Official Title: **A Randomized, Double-Blind, Dose-Ranging Study of INCB018424 Phosphate Cream in Subjects With Vitiligo**

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STATISTICAL ANALYSIS PLAN

INCB 18424-211

A Randomized, Double-Blind, Dose-Ranging Study of INCB018424 Phosphate Cream in Subjects With Vitiligo

IND Number:	**77,101**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803**
Protocol Version:	**Protocol Amendment 1 dated 17 MAY 2017**
CRF Approval Date:	**06 JUN 2017**
SAP Version:	**Original**
SAP Author:	[redacted]**, Biostatistics**
Date of Plan:	**28 JUN 2017**

This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

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LIST OF ABBREVIATIONS

Abbreviation	Term
AE	adverse event
BID	twice daily
BMI	body mass index
BSA	body surface area
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
DB	double-blind
ECG	electrocardiogram
eCRF	electronic case report form
F-BSA	facial body surface area
F-PaGVA	facial assessment of the Patient's Global Vitiligo Assessment
F-PhGVA	facial assessment of the Physician's Global Vitiligo Assessment
F-VASI	facial assessment of the Vitiligo Area and Severity Index
ITT	intent-to-treat
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
NRI	nonresponder imputation
OL	open-label
PaGIC-V	Patient Global Impression of Change for Vitiligo
palmar method of BSA assessment	1% BSA for each subject is approximately equal to the surface area of their palm plus 5 digits; handprint may be used interchangeably
[redacted]	[redacted]
PP	per protocol
PT	preferred term
QD	once daily
SAE	serious adverse event
SAP	statistical analysis plan
SOC	system organ class

T-BSA	total body surface area
TEAE	treatment-emergent adverse event
T-PaGVA	total body assessment of the Patient's Global Vitiligo Assessment

Abbreviation	**Term**
T-PhGVA	total body assessment of the Physician's Global Vitiligo Assessment
T-VASI	total body assessment of Vitiligo Area and Severity Index
VASI	Vitiligo Area and Severity Index
VASI50	≥ 50% improvement from baseline in Vitiligo Area and Severity Index score
VASI75	≥ 75% improvement from baseline in Vitiligo Area and Severity Index score
VASI90	≥ 90% improvement from baseline in Vitiligo Area and Severity Index score
VETF	Vitiligo European Task Force
[redacted]	[redacted]
WHO	World Health Organization

1. INTRODUCTION

This is a randomized and vehicle-controlled study in subjects with vitiligo who have depigmented areas including at least 0.5% of the T-BSA on the face and at least 3% of the T-BSA on nonfacial areas. The study will consist of 3 parts, including a 24-week, DB, vehiclecontrolled treatment period; a 28-week, continued, DB treatment period; and a 52-week, OL extension period. Section 1 of the Protocol provides a detailed description of the investigational product, target patient population, rationale for doses to be examined, and potential risks and benefits of treatment with INCB018424 cream.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCB 18424-211 Protocol. The scope of this plan includes the interim and final analyses that are planned and will be executed by the Department of Biostatistics or designee [redacted]

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 18424-211 Protocol Amendment 1 dated 17 MAY 2017 and CRFs approved 06 JUN 2017. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objectives

2.2.1. Primary Objective

- To establish the efficacy of 24 weeks of treatment with INCB018424 cream in subjects with vitiligo.

2.2.2. Secondary Objectives

- To estimate the dose-response relationship of INCB018424 cream at Weeks 24 and 52.
- To evaluate the safety and tolerability of INCB018424 cream in subjects with vitiligo.

[redacted]

2.3. Study Endpoints

2.3.1. Primary Endpoint

- Proportion of subjects treated with INCB018424 cream who achieve a ≥ 50% improvement from baseline in F-VASI score (F-VASI50) at Week 24 compared with subjects treated with vehicle cream.

2.3.2. Secondary Endpoints

2.3.2.1. Key Secondary Endpoints

- Proportion of subjects who achieve an F-PhGVA of clear or almost clear at Week 24.
- Proportion of subjects who achieve a ≥ 50% improvement from baseline in T-VASI at Week 52.

2.3.2.2. Other Secondary Endpoints

- Assessment of the dose response on percentage change from baseline in F-VASI during the treatment periods.
- Mean and percentage change from baseline in F-VASI score during the treatment periods.
- Proportion of subjects who achieve an F-VASI50 during the treatment periods.
- Percentage change from baseline in F-BSA repigmentation during the treatment periods.
- Percentage change from baseline in T-BSA repigmentation during the treatment periods.
- Mean and percentage change from baseline in T-VASI score during the treatment periods.
- Mean and percentage change from baseline in VETF during the treatment periods.
- Proportion of subjects in each F-PhGVA and T-PhGVA category during the treatment periods.
- Proportion of subjects in each F-PaGVA and T-PaGVA category during the treatment periods.
- Proportions of subjects in each PaGIC-V category during the treatment periods.
- Proportion of subjects who report PaGIC-V of very much improved or much improved during the treatment periods.
- Times to achieve an F-VASI50 and T-VASI50.

- Times to achieve an F-PhGVA and T-PhGVA of clear or almost clear.
- Time to achieve a PaGIC-V of very much improved or much improved.
- Safety and tolerability assessed by monitoring the frequency, duration, and severity of AEs, physical examination, vital signs, and laboratory data for hematology, serum chemistry, and urinalysis.

[redacted]

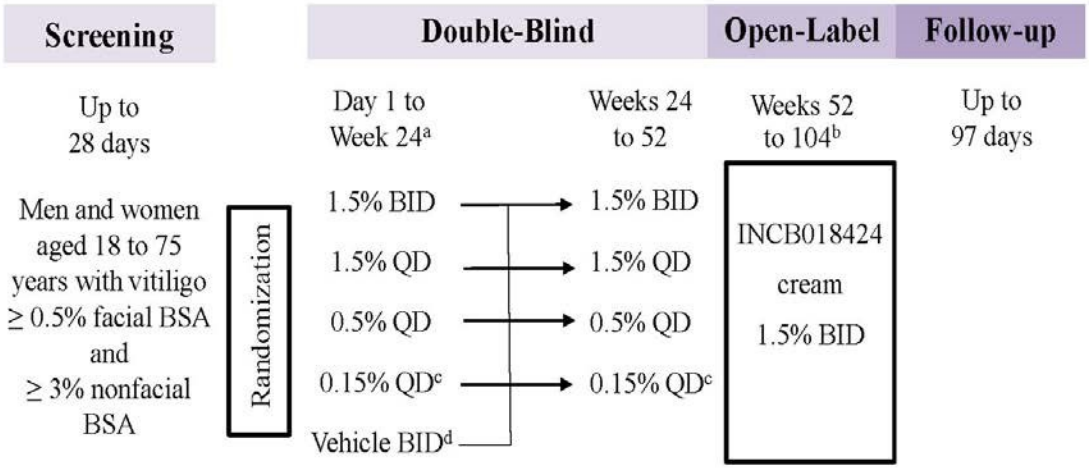
3. STUDY DESIGN

This is a 3-part, randomized, DB, and vehicle-controlled study in subjects with vitiligo who have depigmented areas including at least 0.5% of the T-BSA on the face and at least 3% of the T-BSA on nonfacial areas as determined by the palmar (or handprint- palm plus 5 digits) method. Approximately 150 subjects, aged 18 to 75 years, will be randomized to 1 of 4 dose strengths of INCB018424 cream (1.5% BID, 1.5% QD, 0.5% QD, 0.15% QD) or vehicle cream in a 1:1:1:1:1 ratio and stratified by age (≤ 30 or > 30 years), with no more than 50% of the population being over 30 years of age.

