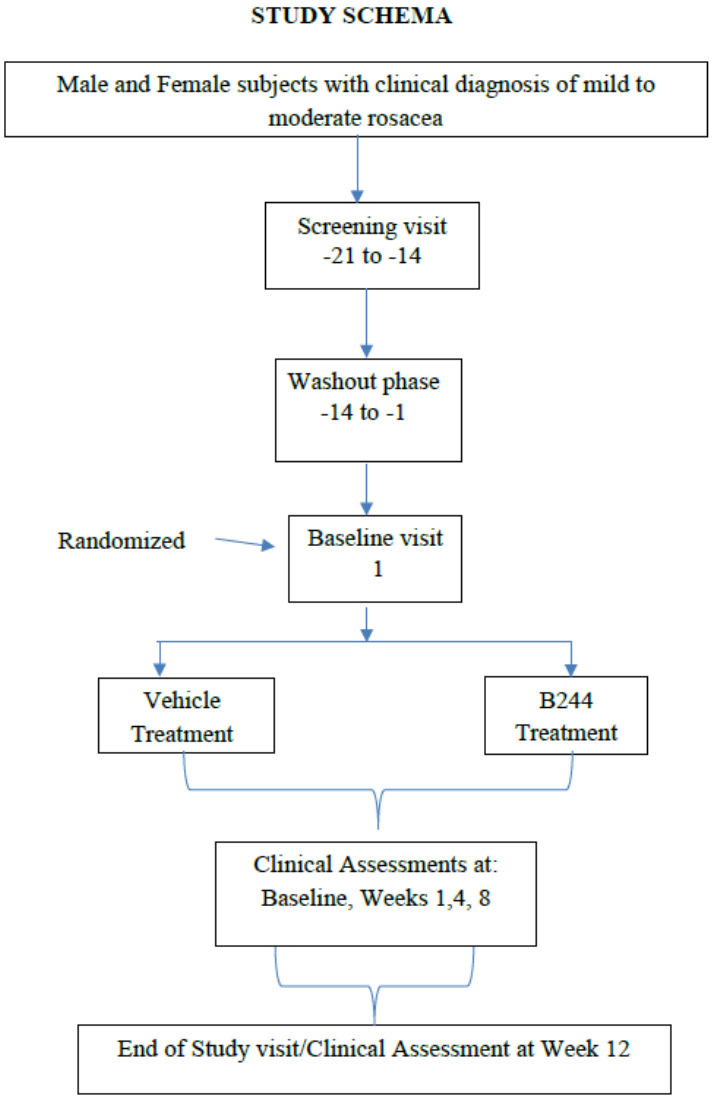
Approximately 130 subjects are planned to be enrolled, and assuming a 20% drop out rate, the planned overall sample size for this clinical trial is approximately 104 adult male and female subjects, 18 years of age and older with mild to moderate rosacea. Subjects will be randomized at a 1:1 ratio (B244: Vehicle) at about 8 clinical research centers in the United States.

The entire study will consist of a total of 6 visits:

- Visit 1(Day -21 to -1): Screening will occur at Days -21 to -1, followed by Washout (Days -14 to -1).
- Visit 2(Baseline/ Day 1): Randomization will occur during the baseline visit for the study (Day 1).
- Visit 3 – 5(Day 7 ± 2 [Week 1], Day 28 ± 2 [Week 4], Day 56 ± 2 [Week 8]): Clinical assessments of response to treatment will be made at Week 1(Day 7), Week 4 (Day 28), and Week 8 (Day 56).
- Visit 6(Day 84 ± 2): Subjects will come back for a 4-week post-treatment follow up visit at Week 12 (Day 84).

2.2 Study Flowchart

Figure 1. Study Flowchart



2.3 Schedule of Activities

Table 1: Schedule of Study Activities

Visit Name	Screening	Baseline/ DAY 1	Week 1	Week 4	Week 8	Week 12/ End of Study Visit	Early Termination Visit
Visit number	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	
Visit window in days	**-21 to -1**	**1**	**7+/-2**	**28 +/- 2**	**56 +/- 2**	**84 +/- 2**	
Informed Consent	X						
Inclusion/Exclusion Criteria	X	X					
Demographics	X						
Medical History	X	X					
Concomitant Medications	X	X	X	X	X	X	X
Physical Exam	X	X				X	X
BP & Pulse[2]	X	X	X	X	X	X	X
Urine pregnancy test for WOCBP[1]	X	X	X	X	X	X	X
Clinical chemistry and hematology and urinalysis[3]	X	X		X	X		X
Biomarkers[4]		X			X		X
CEA	X	X	X	X	X	X	X
IGA	X	X	X	X	X	X	X
Skindex 16	X	X	X	X	X	X	X
PSA score	X	X	X	X	X	X	X
Telangiectasia Evaluation		X			X		X
Fitzpatrick skin type	X						
IWRS		X		X			
Dispense Investigational product to Subject [5/6]		X		X			
Collect Investigational product from Subject[5]				X	X		X

Visit Name	Screening	Baseline/ DAY 1	Week 1	Week 4	Week 8	Week 12/ End of Study Visit	Early Termination Visit
Visit number	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	
Visit window in days	**-21 to -1**	**1**	**7+/-2**	**28 +/- 2**	**56 +/- 2**	**84 +/- 2**	
Investigational product Compliance[5]		X		X	X		X
Study Cleanser and moisturizer dispensation[9]		X		X			
Study Cleanser and moisturizer collection					X		X
Study Diary[8]		X	X	X	X		X
Study Counseling[7]		X	X	X	X		
AE Collection and Assessment	X	X	X	X	X	X	X

1. Urine pregnancy test for WOCBP will be done at every visit.
2. Blood pressure readings will be obtained at every visit. Subject should be allowed to rest for more than 5 minutes sitting, then BP measurements and pulse (x3) will be performed, using the non-dominant arm with a calibrated electronic sphygmomanometer. The average of the second and third readings will be documented.
3. Subjects should fast for at least 8 hours before the test. Laboratory work includes: hematology and Lipid Panel, Albumin, Alkaline Phos, ALT, AST, Total Bilirubin, BUN, BUN: Creatinine ratio, Calcium, Chloride, Creatinine, eGFR, Glucose, Potassium, Sodium, Uric Acid, and urinalysis. HIV Ab, HCV Ab, HBsAg. will only be done at screening.
4. Subjects should fast for at least 8 hours before the test.
5. Weight of the investigational product kit will be obtained at the Baseline visit. Study staff will be asked to weigh all dispensed bottles without the carton box PRE- FIRST DOSE. Weight will be recorded in grams.
6. Subjects will be asked to bring all dispensed bottles back for the Week 4 and Week 8 visits. Upon return for the study visit, all bottles will be weighed again without the carton box. Subjects will be asked to apply the investigational product twice daily. First investigational product application will happen at the site under medical supervision.
7. Subjects will be counseled on the use of study medication and answer any questions subject may have.
8. Subjects will be asked to fill out study diary for the duration of the study.
9. Cleanser and moisturizer will be dispensed at the Baseline visit. Subjects will be asked to refrain, if possible, from using any other cleanser and/or moisturizer on their face and apply the provided product while they are participating in the trial. Any leftover moisturizer /cleanser will be collected at Week 8 visit, at which point subjects will be asked to go back to their regular routine.

3 STUDY OBJECTIVE AND ENDPOINTS

3.1 Study Objectives

3.1.1 Primary Objective

To assess the safety and tolerability of B244 applied twice daily (BID) to the face for 8 weeks in subjects with mild to moderate rosacea.

3.1.2 Exploratory Objectives

To assess the efficacy of B244 in subjects with mild to moderate rosacea.

- Proportion of subjects with IGA improvement at Week 8 relative to baseline.
- Proportion of subjects with CEA improvement at Week 8 relative to baseline.
- Change in IGA from Week 8 to Baseline.
- Change in CEA from Week 8 to Baseline.
- Proportion of Subjects with improvement in IGA or CEA at Week 1, Week 4, and Week 12.
- Change in Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8, and Week 12.
- Proportion of subjects with change in PSA at Week 1, Week 4, Week 8 and Week 12 from Baseline.
- Evaluation of Telangiectasia Score at Baseline/Day 1 and Week 8

3.2 Study Endpoints

3.2.1 Safety & Tolerability (Primary)

Safety and tolerability endpoints will consist of all adverse events reported during the study duration.

3.2.2 Efficacy (Exploratory)

- Change of IGA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of CEA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of PSA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8 and Week 12.
- IGA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in IGA score from baseline to the end of treatment.
- CEA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in CEA score from baseline to the end of treatment.

4 STUDY DESIGN

4.1 Summary of Study Design

This is a Prospective, Vehicle Controlled, Double Blind, Multicenter, Randomized Phase II trial, Comparing the effect of twice daily B244 application for 8 weeks vs. vehicle application on treatment of mild to moderate rosacea. We will enroll approximately 130 subjects and complete 104 subjects.

At Screening and Baseline, all subjects must have clinical diagnosis of mild to moderate rosacea and must have IGA score of 2-3 and CEA score of 2-3 to qualify for the study. After screening and recruitment, participants will be randomized to active or vehicle application for 8 weeks. Subjects will apply a total of 4 pumps of IP per application to the face twice-a-day. Randomization will be 1:1 B244 to Vehicle. Subjects will be provided with cleanser and moisturizer to use for the duration of the study. All B244 randomized subjects will be treated at the dose of $4x10^9$ cells/ml via spray application. Screening will occur at Days -21 to -1. Washout will occur after Screening visit (Days -14 to -1) and randomization will occur during the baseline visit for the study (Day 1).

Efficacy will be assessed using Investigator Global Assessment (IGA) score, Clinician's Erythema Assessment (CEA) score, Patient Self-Assessment (PSA) score and patient reported Skindex 16. Clinical assessments of response to treatment will be made at Week 1(Day 7), Week 4 (Day 28), and Week 8 (Day 56). At Baseline visit, subjects will receive a kit containing the drug product. Each bottle will be used for 2 weeks. At Week 4, subjects will return the used bottles from the kit and will be issued a new kit of drug product to be used from Week 4 through Week 8. Subjects will stop applying investigational product at Week 8 and will return investigational product at that visit. Subjects will come back for a 4-week post-treatment follow up visit at Week 12 (Day 84). Participant's safety will be monitored throughout the study. Safety will be assessed by monitoring reported adverse events, vital signs, clinical chemistry and hematology and overall tolerability of the investigational product.

Subjects would be required to discontinue the investigational product under the following circumstances:

- Development of an intercurrent illness that would jeopardize the safety, or significantly affect assessments of clinical status of a subject
- Either at the discretion of the Investigator or at the participant's request
- Development of any investigational product-related SAE
- Suspected or laboratory-confirmed pregnancy

4.2 Definition of Study Drugs

Study drug includes Test and Placebo drug products. The Sponsor will supply study drug as matching 30ml/bottle, labeled for a blinded study.

- Test Drug: B244, 30ml/bottle (AOBiome, LLC)
- Placebo: Vehicle, 30ml/bottle (AOBiome, LLC)

4.3 Sample Size Considerations

Approximately 130 subjects are planned to be enrolled, and assuming a 20% drop out rate, the planned overall sample size for this clinical trial is approximately 104 adult male and female subjects, 18 years of age and older with mild to moderate rosacea. Subjects will be randomized at a 1:1 ratio (B244: Vehicle) at about 9 clinical research centers in the United States.

4.4 Study Withdrawal

A subject may voluntarily withdraw from the study at any time and for any reason without prejudice to his or her future medical care. The Investigator, Sponsor, or Medical Monitor may also withdraw a subject at any time if it is medically necessary or in the interest of subject's safety. Additional reasons for premature discontinuation of investigational product may include adverse events and major non-compliance with study procedures, as described below. The withdrawal of a subject from investigational product by the Investigator will be discussed with the Medical Monitor before the subject stops investigational product, whenever possible.

A subject will be discontinued from this study if any of the following criteria are met:

- Withdrawal of consent by the subject is received.
- In the opinion of the Investigator, Medical Monitor or Sponsor, it is not in the subject's best interests to continue in the study.
- Significant non-compliance with study procedures that would interfere with the study results or increase the subject's risks in the study, as determined by the Investigator.
- Development of an intercurrent illness that would jeopardize the safety, or significantly affect assessments of clinical status of a subject.
- Development of any investigational product-related SAE.
- Suspected or laboratory-confirmed pregnancy.

Subjects who discontinued early from the study due to lack of treatment effect after completing at least four weeks of treatment (Day 28) will be included in the mITT and PP population as treatment failures and the change in IGA and CEA from the baseline visit to the last completed visit prior to discontinuation due to lack of efficacy will be carried forward in the primary endpoint analysis. Subjects discontinued early for other reasons will be excluded from the PP population.

4.5 Early Discontinuation

If a subject discontinues prematurely, the Investigator will perform Early Termination (ET) visit, capturing the reason for discontinuation.

If a subject does not return for a scheduled visit, every effort will be made to contact the subject and document the End of Study visit assessments. The Investigator must document the primary reason for discontinuation of a study subject in the source document and on the appropriate electronic case report form (eCRF).

5 PLANNED ANALYSIS

5.1 Final Analysis

Final analysis is planned for the study after the database lock. The final analysis will follow instructions presented in this SAP.

6 GENERAL CONSIDERATION FOR DATA ANALYSIS AND HANDLING

6.1 General Summary Table and Individual Subject Data Listing

Summary tables and listings (e.g., post text tables and individual subject data listings are prepared according to ICH Guideline E3) include a “footer” providing explanatory notes that indicate as a minimum:

- SAS program name.
- Programmer.
- Date of data extraction.
- Date of output generation.

Post text tables also include reference(s) to the subject data listing(s) that supports the summary data. The data extraction date links the output to the archived database that is locked to ensure the replication of the results.

Post text tables will be organized with respect to treatment group and a column will be included to summarize all treated subjects. The order of drug presentation will be investigational drug first followed by the vehicle control. A total column will appear as the last column. The summary tables clearly indicate the number of subjects to which the data apply and unknown or not performed are distinguished from missing data.

Summary tables for medications and medical conditions are coded according the WHO Drug Dictionary. Adverse event preferred terms and body/organ systems are coded using

the MedDRA dictionary. The MedDRA dictionary can be used, as well, in the coding of signs and symptoms, medical history, physical examination abnormalities, and clinical diagnoses.