Subjects will receive blinded treatment for up to 52 weeks to examine efficacy, safety, and tolerability. The 3 parts of the study include a 24-week, DB, vehicle-controlled treatment period; a 28-week, continued, DB treatment period; and a 52-week, OL extension period (see Figure 1). The primary endpoint of F-VASI50 will be evaluated at Week 24. After completion of the Week 24 assessments, subjects randomized to vehicle will be randomized to 1 of the 3 higher active treatment groups in a 1:1:1 ratio while maintaining the blind. Subjects in the INCB018424 0.15% QD group who do not achieve a ≥ 25% improvement from baseline on F-VASI (nonresponders of F-VASI25) will be re-randomized to 1 of the 3 higher active treatment groups while maintaining the blind. Subjects randomized to INCB018424 0.15% QD who achieve a ≥ 25% improvement from baseline on F-VASI will remain on the same dose until Week 52. Subjects randomized to INCB018424 1.5% BID, 1.5% QD, and 0.5% QD will remain on the same dose until Week 52.

After completion of the Week 52 assessments, subjects who continue to be eligible for the study have the opportunity to receive an additional 52 weeks of OL treatment with INCB018424 1.5% cream BID.

Figure 1: Study Design Schema



Note: Subjects will be randomized equally to 1 of the 5 treatment groups and stratified by age (≤ 30 or > 30 years).
Note: Body surface area will be calculated using the palmar method, where the subject's palm is approximately equal to 0.5% BSA, and 1% BSA is approximately equal to a handprint (palm including 5 digits). [a] QD regimens will apply vehicle in the evening.

[b] At Weeks 52 and 80, subjects with an F-PhGVA of clear (0) may stop application on the face, decrease to QD, or continue BID.

[c] Re-randomize to a higher dose if < 25% improvement in F-VASI score at Week 24. If ≥ 25% improvement in F-VASI, remain on the same dose until Week 52.

[d] Re-randomized to 1.5% BID, 1.5% QD, or 0.5% QD at Week 24 in a 1:1:1 ratio.

3.1. Randomization

Approximately 150 subjects will be randomized to 1 of 4 dose strengths of INCB018424 cream (1.5% BID, 1.5% QD, 0.5% QD, or 0.15% QD) or vehicle cream in a 1:1:1:1:1 ratio, and stratified by age (≤ 30 or > 30 years), with no more than 50% of the population being over 30 years of age. After completion of the Week 24 assessments, subjects randomized to vehicle will be randomized to 1 of the 3 higher active treatment groups while maintaining the blind. Subjects in the INCB018424 0.15% QD group who do not achieve a ≥ 25% improvement from baseline on F-VASI (nonresponders of F-VASI25) will be re-randomized to 1 of the 3 higher active treatment groups while maintaining the blind. Subjects randomized to INCB018424 0.15% QD who achieve a ≥ 25% improvement from baseline on F-VASI will remain on the same dose until Week 52. Subjects randomized to INCB018424 1.5% BID, 1.5% QD, and 0.5% QD will remain on the same dose until Week 52.

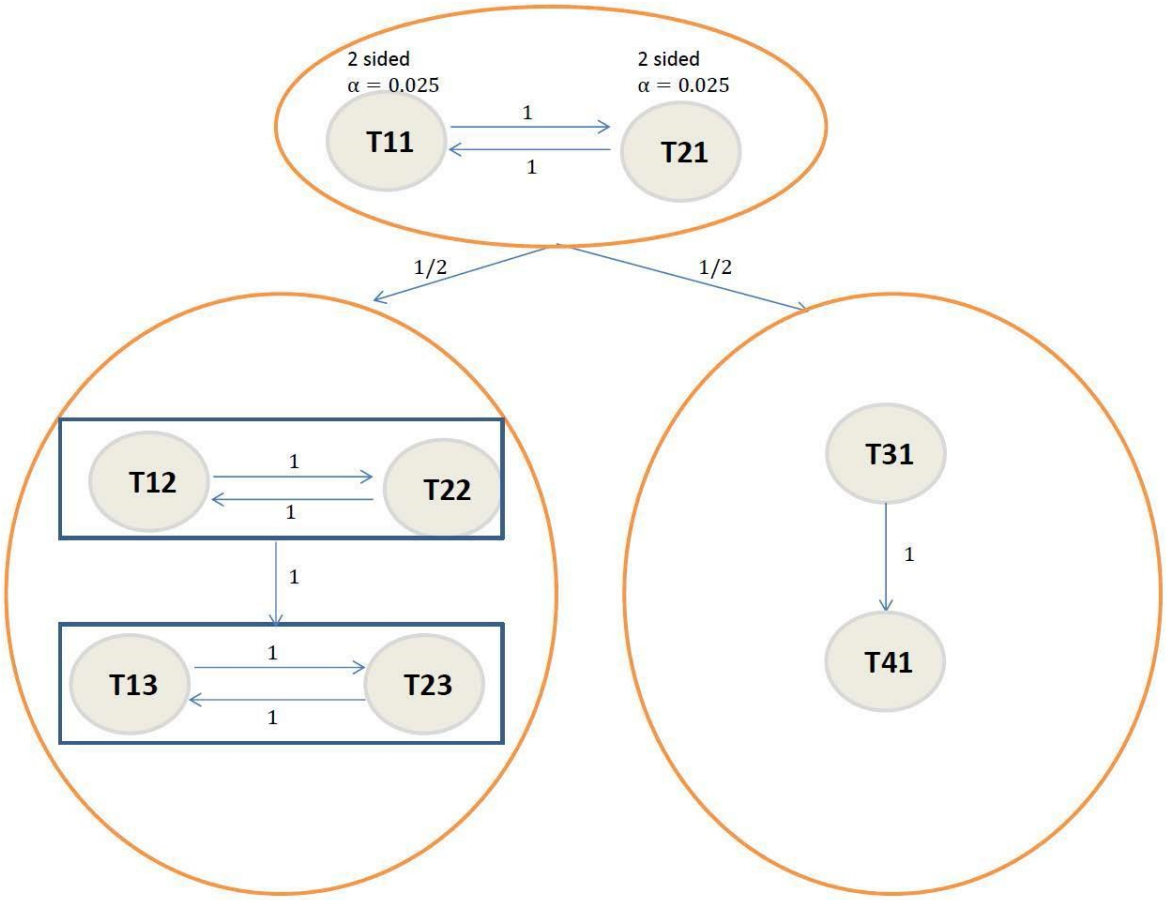
3.2. Control of Type I Error

For the primary endpoint and key secondary endpoints, the overall 2-sided Type I error is 0.05.