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

6.2 General Summary Table and Individual Subject Data Listing Considerations

The default convention is to number tables and listings using a decimal system to reflect main levels of unique tables and listings and sub-levels of replicate tables and listings with two digits per level (e.g., Table XX.YY.ZZ. …).

- The first level number should be consistent with the corresponding CSR appendix in which the tables or listings will appear. For example, the post text tables usually occupy Appendix 14 and the individual subject data listings are put in Appendix 16. All post text tables should have a main number level 14 and listings 16. The subject accounting and disposition table is usually first in the first section of the report and should be numbered Table 14.1. The supportive subject data listing would be Listing 16.1. A subset by sex 2. Subject accounting and final disposition should appear as the second level number (Table 14.1 series). Baseline and demographic profile occupy the next sub-level (Table 14.2 series). Efficacy should come next (Table 14.3 series) followed by safety Table 14.4 series). Reasons for subjects' being excluded from efficacy and protocol violation summary tables should appear as the last level (Table 14.5 series). Similar conventions should be applied to the subject data listings.

- The title should be complete, accurate, and concise. The last line of the title should provide the analysis group being summarized (e.g., Intent-to-Treat Subjects or Per-Protocol Efficacy Subjects). If possible, the units of measurement for data contained in the table can appear in parentheses to conserve space in the body of the table. For example, the summary of vital signs title could read "Summary of Sitting and Standing Blood Pressure (mmHg) and Heart Rate (bpm)." Whether in the title or body of a table or listing, units must always be specified for all appropriate data.

- If possible, variables being summarized, and statistics reported should appear in the left most column of a table. The next columns for treatment groups should report the data from left to right for the investigational drug, placebo, comparative agents, and (optional) all treated subjects, respectively.

In general, the listings should be sorted and presented by treatment assignment, investigational site, and subject number. Treatment assignment and site can appear in the banner of the listing. From left to right, the subject number, visit number, visit date, and relative day should appear.

All tables and listings must have explanatory notes that give, as a minimum, data extraction date, output generation date, complete program name and path where it is stored, as appropriate. The definition of all derived variables and decodes for coded data must appear in the notes. Due to space limitations, tables and listings may require a page of notes as a one-time preface to the output.

6.3 Data Management

Biorasi will create SDTM data sets and ADaM analysis data sets using (SAS®) software. Data analyses and summary tables are generated using SAS version 9.4 or above

6.4 Data Presentation Conventions

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

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

- For continuous variables, all mean and median values are formatted to one more decimal place than the measured value. Standard deviation values are formatted to two more decimal places than the measured value. Minimum and maximum values are presented with the same number of decimal places as the measured value.
- For categorical variables, the number and percentage of responses are presented in the form XX (XX.X %) where the percentage is in the parentheses.
- Date variables are formatted as DDMMMYYYY for presentation. Time is formatted in military time as HH:MM for presentation.
- Wherever possible, data will be decimal aligned.
- P-values, if applicable, will be presented to 4 decimal places. If the p-value is less than 0.0001 then it will be presented as <0.0001.

Unless otherwise stated, any statistical tests performed will use 2-sided tests at the 5% significance level.

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

6.5 Analysis Populations

6.5.1 Screen Failures

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

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

6.5.2 Safety Population

The safety population includes all randomized subjects who received investigational product.

6.5.3 mITT Population

A modified intent-to-treat population includes all subjects who are randomized, applied at least one dose of assigned product, and returned for at least one post-baseline evaluation visit.

6.5.4 Per-Protocol (PP) Population

The PP population includes all randomized subjects who met all inclusion/exclusion criteria, were compliant with the assigned study treatment, returned to the study site for the primary endpoint visit within the specified window (±2 days) OR discontinued from the study as a treatment failure, and did not have any major protocol violations.

Subjects who administered at least 50 % of IP, have at least one baseline and post baseline in clinic visit and did not have any major protocol violations.

Subjects who discontinued early from the study due to lack of treatment effect after completing at least eight weeks of treatment should be included in the mITT and PP population as treatment failures and the change in IGA and CEA from the baseline visit to the last completed visit prior to discontinuation due to lack of efficacy should be carried forward in the primary endpoint analysis. Subjects discontinued early for other reasons should be excluded from the PP population but included in the mITT population.
The results in the mITT population will be considered definitive for superiority of each active treatment to vehicle with those in the PP population considered supportive. Safety analyses will be performed using the Safety population.

6.6 Baseline Definition

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

6.7 Derived and Transformed Data

6.7.1 Baseline Age

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

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

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

6.7.2 Study Day

Day 1 is defined as the day after the baseline when the subject will receive the first dose.

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

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

6.7.3 Multiple Assessments

No multiple assessment for same visit are scheduled.

6.7.4 Handling of Missing Data & Sensitivity Analysis

For the primary and secondary analysis no missing values will be imputed. A sensitivity analysis will be performed by Multiple Imputation Regression Analysis using the following factors: treatment, age, gender, race, baseline IGA, baseline CEA, baseline PSA, smokers/non-smokers and the results of the same variable from previous visits.

6.7.5 Missing Start and Stop Dates for Prior and Concomitant Medication

Start date:

- If start date is completely missing, start date will not be imputed.
- If (year is present, and month and day are missing) or (year and day are present, and month is missing), set month and day to January 1.
- If year and month are present and day is missing, set day to the 1st day of month.

Stop date:

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

6.7.6 Safety Parameters

Safety and tolerability endpoints will consist of all adverse events (AEs) reported during the study duration from the date of randomization through Week 12 (End of Study Visit).

Specific AEs are defined below.

Treatment-Emergent Adverse Events (TEAE): Any AE with onset after the first dose of study medication through 56 days after the last dose of study medication.

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

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

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

6.7.7 Missing Start and Stop Dates for Adverse Events

Start date:

- If start date is completely missing, start date is set to date of first dose.

- If (year is present, and month and day are missing) or (year and day are present, and month is missing):

  If year = year of first dose, then set month and day to month and day of first dose.
  If year < year of first dose, then set month and day to December 31st.
  If year > year of first dose, then set month and day to January 1st.
- If month and year are present and day is missing:

  If year = year of first dose and

  - If month = month of first dose, then set day to day of first dose date.
  - If month < month of first dose, then set day to last day of month.
  - If month > month of first dose, then set day to 1st day of month.

  If year < year of first dose, then set day to last day of month.
  If year > year of first dose, then set day to 1st day of month.

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

- If stop date is completely missing, stop date is set to date of study discontinuation.
- If (year is present, and month and day are missing) or (year and day are present, and month is missing):

  If year = year of study discontinuation, then set month and day to month and day of study discontinuation.
  If year < year of study discontinuation, then set month and day to December 31st.
  If year > year of study discontinuation, then set month and day to December 31st.
- If month and year are present and day is missing:

  If year = year of study discontinuation and

  - If month = month of study discontinuation, then set day to day of study discontinuation date.
  - If month < month of study discontinuation, then set day to last day of month.
  - If month > month of study discontinuation, then set day to last day of month.

  If year < year of study discontinuation, then set day to last day of month.
  If year > year of study discontinuation, then set day to last day of month.

7 DATA ANALYSES

The data analysis will be conducted on all participant data when the trial ends. Subjects will be pooled across all sites. Data will be presented by treatment group and overall. Categorical variables will be summarized by frequency distributions (number and percentages of subjects) and continuous variables will be summarized by descriptive statistics (mean, standard deviation, etc.).

Adverse events will be summarized by treatment group using the Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred term. Separate tabulations will be produced for all treatment-emergent AEs (TEAEs), treatment-related AEs (those considered by the Investigator as at least possibly drug related), SAEs, discontinuations due to AEs, and AEs ≥Grade 3 severity. By-subject listings will be provided for any deaths, SAEs, and AEs leading to discontinuation.

Descriptive statistics for each treatment group will be provided for clinical laboratory values (e.g., hematology, serum chemistry, and urinalysis) and vital signs data, presented as both actual values and changes from baseline relative to each on-study evaluation. Abnormal clinical laboratory values will be listed.

All data will be provided in by-subject listings.

7.1 Subjects Disposition

The subject disposition summary will include the number screened, the number of screen failures, the number enrolled, the number in each patient population for analysis, the number who completed the study, the number who discontinued the study and reason for discontinuation from the study. Disposition data will be summarized by treatment and overall.
A by-subject data listing of study completion information including the reason for study discontinuation will be presented. A by-subject listing of inclusion/exclusion criteria not met will also be presented.

7.2 Protocol Deviations

A summary of all protocol deviations on ITT population by type will be generated. Protocol deviation data will be summarized by treatment and overall. A by-subject data listing of protocol deviations will also be presented.

All protocol deviations will be presented in a data listing.

7.3 Demographic and Baseline Characteristics

Demographic and baseline characteristic data summarization will be performed to descriptively assess the comparability of treatment groups. Data to be tabulated will include age, race, ethnicity, height, weight, and BMI, as well as baseline characteristics related to medical history, including hypertension, diabetes, smoking history.

7.4 Study Drug Exposure

At Baseline visit, Subjects will receive a kit containing (2) two 30 ml white bottles. Each bottle will be used for 2 weeks. At Week 4, subjects will return the used bottles from the kit and will be issued a new kit of two 30mL white bottles to be used from Week 4 through Week 8.

The cumulative amount of study drug exposure will be estimated by calculating the difference between the weight of the 2 bottles of drug at the time the drug was dispensed at Baseline/Week 4 and the weight of the 2 bottles at Week 4/Week 8. Differences will be summed together.

The amount of product used per day will be estimated by dividing the change by the number of days the subject was on treatment. These weights will be compared to the weight of the product that would be used if the subject was compliant with the protocol. Percent compliance will be calculated as follows:

$$\text{Percent compliance} = \left[\frac{\text{Net Weight of Study Drug}}{\text{(1.12g/day*Number of days in the study)} = \text{xx.xx g}} \right] * 100\%$$

The number of days the subject administered study drug, the amount of product used, and the percent compliance will be summarized by treatment group and presented in a by-subject data listing. The subject listing will also include by-visit IP weights. Percent compliance will be calculated only for subjects who returned the study drug at the end of the treatment. In the listing, subjects who withdrew from the study early will be flagged.

7.5 Medical History

A by subject data listing of medical history will be presented. Medical history will be coded using MedDRA v20.0, and the number and percentage of patients experiencing at least 1 such diagnosis by MedDRA System Organ Class (SOC) and preferred term (PT) will be reported.

7.6 Concomitant Medication

Concomitant medications will be coded using the World Health Organization (WHO) dictionary. Results will be tabulated by anatomic therapeutic class (ATC) and preferred term.

This data will be summarized by treatment group. Previous and concomitant medications will be presented in a data listing.

7.7 Vital Signs and Physical Examination

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

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

7.8 Laboratory Data

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

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

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

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

7.9 Visit Windows

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

8 STATISTICAL ANALYSES

8.1 Sample Size Determination

Sample size of 104 randomized 1:1 Active to Vehicle based on 80% power to detect 33% IGA response in Active group versus 10% in the Vehicle group, with two-sided test and alpha =0.05. Until mentioned all alpha value is set at 0.05.

8.2 Safety Analysis

Safety analyses will be conducted using the Safety population

8.2.1 Primary Safety Endpoint

Assess the safety and tolerability of B244 applied twice daily to the face for 8 weeks in subjects with mild to moderate rosacea.

The reporting of safety data is descriptive and will include all subjects who receive at least one dose of investigational product. The variables for safety endpoints are number of subjects with AEs, SAEs, vital signs measurements, clinical chemistry and hematology. AEs will be summarized based on the frequency of AEs and their severity for all treated subjects. All AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA) and summarized by treatment group. Data will be summarized using preferred term and primary system organ class.

If a subject experiences multiple events that map to a single preferred term, the greatest severity and strongest Investigator assessment of relation to investigational product will be assigned to the preferred term for the appropriate summaries. Should an event have a missing severity or relationship, it will be classified as having the highest severity and/or strongest relationship to investigational product.

Summaries of AEs will include any AEs reported beginning with the first dose of investigational product on Day 1. The occurrence of adverse events will be summarized by treatment group using preferred terms, system organ classifications, and severity. Separate summaries of serious adverse events, adverse events related to investigational product, and events leading to the discontinuation of investigational product will be generated. All adverse events reported will be listed for individual subjects showing both verbatim and preferred terms.

8.3 Efficacy Analysis

All efficacy endpoints are exploratory endpoints.

Assessment of Superiority:

- IGA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in IGA score from baseline to the end of treatment (Week 8).
- CEA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in CEA score from baseline to the end of treatment (Week 8).

  Superiority will be based on the proportion of subjects for whom treatment was successful. The comparison will be through a continuity-corrected Z-tests. The Evaluable Period for the outcome variables will be weeks 1, 4, 8 and 12. The superiority of the drug over the vehicle will be tested at week 8 based on the probability of

improvement from baseline with a continuity-corrected Z-tests comparing the change from baseline of treatments vs Placebo. For all other evaluable periods, descriptive statistics for the change from baseline will be shown.

The null and alternative statistical hypotheses for the primary effectiveness endpoints are given by:

(*Ho*): The null hypothesis is that the probability of improving (baseline to week 8) with drug T (*PrT*)is less than or equal to the probability of improving with vehicle (*PrV*).
$H_o: Pr_T \leq Pr_V \neq 0; Pr_T - Pr_V \neq 0$

(*Ha*): The alternative hypothesis is that the probability of improving with drug T (*PrT*) is greater than to the probability of improving with vehicle (*PrV*).
Ha: PrT > PrV; PrT – PrV ≠0

For testing the superiority, the following SAS code will be used:

```
proc freq data = dataset;
tables treat*outcome/riskdiff (equal);
run;
```

- Change of Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8 and Week 12

  The change from baseline score of Skindex-16 will be compared among treatments at Week 12 using an ANOVA, to test the Skindex16 score change from Baseline to Week 12 for the two treatments. Also, descriptive stats will be used to assess the change from Baseline to Week 1, 4, 8 & 12.

- Change of IGA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of CEA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of PSA score at Baseline to Week 1, Week 4, Week 8 and Week 12.

  Descriptive stats will be used to show the change from Baseline to Week 1, 4, 8 & 12.

8.4 Sensitivity Analysis

A sensitivity analysis will be performed by Multiple Imputation Regression Analysis using the following factors: treatment, age, gender, race, baseline IGA, baseline CEA, baseline PSA, smokers/non-smokers and the results of the same variable from previous visits. The Proc MI SAS code will be used to perform the analysis based on the mentioned factors.

9 REFERENCES

- Protocol Number: RB244-001, VER 4.0 "A Vehicle-Controlled, Double-Blind, Randomized Phase II Study of B244 Delivered as a Topical Spray to Determine Safety and Efficacy in Subjects with Mild to Moderate Rosacea."
- Wang, Wei. (1988, October 28). Calculating Age in One Line of Code. Paper presented at annual meeting of Northeast SAS Users Group, New York, New York. Paper retrieved from http://www.lexjansen.com/nesug/nesug01/cc/cc4022.pdf.
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10 APPENDIX

10.1 APPENDIX A: Tables

10.1.1 General

Display Number	Title	Population	Unique/Repeat
14.1.1.1	Subject Enrollment and Disposition	All Subjects	Unique
14.1.1.2	Subject Enrollment and Disposition	Enrolled Subjects	Repeat
14.1.1.3	Analysis Population and Exclusions	All Subjects	Unique
14.1.2.1	Summary of Protocol Deviations (PD)/Violations (PV)	mITT	Unique
14.1.2.2	Summary of Protocol Deviations (PD)/Violations (PV)	Safety	Repeat
14.1.3.1	Summary of Demographic and Baseline Characteristics	mITT	Unique
14.1.3.2	Summary of Demographic and Baseline Characteristics	PP	Repeat
14.1.3.3	Summary of Demographic and Baseline Characteristics	Safety	Repeat
14.1.4.1	Summary of Vital Sign	mITT	Unique
14.1.4.2	Summary of Vital Sign	PP	Repeat
14.1.4.3	Summary of Vital Sign	Safety	Repeat
14.1.5.1	Summary of Physical Examination	mITT	Unique
14.1.5.2	Summary of Physical Examination	PP	Repeat
14.1.5.3	Summary of Physical Examination	Safety	Repeat
14.1.6	Summary of Study Drug Accountability: Dose Dispensed & Collected by Visit	Safety	Unique
14.1.7.1	Summary of Study Drug Compliance	Safety	Unique
14.1.7.2	Summary of Percent Compliance based on Cumulative Net Weight of Study Drug	Safety	Unique
14.1.8	Summary of Prior Medications	Safety	Unique
14.1.9	Summary of Concomitant Medications	Safety	Unique
14.1.10	Summary of Medical History	Safety	Unique
14.1.11	Summary of Substance Abuse	Safety	Unique
14.1.12	Summary of Dairy Details	Safety	Unique

Table 14.1.1.1
Subject Enrollment and Disposition

All Subjects

Disposition	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Screened	xx (xx.x)	xx (xx.x)	xx (xx.x)
Randomized	xx (xx.x)	xx (xx.x)	xx (xx.x)
Treated	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 8	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 12	xx (xx.x)	xx (xx.x)	xx (xx.x)
Discontinued	xx (xx.x)	xx (xx.x)	xx (xx.x)
Screen Failure	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal of consent	xx (xx.x)	xx (xx.x)	xx (xx.x)
In the opinion of the Investigator, it is not in the subject's best interests to continue in the study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pregnancy	xx (xx.x)	xx (xx.x)	xx (xx.x)
Occurrence of an Adverse Event (AE) or Serious Adverse Event (SAE), which, in the opinion of the Investigator warrants discontinuation of the subject from the study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Significant non-compliance with study procedures that would interfere with the study results or increase the subject's risks in the study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject is deemed to be a treatment failure, which is defined as worsening of condition and requiring alternate or supplemental therapy	xx (xx.x)	xx (xx.x)	xx (xx.x)

for the treatment of external anogenital warts during the study			
The subject's medication code is unblinded	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject did not meet, or no longer meets, the entry criteria	xx (xx.x)	xx (xx.x)	xx (xx.x)
The subject is lost to follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)
Investigator discretion	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)

NOTE: The percentages are based on the number of randomized subjects.

Snapshot Data DD-MMM-YYYY

Source: <Dataset> Program Name: <Pgm name>

Repeat as 14.1.1.2 for Enrolled Subject.

Table 14.1.1.3
Analysis Population and Exclusions
All Subjects

Number of Subjects	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Enrolled	xx	xx	xx
Randomized	xx	xx	xx
Included in Safety Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reasons for Exclusion from Safety Population			
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Included in Full Analysis Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reasons for Exclusion from Safety Population			
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Included in Per Protocol Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reasons for Exclusion from Per Protocol Population			
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Did not receive randomized therapy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

NOTE: The percentages are based on the number of randomized subjects.

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Source: <Dataset>

Table 14.1.2.1
Summary of Protocol Deviations (PD)/Violations (PV)
mITT Population

Deviation/Violation	PD/PV	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Description of Violation/deviation	"PD" or "PV"	n (%) xx	n (%) xx	n (%) xx

N: Number of Patients
Xx: Number of deviations/violations

Source: <Dataset>

Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

Repeat for Safety Population

Table 14.1.3.1
Summary of Demographic and Baseline Characteristics
mITT Population

Variable	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Age	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)

Variable	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Sex				
Male	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity				
Hispanic or Latino	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Hispanic or Latino	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race				
American Indian or Alaskan Native	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black or African American	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
White	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

Source: <Dataset>

Repeat for PP and Safety population

Table 14.1.4.1
Summary of Vital Signs,
mITT Population

Visit	Vital Sign	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Baseline	Height	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Weight	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Temperature	N	xx	xx	xx

Visit	Vital Sign	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
					xx.x
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	(xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Heart Rate	N	xx	xx	xx
					xx.x
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	(xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Systolic BP	N	xx	xx	xx
					xx.x
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	(xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Diastolic BP	N	xx	xx	xx
					xx.x
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	(xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for every visit showing Change from Baseline					

Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

CRF pages 05-06

Source: <Dataset>

Repeat for PP and Safety population

Table 14.1.5.1
Summary of Physical Examination,
mITT Population

Visit	Physical Examination	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Baseline	Height	N	xx	xx	xx

Visit	Physical Examination	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Weight	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	General Appearance				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Heart Cardiovascular				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Lungs				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Gastrointestinal				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Ear/Nose/Throat				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Extremities				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Skin				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Repeat for every week					

CRF pages 05-06 Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for PP and Safety populations

Table 14.1.6
Summary of Study Drug Accountability: Dose Dispensed & Collected by Visit
Safety Population

Weight of the Dose	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Dose Dispensed	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
	CV	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for Dose Collected				
Total Dose Dispensed	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
	CV	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for Total Dose Collected				

N: Number of Patients
Means, SD, Median, Min, and Max in Grams.

CRF pages 28-30
Source: <Dataset>

Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

Table 14.1.7.1
Summary of Study Drug Compliance
Safety Population

	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Number of Subjects with Compliance				
Yes	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
If No, Applications Missed				
Missed Applications	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
	CV	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x

	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Applications: Number of applications per patients/day (expected 4 Pumps twice a Day)

Compliance: The expected amount of study drug used per week is approximately 7.84 g/week for 8 sprays/application per day

CRF pages 30

Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Table 14.1.7.2
Summary of Percent Compliance based on Cumulative Net Weight of Study Drug
Safety Population

	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Cumulative Net Weight of Study Drug				
	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
	CV	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Percent Compliance greater than 50%				
Yes	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Applications: Number of applications per patients/day (expected 4 Pumps twice a Day)

The cumulative amount of study drug exposure will be estimated by calculating the difference between the weight of the 2 bottles of drug at the time the drug was dispensed at Baseline/Week 4 and the weight of the 2 bottles at Week 4/Week 8. Differences will be summed together.

% Compliance: The net weight of study drug divided by 1.12g /Day * Number of Days in the Study

CRF pages 30

Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Table 14.1.8
Summary of Prior Medications,
Safety Population

WHO-DD ATC Class Level 1 WHO-DD ATC Class Level 2 WHO-DD Preferred Term	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Number of subjects with at least one prior medication	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			
WHO-DD ATC Class Level 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			

NOTE: The percentages are based on the number of Safety Population.

CRF page 11
Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Table 14.1.9
Summary of Concomitant Medications,
Safety Population

WHO-DD ATC Class Level 1 WHO-DD ATC Class Level 2 WHO-DD Preferred Term	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Number of subjects with at least one concomitant medication	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			
WHO-DD ATC Class Level 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages 12-13
Source: <Dataset>

Program Name: <Pgm name>

Table 14.1.10
Summary of Medical History
Safety Population

WHO-DD SOC WHO-DD Preferred Term	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Number of subjects with at least one Medical History	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD SOC	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages
Source: <Dataset>

Program Name: <Pgm name>

Table 14.1.11
Summary of Substance Abuse
Safety Population

	Statistics	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Total Number of Substance Abuse	n	xx	xx	xx
		xx	xx	xx
		xx	xx	xx
Number of Subjects with Substance Abuse History	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		xx (xx.x)	xx (xx.x)	xx (xx.x)

		xx (xx.x)	xx (xx.x)	xx (xx.x)

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages
Source: <Dataset>

Program Name: <Pgm name>

Table 14.1.12
Summary of Diary Details
Safety Population

	Statistics	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Number of Subjects with diary Dispensed	n	xx	xx	xx
Number of Subjects with diary Collected	n	xx	xx	xx
		xx	xx	xx
Number of Subjects with Sunscreen use	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Subjects with Makeup use	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages
Source: <Dataset>

Program Name: <Pgm name>

10.1.2 Efficacy

Display Number	Title	Population	Unique/Repeat
14.2.1.1	Change from baseline in IGA score by Visit	mITT	Unique
14.2.1.2	Change from baseline in IGA score by Visit	PP	Repeat
14.2.2.1	Change from baseline in CEA score by Visit	mITT	Repeat
14.2.2.2	Change from baseline in CEA score by Visit	PP	Repeat
14.2.3.1	Change from baseline in PSA score by Visit	mITT	Repeat
14.2.3.2	Change from baseline in PSA score by Visit	PP	Repeat
14.2.4.1	Summary of Change from baseline in Skindex 16 score by Visit	mITT	Unique
14.2.4.2	Summary of Change from baseline in Skindex 16 score by Visit	PP	Repeat
14.2.5	Summary of Sensitivity Analysis	mITT	Unique
14.2.6.1	Summary of 2-grade improvement in IGA score from baseline to the end of treatment (Week 8).	mITT	Unique
14.2.6.2	Summary of 2-grade improvement in IGA score from baseline to the end of treatment (Week 8).	PP	Repeat
14.2.7.1	Summary of 2-grade improvement in CEA score from baseline to the end of treatment (Week 8).	mITT	Repeat
14.2.7.2	Summary of 2-grade improvement in CEA score from baseline to the end of treatment (Week 8).	PP	Repeat
14.2.8.1	Summary of Treatment success with IGA score of 0/1 from Baseline to End of Treatment.	mITT	Unique
14.2.8.2	Summary of Treatment success with IGA score of 0/1 from Baseline to End of Treatment.	PP	Repeat
14.2.9.1	Summary of Treatment success with CEA score of 0/1 from Baseline to End of Treatment.	mITT	Repeat
14.2.9.2	Summary of Treatment success with CEA score of 0/1 from Baseline to End of Treatment.	PP	Repeat

Table 14.2.1.1
Change from baseline in IGA Score by Visit.
mITT Population

Visit	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Week 1			
Change from Baseline			
1-grade	n (%)		
2-grade	n (%)		
3-grade	n (%)		
Repeat for all the visits			

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for CEA and PSA for mITT & PP population.

Table 14.2.4.1
Summary of Change from baseline in Skindex 16 score by Visit
mITT Population

Visit	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Baseline			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
CV	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Change from Baseline at Week 1			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
CV	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for All weeks			
Final Analysis for Week 12			
Differences of LS Means			x.xxxx

SE	x.xxxx
CI	(x.xxxx, x.xxxx)
P-value	x.xxxx

SE: Standard Error of the LS Means
P- Value: Probability of Change from Baseline at Week 12

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for PP population.

Table 14.2.5
Summary of Sensitivity Analysis for the Absolute Scores of IGA, CEA & PSA
mITT Population

Imputation	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Imputation#1			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Imputation#2			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for all imputations			
Analysis Summary			
Parameter1			xx.x (xx.xxx)
Mean (SD)			x.xx, x.xx
CI			x.xxx
P-Value			
Parameter2			
Parameter3			

SD: Standard Error of the Parameters
P- Value: Significance of the Parameters effecting the imputation

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Table 14.2.6.1
Summary of 2-grade improvement in IGA score from baseline to the end of treatment (Week 8).
mITT Population

	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Subjects with 2-Grade improvement from Baseline to Week 8	n (%)	n (%)	n (%)
Risk Difference			x.xxx
CI			(x.xx, x.xx)
One Sided P-value			x.xxxx

CI: Confidence Interval
P-value: Probability of Superiority from the Placebo

Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for PP Population and for CEA (mITT & PP).

Table 14.2.8.1
Summary of Treatment success with IGA score of 0 or 1.
mITT Population

	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Subjects with IGA Score of 0/1 at End of Treatment	n (%)	n (%)	n (%)
CI			(x.xx, x.xx)
P-value			x.xxxx

CI: Confidence Interval
P-value: Probability of achieving Treatment Success defined as a score of 0/1.

Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for PP Population and for CEA (mITT & PP)

10.1.3 Safety

Display Number	Title	Population	Unique/Repeat
14.3.1	Overall Summary of Treatment Emergent Adverse Events	Safety	Unique
14.3.1.1	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety	Unique
14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity	Safety	Repeat
14.3.1.3	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug	Safety	Repeat
14.3.2	Summary of Serious Adverse Events by System Organ Class and Preferred Term	Safety	Repeat
14.3.3	Summary of Deaths	Safety	Unique

Table 14.3.1
Overall Summary of Treatment Emergent Adverse Events.
Safety Population

	Statistics	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Total Number of TEAEs	N	xx	xx	xx
Total Number of TESAEs	N	xx	xx	xx
Number of Subjects with:				
At Least One TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Related TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Severe (Grade 3) TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TEAE Leading to Discontinuation	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TEAE Leading to Death	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TESAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Related TESAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

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

	Statistics	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Total Number of TEAEs	n	xx	xx	xx
Number of Subjects with at Least One TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.				
System Organ Class #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.				