A graphical procedure with gatekeeping testing strategy for the primary and key secondary analyses will be implemented to control the overall Type I error rate.

A family of 8 elementary hypotheses, corresponding to treatment comparisons between active treatment and vehicle groups, is evaluated in Figure 2, which is based on F-VASI50 and F-PhGVA at Week 24 and T-VASI50 at Week 52.

Figure 2: Illustration of the Statistical Treatment Comparisons



T = treatment group comparison.

3.2.1. Primary Analysis

The primary endpoint is the proportion of subjects treated with INCB018424 cream who achieve a ≥ 50% improvement from baseline in F-VASI score (F-VASI50) at Week 24 compared with subjects treated with vehicle cream. The comparison of the primary endpoint will be performed for the superiority of either INCB018424 1.5% BID or INCB018424 1.5% QD versus vehicle (T11 and T21, respectively, in Figure 2) using the Bonferroni-Holm procedure at an overall 2-sided α = 0.05 level. The tests on the primary endpoint will be used as a gatekeeper for the 6 statistical tests on key secondary endpoints (see Figure 2).

3.2.2. Secondary Analysis

The key secondary endpoint includes 6 comparisons as depicted in Figure 2.

- T31: INCB018424 0.5% QD is superior to vehicle at Week 24 on F-VASI50.
- T41: INCB018424 0.15% QD is superior to vehicle at Week 24 on F-VASI50.

- T12: INCB018424 1.5% BID is superior to vehicle at Week 24 on F-PhGVA response.
- T22: INCB018424 1.5% QD is superior to vehicle at Week 24 on F-PhGVA response.
- T13: INCB018424 1.5% BID is superior to 0.5% QD at Week 52 on T-VASI50.
- T23: INCB018424 1.5% QD is superior to 0.5% QD at Week 52 on T-VASI50.

The initial allocation of the overall significance level to Branch 1 (T12 and T22) and Branch 2 (T31 and T41) is 0.025, respectively. The weights of the level to be passed on if 1 hypothesis is rejected are specified in Figure 2.

3.2.2.1. Tests in Branch 1

The alternative hypotheses for T12 and T22 will be tested using the Bonferroni-Holm procedure at an overall 2-sided $\alpha = 0.025$ level if the null hypotheses on primary endpoints are rejected.

If both T12 and T22 are rejected, T13 and T23 will be tested using Bonferroni-Holm procedure with overall 2-sided $\alpha = 0.025$ level.

3.2.2.2. Tests in Branch 2

T31 (superiority of INCB018424 0.5% QD compared with vehicle) and T41 (superiority of INCB018424 0.15% QD compared with vehicle) will be tested sequentially at a 2-sided $\alpha = 0.025$ level if the null hypotheses on the primary endpoints are rejected.

3.3. Sample Size Considerations

In order to provide a large safety database and to provide adequate power for efficacy variables, the total sample size for the study is 150 subjects randomized in a 1:1:1:1:1 ratio (stratified by age) to INCB018424 1.5% BID, INCB018424 1.5% QD, INCB018424 0.5% QD, INCB018424 0.15% QD, or vehicle. The sample size selection is based on the assumed response rates of 55% for the INCB018424 1.5% cream BID group, 50% for the INCB018424 1.5% cream QD group, and 5% for the vehicle cream BID group. Using a 2-sided Bonferroni corrected α of 0.025, 25 subjects per group will have a > 90% power to detect such a difference between each of the active treatment groups and the vehicle group based on Fisher's exact test due to small expected frequency of responders in the vehicle group. Assuming a 20% dropout rate during the first 24 weeks, approximately 150 subjects will need to be randomized.

3.4. Schedule of Assessments

See Protocol Amendment 1 dated 17 MAY 2017 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

Table 1: Definition of Day 1, Baseline, and Last Available Value

Study Period	Treatment Group*	Day 1	Baseline	Last Available Value
DB period	INCB018424 cream 1.5% BID 1.5% QD 0.5% QD 0.15% QD Vehicle BID	Date of first application or date of randomization for subjects randomized but not treated in the DB period.	The last nonmissing measurement obtained on or before the day of the first application.	The last nonmissing measurement obtained after the first application, and within 30 days after the last application in the DB period or before the first application in the extension period, whichever is earlier.
OL period	INCB018424 cream 1.5% BID	Date of first application date in DB period.	The last nonmissing measurement obtained on or before the day of the first application in DB period.	The last nonmissing measurement obtained after the first application and within 30 days after the last application.
	INCB018424 cream 1.5% QD 0.5% QD 0.15% QD Vehicle BID	Date of first application in OL period.	The last nonmissing measurement obtained on or before the day of the first application in the OL period.	The last nonmissing measurement obtained after the first application and within 30 days after the last application.

* Treatment group initially assigned or actual treatment received during the DB period.

4.1.1. Study Day

Study Day 1 is used to calculate the study day for mapping scheduled visits. Study Day 1 is the date of the first application of INCB018424 cream or vehicle in the DB treatment period.

If a visit/reporting date is on or after Study Day 1, then the study day at the visit/reporting date will be calculated as

Study Day # = (Visit/Reporting Date – Study Day 1 date + 1).

If the visit/reporting date is before Study Day 1, then the study day at the visit/reporting date will be calculated as

Study Day # = (Visit/Reporting Date – Study Day 1 date).

A study day of -1 indicates 1 day before Study Day 1.

4.2. Variable Definitions

4.2.1. Age

Subject age will be calculated as the integer part of the number of years from date of birth to the date of signing the informed consent form, using the following formula:

Age = integer part of (date of informed consent – date of birth + 1) / 365.25

4.2.2. Body Mass Index

BMI will be calculated as follows:

BMI (kg/m^2) = [weight (kg)] / [height (m)]^2

4.2.3. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first application of INCB018424 cream or vehicle cream.