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

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

	Statistics	Severity	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Total Number of TEAEs	n	Mild	xx	xx	xx
		Moderate	xx	xx	xx
		Severe	xx	xx	xx
		Total	xx	xx	xx
Number of Subjects with at Least One TEAE	n (%)	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)

System Organ Class #1	n (%)	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.					

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

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

	Statistics	Relationship	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Total Number of TEAEs	n	Not Related	xx	xx	xx
		Related	xx	xx	xx
		Total	xx	xx	xx
Number of Subjects with at Least One TEAE	n (%)	Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class #1	n (%)	Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.					

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Table 14.3.2
Summary of Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

	Statistics	Relationship	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Total Number of SAEs	n	Yes	xx	xx	xx
		No	xx	xx	xx
		Total	xx	xx	xx
Number of Subjects with at Least One SAE	n (%)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
		No	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class #1	n (%)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
		No	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
		No	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.					

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Table 14.3.3
Summary of Deaths
Safety Population

	Statistics	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Number of deaths	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related to disease under study	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
AE outcome = death	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related to disease under study and AE outcome = death	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

10.2 APPENDIX B: Listings

Display Number	Title	Population
Listing 16.2.1.1	Subject Enrollment and Disposition by Study Site	All Subjects
Listing 16.2.1.2	Protocol Deviations (PD)/Violations (PV)	Randomized
Listing 16.2.1.3	Demographic Characteristics	Randomized
Listing 16.2.1.4	Vitals Signs by Subject and Visit	Safety
Listing 16.2.1.5	Physical Examination by Subject	Safety
Listing 16.2.1.6	Drug Exposure and Compliance	Safety
Listing 16.2.1.8	Prior Medications	Safety
Listing 16.2.1.9	Concomitant Medications	Safety
Listing 16.2.2.1	IGA score by Subjects and Visits	Randomized
Listing 16.2.2.2	CEA score by Subjects and Visits	Randomized
Listing 16.2.2.3	PSA score by Subjects and Visits	Randomized
Listing 16.2.2.4	Skindex-16 score by Subjects and Visits	Randomized
Listing 16.2.3.1	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, Severity and Relationship to Study Drug	Safety
Listing 16.2.3.2	Serious Adverse Events by System Organ Class and Preferred Term	Safety
Listing 16.2.3.3	Deaths	Safety
Listing 16.2.4.1	Hematology Parameters	Safety
Listing 16.2.4.2	Clinical Chemistry Parameters	Safety
Listing 16.2.4.3	Urinalysis Parameters	Safety
Listing 16.2.4.4	Serology Parameters	Safety

10.3 APPENDIX C: Figures

Display Number	Title	Population
Figure 14.2.1.1	Frequency table Change from baseline for IGA score by Visit	mITT
Figure 14.2.1.2	Frequency table Change from baseline for IGA score by Visit	PP
Figure 14.2.2.1	Frequency table Change from baseline for CEA score by Visit	mITT
Figure 14.2.2.2	Frequency table Change from baseline for CEA score by Visit	PP
Figure 14.2.3.1	Frequency table Change from baseline for PSA score by Visit	mITT
Figure 14.2.3.2	Frequency table Change from baseline for PSA score by Visit	PP
Figure 14.2.4.1	Box Plot of Skindex16 score by Visit	mITT
Figure 14.2.4.2	Box Plot of Skindex16 score by Visit	PP
Figure 14.2.8.1	Bar Plot for Treatment Success (0/1) for IGA score at Week 12	mITT
Figure 14.2.8.2	Bar Plot for Treatment Success (0/1) for IGA score at Week 12	PP
Figure 14.2.9.1	Bar Plot for Treatment Success (0/1) for CEA score at Week 12	mITT
Figure 14.2.9.2	Bar Plot for Treatment Success (0/1) for CEA score at Week 12	PP

STATISTICAL ANALYSIS PLAN
PHASE II

VERSION: 2.0

DATE:

April 02, 2019

BASED ON:

Protocol Version 4.0 Date:07-Jan-19

Data Management Plan Final Version 1.0 Date: 12-Apr-18

Study Drug:

B244 Topical application

Protocol Number:

RB244-001

Study Title:

Vehicle-Controlled, Double-Blind, Randomized Phase II Study of B244 Delivered as a Topical Spray to Determine Safety and Efficacy in Subjects with Mild to Moderate Rosacea.

Sponsor:

AOBiome, LLC

125 Cambridgepark Drive

Cambridge, MA 02140

STATISTICAL ANALYSIS PLAN REVIEW AND APPROVAL

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

Prepared by:

Rahul Paul Choudhury, Lead Bio-Statistician — 30 APR 2019 — Date

Statistical Review:

Jose Nabue, Sr. Specialist Bio-Statistician — 02 May 2019 — Date

Sponsor Review:

Judith Ng-Cashin, M.D, Chief Medical Officer — 2 MAY 2019 — Date

Spiros Jamas, Sc. D., SVP of Therapeutic Development — 2/May/2019 — Date

PROTOCOL SYNOPSIS

Study Title	A Vehicle-Controlled, Double-Blind, Randomized Phase II Study of B244 Delivered as a Topical Spray to Determine Safety and Efficacy in Subjects with Mild to Moderate Rosacea.
Protocol Number	RB244-001
Development Phase	Phase II
Type of Study	Safety Analysis and Superiority of the Study drug over Vehicle
Study Medications	1) B244 Topical Spray (Test formulation), manufactured by AOBiome Therapeutics. 2) Vehicle of test product manufactured by AOBiome Therapeutics.
Name of Active Ingredient	B244
Route of administration	Topical application
Sponsor	AOBiome, LLC,125 Cambridgepark Drive, Cambridge, MA 02140
Study Objectives	**PRIMARY** • To assess the safety and tolerability of B244 applied twice daily (BID) to the face for 8 weeks in subjects with mild to moderate rosacea. **EXPLORATORY** To assess the efficacy of B244 in subjects with mild to moderate rosacea. • Proportion of subjects with IGA improvement at Week 8 relative to baseline • Proportion of subjects with CEA improvement at Week 8 relative to baseline • Change in IGA from Baseline to Week 8 • Change in CEA from Baseline to Week 8 • Proportion of Subjects with improvement in IGA or

	CEA at Week 1, Week 4, and Week 12. • Change in Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8, and Week 12. • Proportion of subjects with change in PSA at Week 1, Week 4, Week 8 and Week 12 from Baseline. • Evaluation of Telangiectasia Score at Baseline/Day1 and Week 8
Study Design	This is a Prospective, Vehicle Controlled, Double Blind, Multicenter, Randomized Phase II trial, comparing the effect of twice daily B244 application for 8 weeks vs. vehicle application on treatment of mild to moderate rosacea. • We will enroll approximately 130 subjects and complete 104 subjects. • At Screening and Baseline: o All subjects must have diagnosis of mild to moderate Rosacea. o Subjects must have IGA score of 2-3 and CEA score of 2-3 to qualify for the study. • After screening and recruitment, participants will be randomized to active or vehicle application for 8 weeks. • Subjects will apply a total of 4 pumps of IP per application to the face twice-a-day • Randomization will be 1:1 B244 to Vehicle. • Subjects will be provided with cleanser and moisturizer to use for the duration of the study • All B244 randomized subjects will be treated at the dose of $4x10^9$ cells/ml via spray application • Screening period will occur at Days -21 to -1 • Washout will occur after Screening visit (Days - 14 to -1) • Randomization will occur during the baseline visit for the study Efficacy will be assessed using Investigator Global Assessment (IGA) score, Clinician's Erythema Assessment (CEA) score, Patient Self-Assessment (PSA) score and patient reported Skindex 16. • Clinical assessments of response to treatment will be made at Week 1(Day 7), Week 4 (Day 28), and Week 8 (Day 56) • At Baseline visit, subjects will receive a kit containing the drug product. Each bottle will be used for 2 weeks. At Week 4, subjects will return the used bottles from the kit and will be issued a new kit of drug product to be used from Week 4 through Week 8. • Subjects will stop applying investigational product at Week 8 and will return investigational product at that visit.

	• Subjects will come back for a 4-week posttreatment follow up visit at Week 12 (Day 84). • Participant's safety will be monitored throughout the study. Safety will be assessed by monitoring reported adverse events, vital signs, clinical chemistry and hematology and overall tolerability of the investigational product. • Subjects would be required to discontinue the investigational product under the following circumstances: o Development of an intercurrent illness that would jeopardize the safety, or significantly affect assessments of clinical status of a subject o Either at the discretion of the Investigator or at the participant's request o Development of any investigational product-related SAE o Suspected or laboratory-confirmed pregnancy
Number of Subjects and Sites	Approximately 130 subjects are planned to be enrolled, and assuming a 20% drop out rate, the planned overall sample size for this clinical trial is approximately 104 adult male and female subjects, 18 years of age and older with mild to moderate rosacea. Subjects will be randomized at a 1:1 ratio (B244: vehicle) at about 8 clinical research centers in the United States.
Eligibility Criteria	INCLUSION CRITERIA • Male and female subjects ≥18. • A clinical diagnosis of mild to moderate facial rosacea. • In good general health as determined by a thorough medical history, physical examination, clinical chemistry and hematology. • A Clinician Erythema Assessment (CEA) score of 2-3 at Screening and at Baseline Visits (prior to the investigational product application). • Mild to Moderate IGA score of 2-3 at Screening and at Baseline Visits (prior to the investigational product application). • Willing to refrain from using any topical or systemic treatments for the treatment of rosacea, other than the investigational product. • Females of childbearing potential with a negative urine pregnancy test (UPT) at Screening and Baseline/Day 1 (prior to the investigational product application). • Ability to comprehend and comply with study procedures. • Agree to commit to participate in the current protocol.

	• Provide written informed consent prior to any study procedure being performed. EXCLUSION CRITERIA Any subject who meet one or more of the following criteria are excluded from this study. • Female subjects who are pregnant, lactating or who are trying to conceive will be excluded from participation in this study. • Any uncontrolled chronic or serious disease or medical condition that would normally prevent participation in a clinical trial, or, in the judgment of the Investigator, would put the subject at undue risk, or might confound the study assessments (e.g., other dermatological diseases), or might interfere with the subject's participation in the study, (e.g., planned hospitalization during the study). • Particular forms of rosacea (e.g., rosacea conglobata, rosacea fulminans, isolated rhinophyma, isolated pustulosis of the chin, Ocular rosacea Phymatous rosacea, Steroid-induced rosacea, severe rosacea including pyoderma faciale) or other concomitant facial dermatoses that are similar to rosacea such as peri-oral dermatitis, demodicidosis, facial keratosis pilaris, seborrheic dermatitis, acute lupus erythematosus, or actinic telangiectasia. • Presence of three (3) or more facial inflammatory lesions of rosacea. • Any skin condition which in the investigator's opinion may interfere with the evaluation of rosacea. • Severe papulopustular rosacea requiring systemic treatment. • Participation at the time of eligibility assessment (Screening) in any other investigational drug or device study or may have participated within 30 days prior to Screening. • Commencement of new hormonal therapy or dose change to hormonal therapy within 90 days prior to baseline. Dose and frequency of use of any hormonal therapy started more than 90 days prior to baseline must remain unchanged throughout the study. Hormonal therapies include, but are not limited to, oral, injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS) or other forms of hormonal contraception that have comparable efficacy (e.g. vaginal ring or transdermal hormone contraception).

- Presence of beard or excessive facial hair at Screening which would interfere with the study treatments or study assessments and refusal to remove for duration of study.
- Current treatment with monoamine oxidase (MAO) inhibitors, barbiturates, opiates, sedatives, systemic anesthetics, or alpha-agonists.
- Carcinoid, Pheochromocytoma or other systemic causes of flushing.
- Known sensitivity to B244 or its components.
- Refusal to submit to blood and urine sampling for laboratory analysis.
- Treatment with the following:

Prohibited Topical Treatments:

Topical Treatment	Prohibited Time Frame prior to Baseline
Astringents or abrasives	2 days
RHOFADE™ (oxymetazoline HCl) Cream,1%	1 week
Bleach baths	1 week
Mirvaso (brimonidine) topical cream	1 week
Vinegar	1 week
Topical Prescription/OTC medications for treatment of acne	1 week
Soolantra (Ivermectin 1%) topical cream	1 week
Topical Antibiotic	2 weeks
Use of over the counter antimicrobial	2 weeks
Benzoyl Peroxide	2 weeks
Immunomodulators	4 weeks
Oracea (doxycycline) topical cream	2 weeks
Corticosteroids	4 weeks
Electrocoagulation, Dermabrasion; Facial peels	4 weeks
Dermatologic/surgical procedure on the face	4 weeks
Topical Prescription medications for the treatment of rosacea (e.g. azelaic acid, metronidazole, etc.)	4 weeks
Laser, Phototherapy, Photodynamic Therapy or IPL (intense pulsed light) treatment	4 weeks

	Prescription or over the counter topical retinoid use on the face (e.g., tretinoin, tazarotene, adapalene) — 4 weeks

Prohibited Systemic Treatments:

Topical Treatment	Prohibited Time Frame prior to Baseline
Exposed to excessive ultraviolet (UV) radiation and/or subject was unwilling to refrain from excessive exposure to UV radiation during the course of the study.	1 week
Prescription anti inflammatory	2 weeks
Prescription/OTC anti-inflammatory medications (excludes low dose aspirin)	2 weeks
Systemic Antibiotics	4 weeks
Prescription medications for the treatment of rosacea (e.g. doxycycline, tetracycline, macrolides)	4 weeks
Prescription medications for treatment of acne	4 weeks
Corticosteroids (oral or injectable)	4 weeks
Immunomodulators	12 weeks
Oral retinoid use (e.g., isotretinoin), vitamin A supplements greater than 10,000 units/day	6 months

Withdrawal and Early Discontinuation	A subject may voluntarily withdraw from the study at any time and for any reason without prejudice to his or her future medical care. The Investigator, Sponsor, or Medical Monitor may also withdraw a subject at any time if it is medically necessary or in the interest of subject's safety. If a subject discontinues prematurely, the Investigator will perform Early Termination (ET) visit, capturing the reason for discontinuation. Further details are provided in section 5.2 & 5.3 of the Protocol RB244-001 v4.0.
Prohibited Concomitant Medication	Prohibited Therapies are those medicinal products and treatment methods that are not allowed during the study period and within the timeframes specified in the section 8.1 of the Protocol RB244-001 v 4.0.
Study Drug	Study drug includes Test and Placebo drug products. The Sponsor will supply study drug as matching 30ml/bottle, labeled for a blinded study. • Test Drug: B244, 30ml/bottle (AOBiome, LLC) • Placebo: Vehicle, 30ml/bottle (AOBiome, LLC)

Duration of Patient Study Participation	Up to 84 ± 2 days
Study Endpoints	**PRIMARY** • The primary safety endpoint is to assess the safety and tolerability of B244 applied twice daily (BID) to the face for 8 weeks in subjects with mild to moderate rosacea based on the number of AE & SAE. **EXPLORATORY** To assess the efficacy of B244 in subjects with mild to moderate rosacea. • Change of IGA score at Baseline to Week 1, Week 4, Week 8 and Week 12 • Change of CEA score at Baseline to Week 1, Week 4, Week 8 and Week 12. • Change of PSA score at Baseline to Week 1, Week 4, Week 8 and Week 12. • Change of Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8 and Week 12 • IGA treatment success, defined as "clear" or "almost clear" with a 2-grade improvement in IGA score from baseline to the end of treatment. • CEA treatment success, defined as "clear" or "almost clear" with a 2-grade improvement in CEA score from baseline to the end of treatment
Statistical Analysis	**SAFETY ANALYSIS** The reporting of safety data is descriptive (arithmetic mean, standard deviation (SD), coefficient of variation (CV), median, minimum, and maximum) will be calculated for quantitative safety data as well as for the difference from baseline, when appropriate. The analysis will include all subjects who receive at least one dose of investigational product. The variables for safety endpoints are AEs, Local Application Site Reactions, vital signs measurements, clinical chemistry and hematology. AEs will be summarized based on the frequency of AEs and their severity for all treated subjects. All AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA) and summarized by treatment group. Data will be summarized using preferred term and primary system organ class, including verbatim term, dose level, severity, and relationship to treatment, will be provided.

	Concomitant medications will be listed by treatment and coded using the most recent version of the World Health Organization (WHO) Drug Dictionary (DD). **EFFICACY ANALYSIS** The Evaluable Period for the outcome variables will be weeks 1, 4, 8 and 12. The superiority of the drug over the vehicle will be tested at week 8 based on the probability of improvement from baseline with a continuity-corrected Z-tests comparing the change from baseline of treatments vs Placebo. For all other evaluable periods, descriptive statistics for the change from baseline will be shown. The change from baseline score of Skindex-16 will be compared among treatments at Week 12 using an ANOVA.

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1 LIST OF ABBREVIATION

Abbreviation	Full Form
AE	Adverse Event
AOB	Ammonia-Oxidizing Bacteria
BID	Bis in Die (twice a day)
BP	Blood Pressure
CEA	Clinician Erythema Assessment
CRA	Clinical Research Associate
CI	Confidence Interval
CRF	Case Report Form
CTMF	Clinical Trial Master File
CTP	Clinical Trial Protocol
eCRF	Electronic Case Report Form
EOS	End of Study
ET	Early Termination
ETR	Erythematotelangiectatic rosacea
GCP	Good Clinical Practice
IB	Investigator's Brochure
ICH	International Conference On Harmonization
IEC	Independent Ethics Committee
IGA	Investigator Global Assessment
IGE	Investigator's Global Evaluation
IP	Investigational Product
IPL	Intense Pulsed Light
IRB	Institutional Review Board
ISF	Investigator Site File
IUD	Intrauterine Device
IUS	Intrauterine system
IWRS	Interactive Web Response System
LOCF	Last Observation Carried Forward
mITT	Modified Intent-To-Treat
NSAID	Nonsteroidal Anti-inflammatory Drug
OTC	Over the Counter
PP	Per-Protocol
PRN	Pro Re Nada (as needed)
PRN	Pro Re Nada (as needed)
PSA	Patient Self-Assessment
RR	Relative Risk
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SI	Simple Imputation
SOP	Standard Operating Procedures
SUSAR	Suspected Unexpected Serious Adverse Reactions
TEAE	Treatment Emergent Adverse Event

ULN	Upper Limit of Normal Range
UPT	Urine Pregnancy Test
UV	Ultraviolet
WBC	White Blood Cell Count

2 INTRODUCTION

This document describes the statistical methods and data presentations to be used in the summary and analysis of data from Protocol RB244-001. Background information is provided for the overall study design and objectives. The reader is referred to the study protocol and electronic case report forms (eCRFs) for details of study conduct and data collection.

2.1 Study Overview

The proposed study is aimed to evaluate the safety and efficacy of B244 topical spray. A Vehicle-Controlled, Double-Blind, Multicenter, Randomized Study Design has been Selected to Evaluate the Safety and Efficacy of the B244 Investigational product in the Treatment of Mild-to-Moderate Rosacea.

There is no cure for rosacea and treatment is aimed at alleviating the symptoms. Topical or oral medications are generally prescribed for mild to moderate papulopustular rosacea. These topical medications include: metronidazole, azelaic acid, sodium sulfacetamide and sulfur, erythromycin, and tretinoin8. Currently these approved topical medications may cause local irritation to the skin. The oral medications prescribed for severe disease include tetracycline, doxycycline, minocycline, erythromycin and metronidazole. The systemic therapies may result in systemic adverse events such as gastrointestinal upset and photosensitivity.

It is believed, that topical application of Ammonia-Oxidizing Bacteria (AOB) will reduce survival of pathogenic bacteria present on the skin and thus improve rosacea symptoms in those affected by it. B244 is being developed as a ‘live topical’ to provide a natural source of AOB and NO/NO2 to the human skin.

This is a Prospective, Vehicle Controlled, Double Blind, Multicenter, Randomized Phase II trial, Comparing the effect of twice daily B244 application for 8 weeks vs. vehicle application on treatment of mild to moderate rosacea. At Screening and Baseline all subjects must have clinical diagnosis of mild to moderate rosacea and subjects must have IGA score of 2-3 and CEA score of 2-3 to qualify for the study.

After screening and recruitment, participants will be randomized to active or vehicle application for 8 weeks. Subjects will apply a total of 4 pumps of IP per application to the face twice-a-day. Subjects will be provided with cleanser and moisturizer to use for the duration of the study. All B244 randomized subjects will be treated at the dose of $4x10^9$ cells/ml via spray application.

Efficacy will be assessed using Investigator Global Assessment (IGA) score, Clinician’s Erythema Assessment (CEA) score, Patient Self-Assessment (PSA) score and patient reported Skindex 16. Participant's safety will be monitored throughout the study. Safety

will be assessed by monitoring reported adverse events, vital signs, clinical chemistry and hematology and overall tolerability of the investigational product.

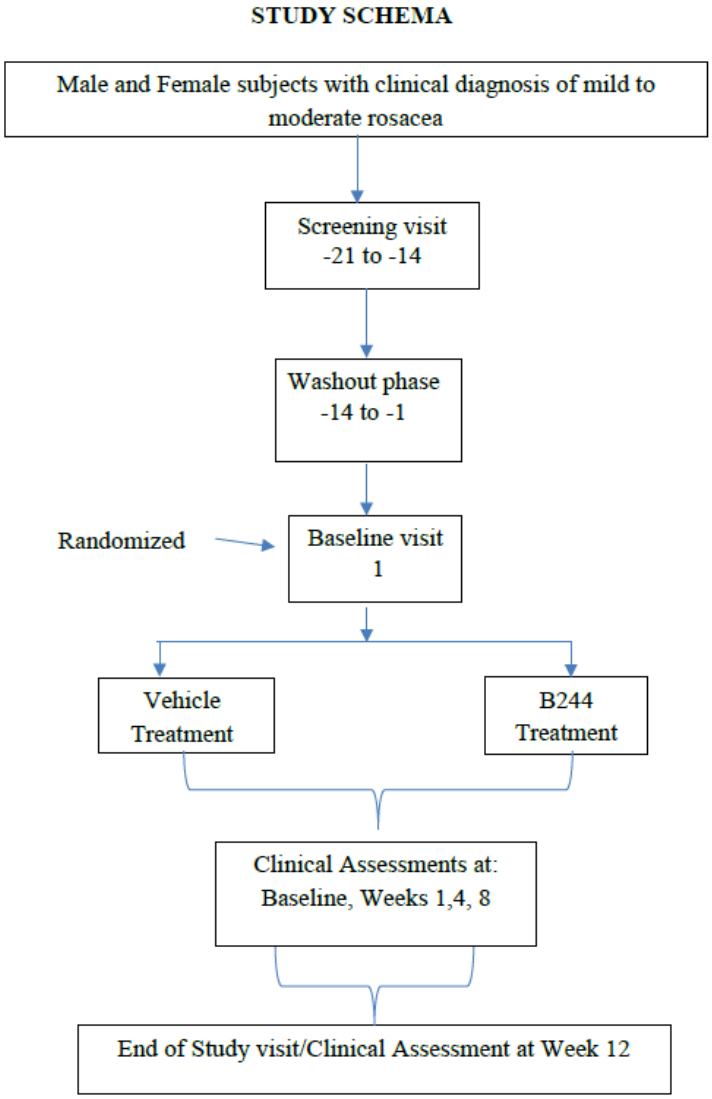
Approximately 130 subjects are planned to be enrolled, and assuming a 20% drop out rate, the planned overall sample size for this clinical trial is approximately 104 adult male and female subjects, 18 years of age and older with mild to moderate rosacea. Subjects will be randomized at a 1:1 ratio (B244: Vehicle) at about 8 clinical research centers in the United States.

The entire study will consist of a total of 6 visits:

- Visit 1(Day -21 to -1): Screening will occur at Days -21 to -1, followed by Washout (Days -14 to -1).
- Visit 2(Baseline/ Day 1): Randomization will occur during the baseline visit for the study (Day 1).
- Visit 3 – 5(Day 7 ± 2 [Week 1], Day 28 ± 2 [Week 4], Day 56 ± 2 [Week 8]): Clinical assessments of response to treatment will be made at Week 1(Day 7), Week 4 (Day 28), and Week 8 (Day 56).
- Visit 6(Day 84 ± 2): Subjects will come back for a 4-week post-treatment follow up visit at Week 12 (Day 84).

2.2 Study Flowchart

Figure 1. Study Flowchart



2.3 Schedule of Activities

Table 1: Schedule of Study Activities

Visit Name	Screening	Baseline/ DAY 1	Week 1	Week 4	Week 8	Week 12/ End of Study Visit	Early Termination Visit
Visit number	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	
Visit window in days	**-21 to -1**	**1**	**7+/-2**	**28 +/- 2**	**56 +/- 2**	**84 +/- 2**	
Informed Consent	X						
Inclusion/Exclusion Criteria	X	X					
Demographics	X						
Medical History	X	X					
Concomitant Medications	X	X	X	X	X	X	X
Physical Exam	X	X				X	X
BP & Pulse[2]	X	X	X	X	X	X	X
Urine pregnancy test for WOCBP[1]	X	X	X	X	X	X	X
Clinical chemistry and hematology and urinalysis[3]	X	X		X	X		X
Biomarkers[4]		X			X		X
CEA	X	X	X	X	X	X	X
IGA	X	X	X	X	X	X	X
Skindex 16	X	X	X	X	X	X	X
PSA score	X	X	X	X	X	X	X
Telangiectasia Evaluation		X			X		X
Fitzpatrick skin type	X						
IWRS		X		X			
Dispense Investigational product to Subject [5/6]		X		X			
Collect Investigational product from Subject[5]				X	X		X

Visit Name	Screening	Baseline/ DAY 1	Week 1	Week 4	Week 8	Week 12/ End of Study Visit	Early Termination Visit
Visit number	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	
Visit window in days	**-21 to -1**	**1**	**7+/-2**	**28 +/- 2**	**56 +/- 2**	**84 +/- 2**	
Investigational product Compliance[5]		X		X	X		X
Study Cleanser and moisturizer dispensation[9]		X		X			
Study Cleanser and moisturizer collection					X		X
Study Diary[8]		X	X	X	X		X
Study Counseling[7]		X	X	X	X		
AE Collection and Assessment	X	X	X	X	X	X	X

1. Urine pregnancy test for WOCBP will be done at every visit.
2. Blood pressure readings will be obtained at every visit. Subject should be allowed to rest for more than 5 minutes sitting, then BP measurements and pulse (x3) will be performed, using the non-dominant arm with a calibrated electronic sphygmomanometer. The average of the second and third readings will be documented.
3. Subjects should fast for at least 8 hours before the test. Laboratory work includes: hematology and Lipid Panel, Albumin, Alkaline Phos, ALT, AST, Total Bilirubin, BUN, BUN: Creatinine ratio, Calcium, Chloride, Creatinine, eGFR, Glucose, Potassium, Sodium, Uric Acid, and urinalysis. HIV Ab, HCV Ab, HBsAg. will only be done at screening.
4. Subjects should fast for at least 8 hours before the test.
5. Weight of the investigational product kit will be obtained at the Baseline visit. Study staff will be asked to weigh all dispensed bottles without the carton box PRE- FIRST DOSE. Weight will be recorded in grams.
6. Subjects will be asked to bring all dispensed bottles back for the Week 4 and Week 8 visits. Upon return for the study visit, all bottles will be weighed again without the carton box. Subjects will be asked to apply the investigational product twice daily. First investigational product application will happen at the site under medical supervision.
7. Subjects will be counseled on the use of study medication and answer any questions subject may have.
8. Subjects will be asked to fill out study diary for the duration of the study.
9. Cleanser and moisturizer will be dispensed at the Baseline visit. Subjects will be asked to refrain, if possible, from using any other cleanser and/or moisturizer on their face and apply the provided product while they are participating in the trial. Any leftover moisturizer /cleanser will be collected at Week 8 visit, at which point subjects will be asked to go back to their regular routine.