Concomitant medication is defined as any nonstudy medication that is:

- Started before the date of first application of INCB018424 cream or vehicle cream and is ongoing throughout the study or ends on/after the date of first application of INCB018424 cream or vehicle cream.
- Started on/after the date of first application of INCB018424 cream or vehicle cream and is ongoing or ends during the course of study treatment.

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after first application of INCB018424 cream or vehicle cream. In the listing, it will be indicated whether a medication is prior-only, concomitant-only, or both prior and concomitant.

For the purposes of analysis, all medications will be considered concomitant medications unless the medications can unequivocally be defined as not concomitant.

4.2.4. Handling of Missing and Incomplete Data

For response endpoints, all nonresponders, as well as all subjects who discontinue study treatment at any time before the timepoint of interest or discontinue from the study for any reason will be defined as nonresponders for NRI analysis.

For other endpoints, missing observations will be handled as detailed in the specific sections addressing each analysis.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc., Cary, NC; v9 or later) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include, but not be limited to, the number of observations, mean,

standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of subjects in each category.

Interim analyses are planned for this study as defined in Section 9.

5.2. Treatment Groups

This is a 3-part study with a 24-week, randomized, DB, and vehicle-controlled treatment period followed by a 28-week, continued, DB treatment period (52 weeks cumulative DB), and an optional 52-week OL treatment period. Data will be summarized by treatment group based on the treatment regimen that was initially assigned or received during the DB period. The results will be summarized and presented separately for the DB period and OL period. Treatment groups are as follows:

- INCB018424 cream 1.5% BID
- INCB018424 cream 1.5% QD
- INCB018424 cream 0.5% QD
- INCB018424 cream 0.15% QD
- Vehicle cream BID

5.3. Analysis Populations

5.3.1. Intent-to-Treat Population

All subjects who are randomized will constitute the ITT population. Treatment groups for this population will be defined according to the treatment assignment at the time of randomization regardless of the actual INCB018424 cream or vehicle cream subjects might apply during their participation in the study.

The ITT population will be used for the summary of demographics, baseline characteristics, subject disposition, and analyses of all efficacy data.

5.3.2. Per Protocol Population

Subjects in the ITT population who are considered to be sufficiently compliant with the Protocol will comprise the PP population.

The PP population will be used in the supportive sensitivity analyses of the primary efficacy endpoints.

5.3.3. Safety Evaluable Population

All randomized subjects who applied at least 1 dose of INCB018424 cream or vehicle cream will constitute the safety evaluable population. Treatment groups for this population will be determined according to the actual treatment the subject received on Day 1 regardless of assigned study drug treatment.

The safety evaluable population will be used for all safety analyses.

[redacted]

5.3.5. Open-Label Evaluable Population

All subjects who applied at least 1 dose of INCB018424 1.5% cream during the OL period will constitute the OL evaluable population.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

Appendix A provides a list of data displays.

6.1. Baseline and Demographics, Physical Characteristics, and Disease History

6.1.1. Demographics

The following demographics will be summarized for the ITT population in the DB period and the OL evaluable population in the OL period: age, sex, race, ethnicity, weight, height, BMI.

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized for the ITT population in the DB period:

- Years since first onset of vitiligo (< 2 years, 2-5 years, > 5 years)
- Age (≤ 30 or > 30 years)
- Baseline F-VASI (25% to < 50% or 50%-100%)
- Vitiligo diagnosed in childhood (No/Yes [age]: 0-5 years, 6-11 years, 12-17 years)
- Type of vitiligo (segmental/nonsegmental)
- Disease status (stable/progressive)
- Skin type (type I/II/III/IV/V/VI)
- Other autoimmune disorders (thyroid disorders/juvenile diabetes mellitus/pernicious anemia/Addison's disease/other)

- Prior therapy given for vitiligo (topical corticosteroids/vitamin D derivatives/calcineurin inhibitors/photochemotherapy/surgical techniques/excimer laser/intralesional/other)
- Current BSA involvement of the face (% of the total face)
- Current T-BSA involvement (% of the total body)

6.1.3. Prior Therapy

Prior medication information for vitiligo will be used to identify medication received by subjects before enrollment into the study. Prior medications for vitiligo will be summarized by treatment group.

6.1.4. Medical History

For subjects in the ITT population in the DB period, medical history will be summarized by assigned treatment group. This summary will include the number and percentage of subjects with significant medical history for each body system/organ class as documented on the eCRF.

6.2. Disposition of Subjects

The number and percentage of subjects who were enrolled, randomized, treated, completed the DB treatment period through Week 24 and Week 52, were treated in the OL period, completed the OL period, and/or discontinued from the study or study treatment with a primary reason for discontinuation in DB or OL treatment period will be summarized for the ITT population in the DB period and the OL evaluable population in the OL period. The number of subjects randomized/enrolled by site will also be provided by treatment group.

6.3. Protocol Deviations and Violations

Protocol deviations and violations recorded on the eCRF will be presented in the subject data listings.

6.4. Exposure

For subjects in the safety population in the DB period and subjects in the OL evaluable population in the OL period, descriptive statistics will be provided by treatment group for duration of treatment, average daily dose, and total dose. Duration of treatment with INCB018424 cream or vehicle cream is defined as the number of days from Day 1 to the last record (defined in Table 2) of INCB018424 cream or vehicle cream application.

Table 2: Definition of Variables for Duration of Treatment

Study Period	Treatment Group[a]	Day 1	Last Record

DB period	INCB018424 cream 1.5% BID 1.5% QD 0.5% QD 0.15% QD vehicle cream BID	Date of first application in DB period.	Date of last record in DB period.
OL period	INCB018424 cream 1.5% BID	Date of first application in DB period.	Date of last record in the OL period.
	INCB018424 cream 1.5% QD 0.5% QD 0.15% QD vehicle cream BID	Date of first application in OL period.	Date of last record in the OL period.

[a] Treatment group initially assigned or actual treatment received during the DB period.

6.5. Study Drug Compliance

For subjects in the safety evaluable population, overall compliance (%) for INCB018424 cream or vehicle cream be calculated for all subjects as

Compliance (%) = 100 × [total amount dispensed – total amount returned] / [total intended dose]

- Total amount dispensed is sum of the weights of tubes dispensed prior to the current visit.
- Total amount returned is the sum of the tubes retuned prior to and on the current visit.
- The intended dose will be based on the earliest study day of permanent discontinuation of the study drug or last study medication record in the database.

6.6. Prior and Concomitant Medication

For subjects in the safety evaluable population in the DB period and the OL evaluable population in the OL period, prior medications and concomitant medications will be coded using the WHO Drug Dictionary and summarized by WHO drug class and WHO drug term. Results will be summarized as number and percentage of subjects with prior and concomitant medications by PT and WHO drug class.

7. EFFICACY

Appendix A provides a list of data displays.