3 STUDY OBJECTIVE AND ENDPOINTS

3.1 Study Objectives

3.1.1 Primary Objective

To assess the safety and tolerability of B244 applied twice daily (BID) to the face for 8 weeks in subjects with mild to moderate rosacea.

3.1.2 Exploratory Objectives

To assess the efficacy of B244 in subjects with mild to moderate rosacea.

- Proportion of subjects with IGA improvement at Week 8 relative to baseline.
- Proportion of subjects with CEA improvement at Week 8 relative to baseline.
- Change in IGA score from Baseline to Week 8.
- Change in CEA score from Baseline to Week 8.
- Proportion of Subjects with improvement in IGA or CEA at Week 1, Week 4, and Week 12.
- Change in Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8, and Week 12.
- Proportion of subjects with change in PSA at Week 1, Week 4, Week 8 and Week 12 from Baseline.
- Evaluation of Telangiectasia Score at Baseline/Day 1 and Week 8

3.2 Study Endpoints

3.2.1 Safety & Tolerability (Primary)

Safety and tolerability endpoints will consist of all adverse events reported during the study duration.

3.2.2 Efficacy (Exploratory)

- Change of IGA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of CEA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of PSA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8 and Week 12.
- IGA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in IGA score from baseline to the end of treatment.
- CEA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in CEA score from baseline to the end of treatment.

4 STUDY DESIGN

4.1 Summary of Study Design

This is a Prospective, Vehicle Controlled, Double Blind, Multicenter, Randomized Phase II trial, Comparing the effect of twice daily B244 application for 8 weeks vs. vehicle application on treatment of mild to moderate rosacea. We will enroll approximately 130 subjects and complete 104 subjects.

At Screening and Baseline, all subjects must have clinical diagnosis of mild to moderate rosacea and must have IGA score of 2-3 and CEA score of 2-3 to qualify for the study. After screening and recruitment, participants will be randomized to active or vehicle application for 8 weeks. Subjects will apply a total of 4 pumps of IP per application to the face twice-a-day. Randomization will be 1:1 B244 to Vehicle. Subjects will be provided with cleanser and moisturizer to use for the duration of the study. All B244 randomized subjects will be treated at the dose of $4x10^9$ cells/ml via spray application. Screening will occur at Days -21 to -1. Washout will occur after Screening visit (Days -14 to -1) and randomization will occur during the baseline visit for the study (Day 1).

Efficacy will be assessed using Investigator Global Assessment (IGA) score, Clinician's Erythema Assessment (CEA) score, Patient Self-Assessment (PSA) score and patient reported Skindex 16. Clinical assessments of response to treatment will be made at Week 1(Day 7), Week 4 (Day 28), and Week 8 (Day 56). At Baseline visit, subjects will receive a kit containing the drug product. Each bottle will be used for 2 weeks. At Week 4, subjects will return the used bottles from the kit and will be issued a new kit of drug product to be used from Week 4 through Week 8. Subjects will stop applying investigational product at Week 8 and will return investigational product at that visit. Subjects will come back for a 4-week post-treatment follow up visit at Week 12 (Day 84). Participant's safety will be monitored throughout the study. Safety will be assessed by monitoring reported adverse events, vital signs, clinical chemistry and hematology and overall tolerability of the investigational product.

Subjects would be required to discontinue the investigational product under the following circumstances:

- Development of an intercurrent illness that would jeopardize the safety, or significantly affect assessments of clinical status of a subject
- Either at the discretion of the Investigator or at the participant's request
- Development of any investigational product-related SAE
- Suspected or laboratory-confirmed pregnancy

4.2 Definition of Study Drugs

Study drug includes Test and Placebo drug products. The Sponsor will supply study drug as matching 30ml/bottle, labeled for a blinded study.

- Test Drug: B244, 30ml/bottle (AOBiome, LLC)
- Placebo: Vehicle, 30ml/bottle (AOBiome, LLC)

4.3 Sample Size Considerations

Approximately 130 subjects are planned to be enrolled, and assuming a 20% drop out rate, the planned overall sample size for this clinical trial is approximately 104 adult male and female subjects, 18 years of age and older with mild to moderate rosacea. Subjects will be randomized at a 1:1 ratio (B244: Vehicle) at about 9 clinical research centers in the United States.

4.4 Study Withdrawal

A subject may voluntarily withdraw from the study at any time and for any reason without prejudice to his or her future medical care. The Investigator, Sponsor, or Medical Monitor may also withdraw a subject at any time if it is medically necessary or in the interest of subject's safety. Additional reasons for premature discontinuation of investigational product may include adverse events and major non-compliance with study procedures, as described below. The withdrawal of a subject from investigational product by the Investigator will be discussed with the Medical Monitor before the subject stops investigational product, whenever possible.

A subject will be discontinued from this study if any of the following criteria are met:

- Withdrawal of consent by the subject is received.
- In the opinion of the Investigator, Medical Monitor or Sponsor, it is not in the subject's best interests to continue in the study.
- Significant non-compliance with study procedures that would interfere with the study results or increase the subject's risks in the study, as determined by the Investigator.
- Development of an intercurrent illness that would jeopardize the safety, or significantly affect assessments of clinical status of a subject.
- Development of any investigational product-related SAE.
- Suspected or laboratory-confirmed pregnancy.

Subjects who discontinued early from the study due to lack of treatment effect after completing at least four weeks of treatment (Day 28) will be included in the mITT and PP population as treatment failures and the change in IGA and CEA from the baseline visit to the last completed visit prior to discontinuation due to lack of efficacy will be carried forward in the primary endpoint analysis. Subjects discontinued early for other reasons will be excluded from the PP population.

4.5 Early Discontinuation

If a subject discontinues prematurely, the Investigator will perform Early Termination (ET) visit, capturing the reason for discontinuation.

If a subject does not return for a scheduled visit, every effort will be made to contact the subject and document the End of Study visit assessments. The Investigator must document the primary reason for discontinuation of a study subject in the source document and on the appropriate electronic case report form (eCRF).

5 PLANNED ANALYSIS

5.1 Final Analysis

Final analysis is planned for the study after the database lock. The final analysis will follow instructions presented in this SAP.

6 GENERAL CONSIDERATION FOR DATA ANALYSIS AND HANDLING

6.1 General Summary Table and Individual Subject Data Listing

Summary tables and listings (e.g., post text tables and individual subject data listings are prepared according to ICH Guideline E3) include a “footer” providing explanatory notes that indicate as a minimum:

- SAS program name.
- Programmer.
- Date of data extraction.
- Date of output generation.

Post text tables also include reference(s) to the subject data listing(s) that supports the summary data. The data extraction date links the output to the archived database that is locked to ensure the replication of the results.

Post text tables will be organized with respect to treatment group and a column will be included to summarize all treated subjects. The order of drug presentation will be investigational drug first followed by the vehicle control. A total column will appear as the last column. The summary tables clearly indicate the number of subjects to which the data apply and unknown or not performed are distinguished from missing data.

Summary tables for medications and medical conditions are coded according the WHO Drug Dictionary. Adverse event preferred terms and body/organ systems are coded using

the MedDRA dictionary. The MedDRA dictionary can be used, as well, in the coding of signs and symptoms, medical history, physical examination abnormalities, and clinical diagnoses.

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

6.2 General Summary Table and Individual Subject Data Listing Considerations

The default convention is to number tables and listings using a decimal system to reflect main levels of unique tables and listings and sub-levels of replicate tables and listings with two digits per level (e.g., Table XX.YY.ZZ. …).

- The first level number should be consistent with the corresponding CSR appendix in which the tables or listings will appear. For example, the post text tables usually occupy Appendix 14 and the individual subject data listings are put in Appendix 16. All post text tables should have a main number level 14 and listings 16. The subject accounting and disposition table is usually first in the first section of the report and should be numbered Table 14.1. The supportive subject data listing would be Listing 16.1. A subset by sex 2. Subject accounting and final disposition should appear as the second level number (Table 14.1 series). Baseline and demographic profile occupy the next sub-level (Table 14.2 series). Efficacy should come next (Table 14.3 series) followed by safety Table 14.4 series). Reasons for subjects' being excluded from efficacy and protocol violation summary tables should appear as the last level (Table 14.5 series). Similar conventions should be applied to the subject data listings.

- The title should be complete, accurate, and concise. The last line of the title should provide the analysis group being summarized (e.g., Intent-to-Treat Subjects or Per-Protocol Efficacy Subjects). If possible, the units of measurement for data contained in the table can appear in parentheses to conserve space in the body of the table. For example, the summary of vital signs title could read "Summary of Sitting and Standing Blood Pressure (mmHg) and Heart Rate (bpm)." Whether in the title or body of a table or listing, units must always be specified for all appropriate data.

- If possible, variables being summarized, and statistics reported should appear in the left most column of a table. The next columns for treatment groups should report the data from left to right for the investigational drug, placebo, comparative agents, and (optional) all treated subjects, respectively.

In general, the listings should be sorted and presented by treatment assignment, investigational site, and subject number. Treatment assignment and site can appear in the banner of the listing. From left to right, the subject number, visit number, visit date, and relative day should appear.

All tables and listings must have explanatory notes that give, as a minimum, data extraction date, output generation date, complete program name and path where it is stored, as appropriate. The definition of all derived variables and decodes for coded data must appear in the notes. Due to space limitations, tables and listings may require a page of notes as a one-time preface to the output.

6.3 Data Management

Biorasi will create SDTM data sets and ADaM analysis data sets using (SAS®) software. Data analyses and summary tables are generated using SAS version 9.4 or above

6.4 Data Presentation Conventions

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

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

- For continuous variables, all mean and median values are formatted to one more decimal place than the measured value. Standard deviation values are formatted to two more decimal places than the measured value. Minimum and maximum values are presented with the same number of decimal places as the measured value.
- For categorical variables, the number and percentage of responses are presented in the form XX (XX.X %) where the percentage is in the parentheses.
- Date variables are formatted as DDMMMYYYY for presentation. Time is formatted in military time as HH:MM for presentation.
- Wherever possible, data will be decimal aligned.
- P-values, if applicable, will be presented to 4 decimal places. If the p-value is less than 0.0001 then it will be presented as <0.0001.

Unless otherwise stated, any statistical tests performed will use 2-sided tests at the 5% significance level.

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

6.5 Analysis Populations

6.5.1 Screen Failures

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

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

6.5.2 Safety Population

The safety population includes all randomized subjects who received investigational product.

6.5.3 mITT Population

A modified intent-to-treat population includes all subjects who are randomized, applied at least one dose of assigned product, and returned for at least one post-baseline evaluation visit.

6.5.4 Per-Protocol (PP) Population

The PP population includes all randomized subjects who met all inclusion/exclusion criteria, were compliant with the assigned study treatment, returned to the study site for the primary endpoint visit within the specified window (±2 days) OR discontinued from the study as a treatment failure, and did not have any major protocol violations.

Subjects who administered at least 50 % of IP, have at least one baseline and post baseline in clinic visit and did not have any major protocol violations.

Subjects who discontinued early from the study due to lack of treatment effect after completing at least eight weeks of treatment should be included in the mITT and PP population as treatment failures and the change in IGA and CEA from the baseline visit to the last completed visit prior to discontinuation due to lack of efficacy should be carried forward in the primary endpoint analysis. Subjects discontinued early for other reasons should be excluded from the PP population but included in the mITT population.
The results in the mITT population will be considered definitive for superiority of each active treatment to vehicle with those in the PP population considered supportive. Safety analyses will be performed using the Safety population.

6.6 Baseline Definition

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

6.7 Derived and Transformed Data

6.7.1 Baseline Age

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

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

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

6.7.2 Study Day

Day 1 is defined as the day after the baseline when the subject will receive the first dose.

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

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

6.7.3 Multiple Assessments

No multiple assessment for same visit are scheduled.

6.7.4 Handling of Missing Data & Sensitivity Analysis

For the primary and secondary analysis no missing values will be imputed. A sensitivity analysis will be performed by Multiple Imputation Regression Analysis using the following factors: treatment, age, gender, race, baseline IGA, baseline CEA, baseline PSA, smokers/non-smokers and the results of the same variable from previous visits.

6.7.5 Missing Start and Stop Dates for Prior and Concomitant Medication

Start date:

- If start date is completely missing, start date will not be imputed.
- If (year is present, and month and day are missing) or (year and day are present, and month is missing), set month and day to January 1.
- If year and month are present and day is missing, set day to the 1st day of month.

Stop date:

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

6.7.6 Safety Parameters

Safety and tolerability endpoints will consist of all adverse events (AEs) reported during the study duration from the date of randomization through Week 12 (End of Study Visit).

Specific AEs are defined below.

Treatment-Emergent Adverse Events (TEAE): Any AE with onset after the first dose of study medication through 56 days after the last dose of study medication.

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

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

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

6.7.7 Missing Start and Stop Dates for Adverse Events

Start date:

- If start date is completely missing, start date is set to date of first dose.

- If (year is present, and month and day are missing) or (year and day are present, and month is missing):

  If year = year of first dose, then set month and day to month and day of first dose.
  If year < year of first dose, then set month and day to December 31st.
  If year > year of first dose, then set month and day to January 1st.
- If month and year are present and day is missing:

  If year = year of first dose and

  - If month = month of first dose, then set day to day of first dose date.
  - If month < month of first dose, then set day to last day of month.
  - If month > month of first dose, then set day to 1st day of month.

  If year < year of first dose, then set day to last day of month.
  If year > year of first dose, then set day to 1st day of month.

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

- If stop date is completely missing, stop date is set to date of study discontinuation.
- If (year is present, and month and day are missing) or (year and day are present, and month is missing):

  If year = year of study discontinuation, then set month and day to month and day of study discontinuation.
  If year < year of study discontinuation, then set month and day to December 31st.
  If year > year of study discontinuation, then set month and day to December 31st.
- If month and year are present and day is missing:

  If year = year of study discontinuation and

  - If month = month of study discontinuation, then set day to day of study discontinuation date.
  - If month < month of study discontinuation, then set day to last day of month.
  - If month > month of study discontinuation, then set day to last day of month.

  If year < year of study discontinuation, then set day to last day of month.
  If year > year of study discontinuation, then set day to last day of month.

7 DATA ANALYSES

The data analysis will be conducted on all participant data when the trial ends. Subjects will be pooled across all sites. Data will be presented by treatment group and overall. Categorical variables will be summarized by frequency distributions (number and percentages of subjects) and continuous variables will be summarized by descriptive statistics (mean, standard deviation, etc.).

Adverse events will be summarized by treatment group using the Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred term. Separate tabulations will be produced for all treatment-emergent AEs (TEAEs), treatment-related AEs (those considered by the Investigator as at least possibly drug related), SAEs, discontinuations due to AEs, and AEs ≥Grade 3 severity. By-subject listings will be provided for any deaths, SAEs, and AEs leading to discontinuation.

Descriptive statistics for each treatment group will be provided for clinical laboratory values (e.g., hematology, serum chemistry, and urinalysis) and vital signs data, presented as both actual values and changes from baseline relative to each on-study evaluation. Abnormal clinical laboratory values will be listed.

All data will be provided in by-subject listings.

7.1 Subjects Disposition

The subject disposition summary will include the number screened, the number of screen failures, the number enrolled, the number in each patient population for analysis, the number who completed the study, the number who discontinued the study and reason for discontinuation from the study. Disposition data will be summarized by treatment and overall.
A by-subject data listing of study completion information including the reason for study discontinuation will be presented. A by-subject listing of inclusion/exclusion criteria not met will also be presented.

7.2 Protocol Deviations

A summary of all protocol deviations on ITT population by type will be generated. Protocol deviation data will be summarized by treatment and overall. A by-subject data listing of protocol deviations will also be presented.

All protocol deviations will be presented in a data listing.

7.3 Demographic and Baseline Characteristics

Demographic and baseline characteristic data summarization will be performed to descriptively assess the comparability of treatment groups. Data to be tabulated will include age, race, ethnicity, height, weight, and BMI, as well as baseline characteristics related to medical history, including hypertension, diabetes, smoking history.

7.4 Study Drug Exposure

At Baseline visit, Subjects will receive a kit containing (2) two 30 ml white bottles. Each bottle will be used for 2 weeks. At Week 4, subjects will return the used bottles from the kit and will be issued a new kit of two 30mL white bottles to be used from Week 4 through Week 8.

The cumulative amount of study drug exposure will be estimated by calculating the difference between the weight of the 2 bottles of drug at the time the drug was dispensed at Baseline/Week 4 and the weight of the 2 bottles at Week 4/Week 8. Differences will be summed together.

The amount of product used per day will be estimated by dividing the change by the number of days the subject was on treatment. These weights will be compared to the weight of the product that would be used if the subject was compliant with the protocol. Percent compliance will be calculated as follows:

$$\text{Percent compliance} = \left[\frac{\text{Net Weight of Study Drug}}{\text{(1.12g/day*Number of days in the study)} = \text{xx.xx g}} \right] * 100\%$$

The number of days the subject administered study drug, the amount of product used, and the percent compliance will be summarized by treatment group and presented in a by-subject data listing. The subject listing will also include by-visit IP weights. Percent compliance will be calculated only for subjects who returned the study drug at the end of the treatment. In the listing, subjects who withdrew from the study early will be flagged.

7.5 Medical History

A by subject data listing of medical history will be presented. Medical history will be coded using MedDRA v20.0, and the number and percentage of patients experiencing at least 1 such diagnosis by MedDRA System Organ Class (SOC) and preferred term (PT) will be reported.

7.6 Concomitant Medication

Concomitant medications will be coded using the World Health Organization (WHO) dictionary. Results will be tabulated by anatomic therapeutic class (ATC) and preferred term.

This data will be summarized by treatment group. Previous and concomitant medications will be presented in a data listing.

7.7 Vital Signs and Physical Examination

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

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

7.8 Laboratory Data

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

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

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

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

7.9 Visit Windows

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

8 STATISTICAL ANALYSES

8.1 Sample Size Determination

Sample size of 104 randomized 1:1 Active to Vehicle based on 80% power to detect 33% IGA response in Active group versus 10% in the Vehicle group, with two-sided test and alpha =0.05. Until mentioned all alpha value is set at 0.05.

8.2 Safety Analysis

Safety analyses will be conducted using the Safety population

8.2.1 Primary Safety Endpoint

Assess the safety and tolerability of B244 applied twice daily to the face for 8 weeks in subjects with mild to moderate rosacea.

The reporting of safety data is descriptive and will include all subjects who receive at least one dose of investigational product. The variables for safety endpoints are number of subjects with AEs, SAEs, vital signs measurements, clinical chemistry and hematology. AEs will be summarized based on the frequency of AEs and their severity for all treated subjects. All AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA) and summarized by treatment group. Data will be summarized using preferred term and primary system organ class.

If a subject experiences multiple events that map to a single preferred term, the greatest severity and strongest Investigator assessment of relation to investigational product will be assigned to the preferred term for the appropriate summaries. Should an event have a missing severity or relationship, it will be classified as having the highest severity and/or strongest relationship to investigational product.

Summaries of AEs will include any AEs reported beginning with the first dose of investigational product on Day 1. The occurrence of adverse events will be summarized by treatment group using preferred terms, system organ classifications, and severity. Separate summaries of serious adverse events, adverse events related to investigational product, and events leading to the discontinuation of investigational product will be generated. All adverse events reported will be listed for individual subjects showing both verbatim and preferred terms.

8.3 Efficacy Analysis

All efficacy endpoints are exploratory endpoints.

Assessment of Superiority:

- IGA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in IGA score from baseline to the end of treatment (Week 8).
- CEA treatment success, defined as “clear” or “almost clear” with a 2-grade improvement in CEA score from baseline to the end of treatment (Week 8).

  Superiority will be based on the proportion of subjects for whom treatment was successful. The comparison will be through a continuity-corrected Z-tests. The Evaluable Period for the outcome variables will be weeks 1, 4, 8 and 12. The superiority of the drug over the vehicle will be tested at week 8 based on the probability of

improvement from baseline with a continuity-corrected Z-tests comparing the change from baseline of treatments vs Placebo. For all other evaluable periods, descriptive statistics for the change from baseline will be shown.

The null and alternative statistical hypotheses for the primary effectiveness endpoints are given by:

(*Ho*): The null hypothesis is that the probability of improving (baseline to week 8) with drug T (*PrT*)is less than or equal to the probability of improving with vehicle (*PrV*).
Ho: PrT ≤ PrV ; PrT – PrV ≠ 0

(*Ha*): The alternative hypothesis is that the probability of improving with drug T (*PrT*) is greater than to the probability of improving with vehicle (*PrV*).
Ha: PrT > PrV; PrT – PrV ≠0

For testing the superiority, the following SAS code will be used:

```
proc freq data = dataset;
tables treat*outcome/riskdiff (equal);
run;
```

- Change of Skindex 16 patient reported outcome from Baseline to Week 1, Week 4, Week 8 and Week 12

  The change from baseline score of Skindex-16 will be compared among treatments at Week 12 using an ANOVA, to test the Skindex16 score change from Baseline to Week 12 for the two treatments. Also, descriptive stats will be used to assess the change from Baseline to Week 1, 4, 8 & 12.

- Change of IGA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of CEA score at Baseline to Week 1, Week 4, Week 8 and Week 12.
- Change of PSA score at Baseline to Week 1, Week 4, Week 8 and Week 12.

  Descriptive stats will be used to show the change from Baseline to Week 1, 4, 8 & 12.

- Supplemental Analysis
  Supplemental analysis will be performed based on any IGA or CEA improvement from Baseline including p-values for the change from Baseline to Week 8 within each treatment group, and IGA and CEA for the subgroup of patients that had a baseline IGA or CEA of 3.

8.4 Sensitivity Analysis

A sensitivity analysis will be performed by Multiple Imputation Regression Analysis using the following factors: treatment, age, gender, race, baseline IGA, baseline CEA, baseline

PSA, smokers/non-smokers and the results of the same variable from previous visits. The Proc MI SAS code will be used to perform the analysis based on the mentioned factors.

9 REFERENCES

- Protocol Number: RB244-001, VER 4.0 "A Vehicle-Controlled, Double-Blind, Randomized Phase II Study of B244 Delivered as a Topical Spray to Determine Safety and Efficacy in Subjects with Mild to Moderate Rosacea."
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10 APPENDIX

10.1 APPENDIX A: Tables

10.1.1 General

Display Number	Title	Population	Unique/Repeat
14.1.1.1	Subject Enrollment and Disposition	All Subjects	Unique
14.1.1.2	Subject Enrollment and Disposition	Enrolled Subjects	Unique
14.1.1.3	Analysis Population and Exclusions	All Subjects	Unique
14.1.2.1	Summary of Protocol Deviations (PD)/Violations (PV)	mITT	Unique
14.1.2.2	Summary of Protocol Deviations (PD)/Violations (PV)	Safety	Repeat
14.1.3.1	Summary of Demographic and Baseline Characteristics	mITT	Unique
14.1.3.2	Summary of Demographic and Baseline Characteristics	PP	Repeat
14.1.3.3	Summary of Demographic and Baseline Characteristics	Safety	Repeat
14.1.4.1	Summary of Vital Sign	mITT	Unique
14.1.4.2	Summary of Vital Sign	PP	Repeat
14.1.4.3	Summary of Vital Sign	Safety	Repeat
14.1.5.1	Summary of Physical Examination	mITT	Unique
14.1.5.2	Summary of Physical Examination	PP	Repeat
14.1.5.3	Summary of Physical Examination	Safety	Repeat
14.1.6	Summary of Study Drug Accountability: Dose Dispensed & Collected by Visit	Safety	Unique
14.1.7.1	Summary of Study Drug Compliance	Safety	Unique
14.1.7.2	Summary of Percent Compliance based on Cumulative Net Weight of Study Drug	Safety	Unique
14.1.8	Summary of Prior or Concomitant Medications	Safety	Unique
14.1.9	Summary of Medical History	Safety	Unique
14.1.10	Summary of Substance Abuse	Safety	Unique
14.1.11	Summary of Dairy Details	Safety	Unique

Table 14.1.1.1
Subject Enrollment and Disposition

All Subjects

Disposition	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Screened	xx	xx	xx (xx.x)
Randomized	xx	xx	xx (xx.x)
Treated	xx	xx	xx (xx.x)
Completed Study	xx	xx	xx (xx.x)
Discontinued	xx	xx	xx (xx.x)
Screen Failure	xx	xx	xx (xx.x)
Withdrawal of consent	xx	xx	xx (xx.x)
In the opinion of the Investigator, it is not in the subject's best interests to continue in the study	xx	xx	xx (xx.x)
Pregnancy	xx	xx	xx (xx.x)
Occurrence of an Adverse Event (AE) or Serious Adverse Event (SAE), which, in the opinion of the Investigator warrants discontinuation of the subject from the study	xx	xx	xx (xx.x)
The subject is lost to follow-up	xx	xx	xx (xx.x)
Other	xx	xx	xx (xx.x)

NOTE: The percentages are based on the number of All subjects.
Subjects may have more than one reason for discontinuation, and they are counted more than once.

Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Table 14.1.1.2
Subject Enrollment and Disposition

Enrolled Subjects

Disposition	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Randomized	xx (xx.x)	xx (xx.x)	xx (xx.x)
Treated	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 8	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Week 12	xx (xx.x)	xx (xx.x)	xx (xx.x)
Discontinued	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal of consent	xx (xx.x)	xx (xx.x)	xx (xx.x)
In the opinion of the Investigator, it is not in the subject's best interests to continue in the study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pregnancy	xx (xx.x)	xx (xx.x)	xx (xx.x)
Occurrence of an Adverse Event (AE) or Serious Adverse Event (SAE), which, in the opinion of the Investigator warrants discontinuation of the subject from the study	xx (xx.x)	xx (xx.x)	xx (xx.x)
The subject is lost to follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)

NOTE: The percentages are based on the number of Randomized subjects.
Subjects may have more than one reason for discontinuation, and they are counted more than once.

Snapshot Data DD-MMM-YYYY

Source: <Dataset>

Program Name: <Pgm name>

Table 14.1.1.3
Analysis Population and Exclusions
All Subjects

Number of Subjects	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Enrolled	xx	xx	xx
Randomized	xx	xx	xx
Included in Safety Population	xx	xx	xx (xx.x%)
Reasons for Exclusion from Safety Population			
	xx	xx	xx (xx.x%)
	xx	xx	xx (xx.x%)
Included in Full Analysis Set	xx	xx	xx (xx.x%)
Reasons for Exclusion from Safety Population			
	xx	xx	xx (xx.x%)
Included in Per Protocol Population	xx	xx	xx (xx.x%)
Reasons for Exclusion from Per Protocol Population			
Lost To Follow Up	xx	xx	xx (xx.x%)
Major Deviation	xx	xx	xx (xx.x%)
Not 50% Ip Compliant	xx	xx	xx (xx.x%)
Screen Failure	xx	xx	xx (xx.x%)
Withdrawal of Consent By Subject	xx	xx	xx (xx.x%)

NOTE: The percentages are based on the number of All subjects.

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Source: <Dataset>

Table 14.1.2.1
Summary of Protocol Deviations (PD)/Violations (PV)
mITT Population

Deviation/Violation	Deviation/Violation Category	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Description of Violation/deviation	"Major" or "Minor"	n (%) xx	n (%) xx	n (%) xx

NOTE: The percentages are based on the number of ITT Population.

Source: <Dataset> Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

Repeat for Safety Population

Table 14.1.3.1
Summary of Demographic and Baseline Characteristics
mITT Population

Variable	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Age	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Sex				
Male	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity				
Hispanic or Latino	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Hispanic or Latino	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race				
American Indian or Alaskan Native	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black or African American	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Variable	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
White	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

NOTE: The percentages are based on the number of ITT Population.

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Source: <Dataset>

Repeat for PP and Safety population

Table 14.1.4.1
Summary of Vital Signs,
mITT Population

Visit	Vital Sign	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Baseline	Height	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Weight	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Temperature	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Heart Rate	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Systolic BP	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)

Visit	Vital Sign	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Diastolic BP	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for every visit showing Change from Baseline					

NOTE: The percentages are based on the number of ITT Population.