7.1. General Considerations

For continuous measurements, summary statistics will include sample size, mean, median, standard deviation, standard error of the mean, minimum, and maximum. For all continuous variables, both the actual value and change and/or percentage from baseline (if available) will be analyzed.

For categorical measurements, summary statistics will include sample size, frequency, and percentages.

All by-visit analyses will include the follow-up period if the data are available.

7.2. Efficacy Measures

7.2.1. Vitiligo Area and Severity Index

Areas affected by depigmentation due to vitiligo will be assessed using the VASI, which is a quantitative clinical tool that is analogous to the Psoriasis Area Severity Index used in psoriasis and is based on a composite estimate of the overall area of vitiligo patches at baseline and the degree of macular repigmentation within these patches over time.

In this study, F-VASI will be determined. F-VASI will be the percentage of depigmented vitiligo skin expressed as a percentage of the total area of skin on the face (100%) and estimated by the investigator using the palmar method. This will be an additional variable to be analyzed in addition to the vitiligo head/neck subscore.

The primary endpoint, which is the proportion of subjects treated with INCB018424 cream who achieve an F-VASI50 at Week 24 compared with subjects treated with vehicle cream, will be assessed using the F-VASI for the ITT population in the DB period. The percentage improvement in F-VASI score from baseline will be computed as:

100 × (Baseline F-VASI score – Observed F-VASI score) / Baseline F-VASI score.

A positive score denotes improvement, and a negative score denotes worsening.

The categorical variable F-VASI50 is defined to be equal to 1 for subjects achieving an improvement in F-VASI of at least 50% and 0 for those achieving improvement of less than 50%. A subject is said to be an F-VASI50 responder or have achieved an F-VASI50 response if F-VASI50 = 1.

The total body VASI (T-VASI) is calculated using a formula that includes contributions from all body regions (possible range, 0-100).

$$VASI = \sum_{all\ body\ sites} [hand\ units]\ x\ [Residual\ Depigmentation]$$

Briefly, the body is divided into the following 6 separate and mutually exclusive sites: head/neck, hands, upper extremities (excluding hands), trunk, lower extremities (excluding feet), and feet. The percentage of vitiligo involvement is estimated in hand units by the same investigator during the entire course of the study to eliminate variations in hand size. The degree of depigmentation for each body site was determined and estimated to the nearest of the following percentages: 0%, 10%, 25%, 50%, 75%, 90%, or 100%. At 100% depigmentation, no pigment is present; at 90%, specks of pigment are present; at 75%, the depigmented area exceeds the pigmented area; at 50%, the depigmented and pigmented area are equal; at 25%, the pigmented area exceeds the depigmented area; at 10%, only specks of depigmentation are present. The VASI is then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each body site and adding the values of all

body sites together (Hamzavi et al 2004, Dicle 2015). See Appendix C of the Protocol for the full assessment tool.

The categorical variable T-VASI50 is defined to be equal to 1 for subjects achieving an improvement in T-VASI of at least 50% and 0 for those achieving improvement in T-VASI of less than 50%. A subject is said to be a T-VASI50 responder or have achieved a T-VASI50 response if T-VASI50 = 1.

7.2.2. Body Surface Area

At each visit, the BSA affected with vitiligo for each of 4 regions (head/neck [H], upper limbs [UL], trunk [T], and lower limbs [LL]) as a percentage of the T-BSA, as well as the face separately (depigmented area as a percent of the total area of the face) will be determined to the nearest 0.1% using, as guides, the palm plus 5 digits, with fingers tucked together and thumb tucked to the side (handprint), as 1% BSA and the thumb as 0.1% BSA.

If the subject has areas that exceed 20% that will not be treated with study drug, the BSA of these areas should be noted.

If worsening of vitiligo is present, then new areas, expansion of existing areas, or both are noted as present since the prior visit.

7.2.3. Vitiligo European Task Force Scale

The VETF proposed a system that combines analysis of extent, stage of disease (staging), and disease progression (spreading). Extent is evaluated using the rule of nines, already used in assessment of atopic dermatitis. Staging is based on cutaneous and hair pigmentation in vitiligo patches, and the disease is staged 0 to 4 on the largest macule in each body region, except hands and feet, which are assessed separately and globally as 1 unique area.

The staging scale is as follows:

- Stage 0: normal pigmentation (no depigmentation in area graded).
- Stage 1: incomplete pigmentation (including spotty depigmentation, trichrome, and homogeneous lighter pigmentation).
- Stage 2: complete depigmentation, a few white hairs do not change stage.
- Stage 3: partial hair whitening < 30%.
- Stage 4: complete hair whitening.

"Spreading" in VETF includes a dynamic dimension, since rapidly progressive vitiligo needs urgent intervention to stabilize the disease. The proposed grid allows scoring this dimension on a simple scale (+1: progressive; 0: stable; −1: regressive).

Spreading is assessed by combining Wood's lamp and electric light examinations in a dark room. Wood's lamp includes a magnifying lens to assess hairs, especially vellus hairs (Taïeb and Picardo 2007, Kawakami and Hashimoto 2011, Komen et al 2015).

See Appendix D of the Protocol for the full assessment tool.

7.2.4. Physician's Global Vitiligo Assessment

The severity of vitiligo will be assessed by the physician using the PhGVA, which has a 5-point scale (Table 3). Response will be reported for face and overall (F-PhGVA and T-PhGVA). Complete facial repigmentation is defined as an F-PhGVA of clear (0).

During the OL extension, for subjects who have complete facial repigmentation at Week 52 or Week 80, relapse is defined as increased areas of depigmentation, as determined by the investigator, by a change in F-PhGVA from 0 (clear) to 1 (almost clear) or from 0 (clear) to ≥ 2 (mild disease).

Table 3: Physician's Global Vitiligo Assessment Scale

Score	Severity	Description
0	Clear	No signs of vitiligo.
1	Almost clear	Only specks of depigmentation present.
2	Mild disease	Pigmented and depigmented areas are equal.
3	Moderate disease	More or complete depigmentation (may include < 30% hair whitening).
4	Severe disease	Complete depigmentation plus > 30% hair whitening.

A subject is said to be an F-PhGVA responder or have achieved an F-PhGVA response if he or she has achieved F-PhGVA of clear or almost clear. T-PhGVA responder and T-PhGVA response are defined in a similar fashion.

7.2.5. Patient's Global Vitiligo Assessment

The severity of vitiligo will be assessed by the subject using the PaGVA, which has a 5-point scale. Response will be reported for face and overall (F-PaGVA and T-PaGVA). The subject will be asked the following:

> How severe is your vitiligo on your face (or total body) with respect to the area covered by white skin?
>
> Responses: No white patches (No vitiligo); Mild; Moderate; Severe; Very Severe.