CRF pages 05-06

Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Repeat for PP and Safety population

Table 14.1.5.1
Summary of Physical Examination,
mITT Population

Visit	Physical Examination	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Baseline					
	General Appearance				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Heart Cardiovascular				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Visit	Physical Examination	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Lungs				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Gastrointestinal				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Ear/Nose/Throat				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Extremities				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Skin				
	Normal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Repeat for every week					

NOTE: The percentages are based on the number of ITT Population.

CRF pages 05-06
Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Repeat for PP and Safety populations

Table 14.1.6
Summary of Study Drug Accountability: Dose Dispensed & Collected by Visit
Safety Population

Weight of the Dose	Visit	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Dose Dispensed	Baseline	N	xx	xx	xx
		Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for Dose Collected by Visits					

N: Number of Patients
Mean(SD) : Mean (Standard Deviation),CV: Coefficient of Variance..

CRF pages 28-30

Source: <Dataset>

Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

Table 14.1.7.1
Summary of Study Drug Compliance
Safety Population

	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Number of Subjects with Compliance				
Yes	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
If No, Applications Missed				
Missed Applications	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
	CV	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Applications: Number of applications per patients/day (expected 4 Pumps twice a Day)

Compliance: The expected amount of study drug used per week is approximately 7.84 g/week for 8 sprays/application per day

CRF pages 30

Source: <Dataset>

Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

Table 14.1.7.2
Summary of Percent Compliance based on Cumulative Net Weight of Study Drug
Safety Population

	Statistic	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Cumulative Net Weight of Study Drug				
	N	xx	xx	xx
	Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
	CV	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Percent Compliance greater than 50%				
Yes	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Applications: Number of applications per patients/day (expected 4 Pumps twice a Day)

The cumulative amount of study drug exposure will be estimated by calculating the difference between the weight of the 2 bottles of drug at the time the drug was dispensed at Baseline/Week 4 and the weight of the 2 bottles at Week 4/Week 8. Differences will be summed together.

% Compliance: The net weight of study drug divided by 1.12g /Day * Number of Days in the Study

Snapshot Data DD-MMM-YYYY

CRF pages 30

Program Name: <Pgm name>

Source: <Dataset>

Table 14.1.8
Summary of Prior or Concomitat Medications,
Safety Population

WHO-DD ATC Class Level 1 WHO-DD ATC Class Level 2 WHO-DD Preferred Term	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Number of subjects with at least one prior medication	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 1	xx (xx.x)	xx (xx.x)	xx (xx.x)

WHO-DD ATC Class Level 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			
WHO-DD ATC Class Level 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD ATC Class Level 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			

NOTE: The percentages are based on the number of Safety Population.

CRF page 11
Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Table 14.1.9
Summary of Medical History
Safety Population

WHO-DD SOC WHO-DD Preferred Term	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Number of subjects with at least one Medical History	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD SOC	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHO-DD Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.			

NOTE: The percentages are based on the number of Safety Population.

CRF pages
Source: <Dataset>

Snapshot Data DD-MMM-YYYY

Program Name: <Pgm name>

Table 14.1.10
Summary of Substance Abuse
Safety Population

Statistics	B244 Topical Spray	Placebo N (xxx)	All Patients N (xxx)

		N (xxx)		
Total Number of Substance Abuse	n	xx xx xx	xx xx xx	xx xx xx
Number of Subjects with Substance Abuse History	n (%)	xx (xx.x) xx (xx.x) xx (xx.x)	xx (xx.x) xx (xx.x) xx (xx.x)	xx (xx.x) xx (xx.x) xx (xx.x)

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages
Source: <Dataset>

Program Name: <Pgm name>

Table 14.1.11
Summary of Diary Details
Safety Population

	Statistics	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Number of Subjects with diary Dispensed	n	xx	xx	xx
Number of Subjects with diary Collected	n	xx xx	xx xx	xx xx
Number of Subjects with Sunscreen use	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Subjects with Makeup use	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages
Source: <Dataset>

Program Name: <Pgm name>

10.1.2 Efficacy

Display Number	Title	Population	Unique/Repeat
14.2.1.1	Change from baseline in IGA score by Visit	mITT	Unique
14.2.1.2	Change from baseline in IGA score by Visit	PP	Repeat
14.2.2.1	Change from baseline in CEA score by Visit	mITT	Repeat
14.2.2.2	Change from baseline in CEA score by Visit	PP	Repeat
14.2.3.1	Change from baseline in PSA score by Visit	mITT	Repeat
14.2.3.2	Change from baseline in PSA score by Visit	PP	Repeat
14.2.4.1	Summary of Change from baseline in Skindex 16 score by Visit	mITT	Unique
14.2.4.2	Summary of Change from baseline in Skindex 16 score by Visit	PP	Repeat
14.2.5.1	Change from baseline in Telangiectasia score by Visit	mITT	Repeat
14.2.5.2	Change from baseline in Telangiectasia score by Visit	PP	Repeat
14.2.6.1	Summary of 2-grade improvement in IGA score from baseline to the end of treatment.	mITT	Unique
14.2.6.2	Summary of 2-grade improvement in IGA score from baseline to the end of treatment	PP	Repeat
14.2.7.1	Summary of 2-grade improvement in CEA score from baseline to the end of treatment	mITT	Repeat
14.2.7.2	Summary of 2-grade improvement in CEA score from baseline to the end of treatment .	PP	Repeat
14.2.8.1	Summary of IGA score of 0/1 at End of Treatment.	mITT	Unique
14.2.8.2	Summary of IGA score of 0/1 at End of Treatment.	PP	Repeat
14.2.9.1	Summary of CEA score of 0/1 at End of Treatment.	mITT	Repeat
14.2.9.2	Summary of CEA score of 0/1 at End of Treatment.	PP	Repeat
14.2.10.1	Summary of Sensitivity Analysis for Change from Baseline Score of IGA	mITT	Unique
14.2.10.2	Summary of Sensitivity Analysis for Change from Baseline Score of CEA	mITT	Repeat
14.2.10.3	Summary of Sensitivity Analysis for Change from Baseline Score of PSA	mITT	Repeat

Table 14.2.1.1
Change from baseline in IGA Score by Visit.
mITT Population

Visit	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Week 1			
Change from Baseline			
1-grade	n (%)		
2-grade	n (%)		
3-grade	n (%)		
Repeat for all the visits			

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for CEA and PSA & Telangiectasia Score for mITT & PP population.

Table 14.2.4.1
Summary of Change from baseline in Skindex 16 score by Visit
mITT Population

Visit	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Baseline			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
CV	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Change from Baseline at Week 1			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
CV	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for All weeks			

Final Analysis for Week 12	
Differences of LS Means	x.xxxx
SE	x.xxxx
CI	(x.xxxx, x.xxxx)
P-value	x.xxxx

SE: Standard Error of the LS Means

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for PP population.

Table 14.2.10.1
Summary of Sensitivity Analysis for Change from Baseline Score of IGA
mITT Population

Imputation	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Imputation#1			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Imputation#2			
N	xx	xx	xx
Mean (SD)	xx.x (xx.xxx)	xx.x (xx.xxx)	xx.x (xx.xxx)
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Repeat for all imputations			
Analysis Summary			
Mean (SD)			x.xx, x.xx
CI			x.xxx
P-Value			

SD: Standard Error of the Parameters
CI: Confidence Interval

Repeat for CEA & PSA.

CRF pages Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Table 14.2.6.1
Summary of 2-grade improvement in IGA score from baseline to the end of treatment.
mITT Population

	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Subjects with 2-Grade improvement from Baseline to End of Treatment	n (%)	n (%)	n (%)
Risk Difference			x.xxx
CI			(x.xx, x.xx)
P-value			x.xxxx

CI: Confidence Interval

Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for PP Population and for CEA (mITT & PP).

Table 14.2.8.1
Summary of IGA score of 0/1 at End of Treatment.
mITT Population

	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Subjects with Score of 0/1 at End of Treatment	n (%)	n (%)	n (%)
Risk Difference			x.xxx
CI			(x.xx, x.xx)
P-value			x.xxxx

CI: Confidence Interval

Snapshot Data DD-MMM-YYYY
Source: <Dataset> Program Name: <Pgm name>

Repeat for PP Population and for CEA (mITT & PP)

10.1.3 Safety

Display Number	Title	Population	Unique/Repeat
14.3.1	Overall Summary of Treatment Emergent Adverse Events	Safety	Unique
14.3.1.1	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety	Unique
14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity	Safety	Repeat
14.3.1.3	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug	Safety	Repeat
14.3.2	Summary of Serious Adverse Events by System Organ Class and Preferred Term	Safety	Repeat
14.3.3	Summary of Deaths	Safety	Unique

Table 14.3.1
Overall Summary of Treatment Emergent Adverse Events.
Safety Population

	Statistics	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Total Number of TEAEs	N	xx	xx	xx
Total Number of TESAEs	N	xx	xx	xx
Number of Subjects with:				
At Least One TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Related TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Severe (Grade 3) TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TEAE Leading to Discontinuation	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TEAE Leading to Death	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TESAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Related TESAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages
Source: <Dataset>

Program Name: <Pgm name>

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

	Statistics	B244 Topical Spray n (%)	Placebo n (%)	All Patients n (%)
Total Number of TEAEs	n	xx	xx	xx
Number of Subjects with at Least One TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.				
System Organ Class #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.				

NOTE: The percentages are based on the number of Safety Population.

Snapshot Data DD-MMM-YYYY

CRF pages
Source: <Dataset>

Program Name: <Pgm name>

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

	Statistics	Severity	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Total Number of TEAEs	n	Mild	xx	xx	xx
		Moderate	xx	xx	xx

		Severe	xx	xx	xx
		Total	xx	xx	xx
Number of Subjects with at Least One TEAE	n (%)	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class #1	n (%)	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.					

CRF pages Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

NOTE: The percentages are based on the number of Safety Population.
Subject has more than 1 AE on a Preferred term, then, it is counted only once on the highest severity.

Source:
<Dataset>

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

	Statistics	Relationship	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Total Number of TEAEs	n	Not Related	xx	xx	xx
		Related	xx	xx	xx
		Total	xx	xx	xx
Number of Subjects with at Least One TEAE	n (%)	Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)

System Organ Class #1	n (%)	Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Related	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.					

NOTE: The percentages are based on the number of Safety Population.

CRF pages
Source: <Dataset>

Snapshot Data DD-MMM-YYYY
Program Name: <Pgm name>

Table 14.3.2
Summary of Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

	Statistics	Relationship	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Total Number of SAEs	n	Yes	xx	xx	xx
		No	xx	xx	xx
		Total	xx	xx	xx
Number of Subjects with at Least One SAE	n (%)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
		No	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class #1	n (%)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
		No	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
		No	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.					

CRF pages

Snapshot Data DD-MMM-YYYY

NOTE: The percentages are based on the number of Safety Population. Program Name: <Pgm name>

Source: <Dataset>

Table 14.3.3
Summary of Deaths
Safety Population

	Statistics	B244 Topical Spray N (xxx)	Placebo N (xxx)	All Patients N (xxx)
Number of deaths	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related to disease under study	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
AE outcome = death	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related to disease under study and AE outcome = death	n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

CRF pages Snapshot Data DD-MMM-YYYY

NOTE: The percentages are based on the number of Safety Population. Program Name: <Pgm name>

Source: <Dataset>

10.2 APPENDIX B: Listings

Display Number	Title	Population
Listing 16.2.1.1	Subject Enrollment and Disposition by Study Site	All Subjects
Listing 16.2.1.2	Protocol Deviations (PD)/Violations (PV)	Randomized
Listing 16.2.1.3	Demographic Characteristics	Randomized
Listing 16.2.1.4	Vitals Signs by Subject and Visit	Safety
Listing 16.2.1.5	Physical Examination by Subject	Safety
Listing 16.2.1.6	Drug Exposure and Compliance	Safety
Listing 16.2.1.8	Prior and Concomitant Medications	Safety
Listing 16.2.1.9	Medical History	Safety
Listing 16.2.2.1	IGA score by Subjects and Visits	Randomized
Listing 16.2.2.2	CEA score by Subjects and Visits	Randomized
Listing 16.2.2.3	PSA score by Subjects and Visits	Randomized
Listing 16.2.2.4	Skindex-16 score by Subjects and Visits	Randomized
Listing 16.2.2.5	Telangiectasia Evaluation by Subjects and Visits	Randomized
Listing 16.2.2.6	Fitzpatrick Classification by Subjects and Visits	Randomized
Listing 16.2.3.1	Treatment Emergent Adverse Events by System Organ Class, Preferred Term, Severity and Relationship to Study Drug	Safety

Listing 16.2.3.2	Serious Adverse Events by System Organ Class and Preferred Term	Safety
Listing 16.2.3.3	Deaths	Safety
Listing 16.2.4.1	Hematology Parameters	Safety
Listing 16.2.4.2	Clinical Chemistry Parameters	Safety
Listing 16.2.4.3	Urinalysis Parameters	Safety

10.3 APPENDIX C: Figures

Display Number	Title	Population
Figure 14.2.1.1	Frequency table Change from baseline for IGA score by Visit	mITT
Figure 14.2.1.2	Frequency table Change from baseline for IGA score by Visit	PP
Figure 14.2.2.1	Frequency table Change from baseline for CEA score by Visit	mITT
Figure 14.2.2.2	Frequency table Change from baseline for CEA score by Visit	PP
Figure 14.2.3.1	Frequency table Change from baseline for PSA score by Visit	mITT
Figure 14.2.3.2	Frequency table Change from baseline for PSA score by Visit	PP
Figure 14.2.4.1	Box Plot of Skindex16 score by Visit	mITT
Figure 14.2.4.2	Box Plot of Skindex16 score by Visit	PP
Figure 14.2.8.1	Bar Plot of IGA & CEA score at End of Treatment	mITT
Figure 14.2.8.2	Bar Plot of IGA & CEA score at End of Treatment	PP
Figure 14.2.9.1	Bar Plot of IGA & CEA score for more than 2-grade improvement from Baseline to End of Treatment.	mITT
Figure 14.2.9.2	Bar Plot of IGA & CEA score for more than 2-grade improvement from Baseline to End of Treatment.	PP