7.2.6. Patient Global Impression of Change-Vitiligo

The PaGIC-V is an assessment of improvement by the subject. It is a 7-point scale comparing the vitiligo areas at baseline with the subject's treated areas of vitiligo at the study visit. The subject will answer the following:

> Since the start of the treatment you've received in this study, your vitiligo in areas treated with the study drug is: (1) very much improved, (2) much improved, (3) minimally improved, (4) no change, (5) minimally worse, (6) much worse, and (7) very much worse.

A subject is said to be a PaGIC-V responder or have achieved a PaGIC-V response if he or she has achieved PaGIC-V of (1) very much improved or (2) much improved.

[redacted]

7.3. Analysis of the Primary Efficacy Parameter

7.3.1. Primary Efficacy Analysis

The primary endpoint is the proportion of subjects treated with INCB018424 cream who achieve an F-VASI50 at Week 24 compared with subjects treated with vehicle cream. The comparison of the primary endpoint will be performed in the ITT population for the superiority of either INCB018424 cream 1.5% BID or 1.5% QD versus vehicle cream using the Bonferroni-Holm procedure at an overall 2-sided $\alpha = 0.05$ level. The graphical approach that controls the Type I error rate can be found in Figure 2. The percentage of subjects achieving an F-VASI50 response at Week 24 will be analyzed by logistic regression using stratification factor of randomization (ie, age ≤ 30 or > 30 years) and treatment group as predictors. Exact logistic regression (Mehta and Patel 1995) will be used for all of the comparisons if any of the dose levels has an expected cell count less than 5. The proportions, along with unadjusted p-values and 95% confidence intervals, will be reported. All nonresponders in the DB period, as well as all subjects who discontinue study treatment at any time before the timepoint of interest or discontinue from the study for any reason, will be defined as nonresponders for the NRI analysis.

7.3.2. Sensitivity and Supportive Analyses for Primary Endpoint

The primary endpoint will be analyzed using the PP population as a sensitivity analysis to the ITT population.

7.4. Analysis of the Secondary Efficacy Parameters

Secondary efficacy analyses will be conducted for the ITT population in the DB period.

7.4.1. Efficacy Analysis for Key Secondary Endpoints

The percentage of F-PhGVA responders at Week 24, as well as the percentage of T-VASI50 responders at Week 52, will be analyzed using similar logistic regression as specified in the primary efficacy analysis. The NRI rule for missing data is the same as in F-VASI50. The graphical approach as specified in Figure 2 will be used to control the family-wise error rate.

7.4.2. Efficacy Analysis for Other Secondary Endpoints

There will be no adjustment for multiple comparisons for secondary endpoints other than the key secondary endpoints.

An E_{max} model will be fit for assessment of the dose-response relationship on percentage change from baseline in F-VASI scores at Week 24, which will provide estimates of the maximum and minimum response levels, ED_{50} (the concentration where the response is the midpoint between the maximum and minimum), and the slope parameter. The 5 dose levels of INCB018424 cream

in the model fitting will be vehicle, 0.15% QD, 0.5% QD, 1.5% QD, and 1.5% BID (equivalent to 3% QD).

Mean, change from baseline, and percentage change from baseline will be summarized by treatment and visit using descriptive statistics for the following:

- F-VASI and T-VASI
- F-BSA and T-BSA
- VETF

Categorical endpoints at postbaseline visits will be summarized by treatment and visit using descriptive statistics, including the following:

- F-VASI50 and T-VASI50
- F-PhGVA and T-PhGVA
- F-PaGVA and T-PaGVA
- F-PhGVA and T-PhGVA of clear and almost clear
- PaGIC-V and PaGIC-V of very much improved or much improved

The Kaplan-Meier product limit method will be used to estimate time to event curves for the following:

- F-VASI50 and T-VASI50
- F-PhGVA and T-PhGVA of clear or almost clear
- PaGIC-V of very much improved or much improved

Treatment comparisons may be performed using the log-rank test stratified by randomization stratification factor, if applicable.

[redacted]

7.6. Subgroup Analyses

Subgroups will be formed based on the following subject characteristics and baseline variables for those subjects whose data are available:

- Age ($\leq$ 30 or > 30)
- F-VASI at baseline (25% to < 50% or 50% to 100%)
- Years since first onset of vitiligo (< 2 years, 2-5 years, > 5 years)

- Skin type (type I/II/III/IV/V/VI)
- Race (White, Black, Asian, American Indian/Alaska Native, Native Hawaiian/Pacific islander/other)

[redacted]

[redacted]

8. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays.

8.1. General Considerations

Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique PTs reported on relatively few subjects.

Unless otherwise stated, table summaries will be limited to AEs occurring within 30 days of the last administration of study drug.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after first application of study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug application.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE. The CTCAE v4.03 is used for this study. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered to be treatment-related. The incidence of AEs and treatmentrelated AEs will be tabulated. In addition, SAEs will also be tabulated.

Any missing onset date, causality, or severity must be queried for resolution. Unresolved missing causality and severity will be handled according to the following rules:

- An unresolved missing causality will be considered treatment-related.
- An unresolved missing severity will be identified as an unknown severity.

For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment emergent.

8.2.2. Adverse Event Summaries

An overall summary of AEs by treatment group will include:

- Number (%) of subjects reporting any TEAEs
- Number (%) of subjects reporting any SAEs
- Number (%) of subjects reporting any Grade 3 or 4 TEAEs
- Number (%) of subjects reporting any treatment-related TEAEs
- Number (%) of subjects who temporarily interrupted study treatment because of TEAEs
- Number (%) of subjects who permanently discontinued study treatment because of TEAEs
- Number (%) of subjects who had a TEAE leading to death

The following summaries will be produced by MedDRA term (if 2 or fewer subjects appear in a table, a listing may be appropriate):

- Summary of TEAEs by SOC and PT
- Summary of TEAEs by PT in decreasing order of frequency
- Summary of TEAEs by SOC, PT, and maximum severity
- Summary of treatment-related AEs by SOC and PT
- Summary of treatment-related AEs by PT in decreasing order of frequency
- Summary of treatment-related AEs by SOC, PT, and maximum severity

- Summary of Grade 3 or 4 AEs by SOC and PT
- Summary of Grade 3 or 4 treatment-related AEs by SOC and PT
- Summary of TEAEs leading to death by SOC and PT
- Summary of treatment-emergent SAEs by SOC and PT
- Summary of treatment-emergent SAEs by PT in descending order of frequency
- Summary of treatment-related SAEs by SOC and PT
- Summary of TEAEs leading to dose interruption by SOC and PT
- Summary of TEAEs leading to discontinuation of treatment by SOC and PT
- Summary of nonserious TEAEs by SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

All laboratory assessments will be performed using a central laboratory except for urine pregnancy tests (as applicable). Laboratory values and change from baseline values will be summarized descriptively by visit. Baseline values will be determined using the nonmissing values collected before the first dose, prioritizing scheduled assessments over unscheduled visits. The last scheduled record before administration will be considered the baseline record. For baseline laboratory candidates with the same date and time in the same priority category, additional rules may be provided after consultation with the medical monitor to delineate which value will be defined as baseline.

8.3.2. Laboratory Value Summaries

Clinical laboratory tests, including hematology, serum chemistry, and urinalysis (refer to Table 5 of the Protocol), will be performed for each subject during the study in accordance with study schedule of assessments. If specific safety issues arise, additional unscheduled laboratory tests/analyses may be performed at the discretion of the investigator.

All test results and associated normal ranges from central laboratories will be reported in SI units. All tests with numeric values will have a unique unit per test.

Laboratory hematology and serum chemistry parameters identified in Table 5 of the Protocol will be summarized. Numeric laboratory values will be summarized descriptively in SI units, and non-numeric test values will be tabulated when necessary. In addition, box-and-whisker plots will be provided for lab parameters if applicable.

For test results that will be summarized with available normal ranges, the number and percentage of subjects with the laboratory values being low, normal, high, and missing will be tabulated by each test and each visit.

A listing of abnormal laboratory values will be provided.

8.4. Vital Signs

Values at each scheduled visit, change, and percentage change from baseline for vital signs, including systolic blood pressure, diastolic blood pressure, pulse, respiratory rate, and body temperature will be summarized descriptively.

Criteria for clinically notable vital sign abnormalities are defined in Table 4. The abnormal values for subjects exhibiting clinically notable vital sign abnormalities will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined range and percentage change greater than 25%. The abnormal values for subjects exhibiting alert vital sign abnormalities will be listed.

Table 4: Criteria for Clinically Notable Vital Sign Abnormalities

Parameter	Raw Value	Percent Change From Baseline
Systolic blood pressure	< 90 or > 150 mmHg	< 25% or > 25%
Diastolic blood pressure	< 50 or > 90 mmHg	< 25% or > 25%
Pulse	< 45 or > 100 beats/min	< 25% or > 25%
Respiratory rate	< 8 or > 20 breaths/min	< 25% or > 25%
Body temperature	< 35.5°C or > 38.0°C	< 25% or > 25%

9. INTERIM ANALYSES

An interim analysis will be conducted when at least half of the randomized subjects reach Week 12 and again at Week 24. The interim analyses will not include any stopping rules for futility or efficacy. There will be no external Data Monitoring Committee. Sites will remain blinded to study drug, but some personnel at Incyte without direct contact with sites will be unblinded. An internal committee will be charged with evaluating the unblinded efficacy and safety results in the interim analysis. As there are no plans for stopping early for efficacy, no adjustments of α or final p-values for repeated testing are necessary.

For analysis of the primary endpoint, a cutoff for clinical data used in the first interim analysis will be based on the earliest date that the first 75 subjects complete the Week 12 visit or discontinue the study or study treatment. All visits occurring on or before this date for these 75 subjects will be included in the first interim analysis. The cutoff for the second interim analysis will be defined in a similar fashion.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 5.

Table 5: Statistical Analysis Plan Versions

SAP Version	Date
Original	28 JUN 2017

10.1. Changes to Protocol-Defined Analyses

Not applicable.

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

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Mehta CR, Patel NR. Exact logistic regression: theory and examples. Stat Med 1995;14:21432160.

Taïeb A, Picardo M, VETF Members. The definition and assessment of vitiligo: a consensus report of the Vitiligo European Task Force. Pigment Cell Res 2007;20:27-35.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the clinical study report. Standard tables will follow the conventions in the Standard Safety Tables initial version. In-text tables are identical in structure and content as appendix tables, but follow a Rich Text Format.

The lists of tables, figures, and listings are to be used as guidelines. Modifications of the list that do not otherwise affect the nature of the analysis will not warrant an amendment to the SAP.

Tables for Double-Blind Period

Table No.	Title	Population	Standard	In-Text
Baseline and Demographic Characteristics				
1.1 Disposition				
1.1.1.1	Analysis Populations	ITT	X	
1.1.1.2	Summary of Subject Disposition	ITT		
1.1.1.3	Summary of Number of Subjects Enrolled by Site	ITT	X	
1.2 Demography				
1.1.2.1	Summary of Demographics	ITT	X	
1.3 Baseline Characteristics				
1.1.3.1	Summary of Baseline Disease Characteristics	ITT		
1.1.3.2	Summary of Medical History	ITT	X	
1.4 Prior and Concomitant Medications				
1.1.4.1	Summary of Prior Medications	ITT	X	
1.1.4.2	Summary of Prior Medications for Vitiligo	ITT	X	
1.1.4.3	Summary of Concomitant Medications	ITT	X	
Efficacy				
2.1 F-VASI				
2.1.1.1	Summary of Subjects Achieving F-VASI50 Response at Week 24 (Primary Endpoint)	ITT		
2.1.1.2	Summary of Subjects Achieving F-VASI50 Response at Week 24	PP		
2.1.1.3	Summary of Subjects Achieving F-VASI50 Response by Visit From Baseline to Week 52	ITT		
2.1.1.4.1	Summary of Subjects Achieving F-VASI50 Response by Visit From Baseline to Week 52 and by Age ≤ 30 and > 30	ITT		

2.1.1.4.2	Summary of Subjects Achieving F-VASI50 Response by Visit From Baseline to Week 52 and by Categorical Baseline F-VASI Score	ITT		
2.1.1.4.3	Summary of Subjects Achieving F-VASI50 Response by Visit From Baseline to Week 52 and by Years Since First Onset of Vitiligo	ITT		

Table No.	Title	Population	Standard	In-Text
2.1.1.4.4	Summary of Subjects Achieving F-VASI50 Response by Visit From Baseline to Week 52 and by Skin Type	ITT		
2.1.1.4.5	Summary of Subjects Achieving F-VASI50 Response by Visit From Baseline to Week 52 and by Race	ITT		
2.1.1.5	Summary and Analysis of F-VASI Score by Visit From Baseline to Week 52	ITT		
2.1.1.6	Summary and Analysis of F-VASI Score by Visit From Baseline to Week 52 and by Age ≤ 30 and > 30	ITT		
2.1.1.7	Summary and Analysis of F-VASI Score by Visit From Baseline to Week 52 and by Categorical Baseline F-VASI Score	ITT		
2.2 T-VASI				
2.1.2.1	Summary of Subjects Achieving T-VASI50 Response by Visit From Baseline to Week 52	ITT		
2.1.2.2.1	Summary of Subjects Achieving T-VASI50 Response by Visit From Baseline to Week 52 and by Age ≤ 30 and > 30	ITT		
2.1.2.2.2	Summary of Subjects Achieving T-VASI50 Response by Visit From Baseline to Week 52 and by Categorical Baseline F-VASI Score	ITT		
2.1.2.2.3	Summary of Subjects Achieving T-VASI50 Response by Visit From Baseline to Week 52 and by Years Since First Onset of Vitiligo	ITT		
2.1.2.2.4	Summary of Subjects Achieving T-VASI50 Response by Visit From Baseline to Week 52 and by Skin Type	ITT		
2.1.2.2.5	Summary of Subjects Achieving T-VASI50 Response by Visit From Baseline to Week 52 and by Race	ITT		
2.1.2.4	Summary and Analysis of T-VASI Score by Visit From Baseline to Week 52	ITT		
2.1.2.5	Summary and Analysis of T-VASI Score by Visit From Baseline to Week 52 and by Age ≤ 30 and > 30	ITT		
2.1.2.6	Summary and Analysis of T-VASI Score by Visit From Baseline to Week 52 and by Categorical Baseline F-VASI Score	ITT		
2.3 F-PhGVA				
2.1.3.1	Summary of F-PhGVA by Visit From Baseline to Week 52	ITT		

2.1.3.2.1	Summary of F-PhGVA by Visit From Baseline to Week 52 and by Age ≤ 30 and > 30	ITT		
2.1.3.2.2	Summary of F-PhGVA by Visit From Baseline to Week 52 and by Categorical Baseline F-VASI Score	ITT		
2.1.3.2.3	Summary of F-PhGVA by Visit From Baseline to Week 52 and by Years Since First Onset of Vitiligo	ITT		
2.1.3.2.4	Summary of F-PhGVA by Visit From Baseline to Week 52 and by Skin Type	ITT		
2.1.3.2.5	Summary of F-PhGVA by Visit From Baseline to Week 52 and by Race	ITT		

Table No.	Title	Population	Standard	In-Text
2.4 T-PhGVA				
2.1.4.1	Summary of T-PhGVA by Visit From Baseline to Week 52	ITT		
2.5 F-PaGVA				
2.1.5.1	Summary of F-PaGVA by Visit From Baseline to Week 52	ITT		
2.6 T-PaGVA				
2.1.6.1	Summary of T-PaGVA by Visit From Baseline to Week 52	ITT		
2.7 F-BSA				
2.1.7.1	Summary of F-BSA by Visit From Baseline to Week 52	ITT		
2.8 T-BSA				
2.1.8.1	Summary of T-BSA by Visit From Baseline to Week 52	ITT		
2.9 VETF				
2.1.9.1	Summary of VETF by Visit From Baseline to Week 52	ITT		
2.10 PaGIC-V				
2.1.10.1	Summary of PaGIC-V by Visit From Baseline to Week 52	ITT		
[redacted]				
Safety				
3.1 Study Drug Exposure				
3.1.1.1	Summary of Drug Compliance	Safety	X	
3.1.1.2	Summary of Study Drug Exposure	Safety	X	

3.2 Adverse Events				
3.1.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X	
3.1.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X	
3.1.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X	
3.1.2.5	Summary of Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.6	Summary of Treatment-Related Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X	
3.1.2.7	Summary of Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X	
3.1.2.8	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.9	Summary of Grade 3 or 4 Treatment-Related TreatmentEmergent Adverse Events by MedDRA Preferred Term in the Open-Label Period	Safety	X	
Table No.	**Title**	**Population**	**Standard**	**In-Text**
3.1.2.10	Summary of TEAEs Leading to Death by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.11	Summary of Treatment-Emergent SAEs by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.12	Summary of Treatment-Emergent SAEs by MedDRA Preferred Term in Descending Order of Frequency	Safety	X	
3.1.2.13	Summary of Treatment-Related SAEs by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.14	Summary of TEAEs Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.15	Summary of TEAEs Leading to Discontinuation of Treatment by MedDRA System Organ Class and Preferred Term	Safety	X	
3.1.2.16[a]	Summary of Nonserious TEAEs by MedDRA System Organ Class and Preferred Term	Safety	X	
3.3 Laboratory				
3.1.3.1	Summary of Laboratory Values - Hematology	Safety	X	
3.1.3.2	Summary of Laboratory Values - Chemistry	Safety	X	
3.4 Vital Signs				

3.1.4.1	Summary of Systolic Blood Pressure	Safety	X	
3.1.4.2	Summary of Diastolic Blood Pressure	Safety	X	
3.1.4.3	Summary of Pulse	Safety	X	
3.1.4.4	Summary of Respiratory Rate	Safety	X	
3.1.4.5	Summary of Body Temperature	Safety	X	
3.1.4.6	Summary of Weight	Safety	X	

[a] Non-SAE table will be generated for the study with the express purpose of clinical trial results posting.

Tables for Open-Label Period

Table No.	Title	Population	Standard	In-Text
Baseline and Demographic Characteristics				
1.1 Disposition				
1.2.1.2	Summary of Subject Disposition	Open-label evaluable		
1.4 Concomitant Medications				
1.2.4.3	Summary of Concomitant Medications	Open-label evaluable	X	
Efficacy				
2.1 F-VASI				
2.2.1.3	Summary of Subjects Achieving F-VASI50 Response by Visit in the Open-Label Period	Open-label evaluable		
2.2.1.6	Summary and Analysis of F-VASI Score by Visit in the Open-Label Period	Open-label evaluable		

Table No.	Title	Population	Standard	In-Text
2.2 T-VASI				
2.2.2.1	Summary of Subjects Achieving T-VASI50 Response by Visit in the Open-Label Period	Open-label evaluable		
2.2.2.4	Summary and Analysis of T-VASI Score by Visit in the Open-Label Period	Open-label evaluable		
2.3 F-PhGVA				
2.2.3.1	Summary of F-PhGVA by Visit in the Open-Label Period	Open-label evaluable		
2.4 T-PhGVA				
2.2.4.1	Summary of T-PhGVA by Visit in the Open-Label Period	Open-label evaluable		
2.5 F-PaGVA				

2.2.5.1	Summary of F-PaGVA by Visit in the Open-Label Period	Open-label evaluable		
2.6 T-PaGVA				
2.2.6.1	Summary of T-PaGVA by Visit in the Open-Label Period	Open-label evaluable		
2.7 F-BSA				
2.2.7.1		Summary of F-BSA by Visit in Open-Label Period	Open-label evaluable	
2.8 T-BSA				
2.2.8.1		Summary of T-BSA by Visit in the Open-Label Period	Open-label evaluable	
2.9 VETF				
2.2.9.1	Summary of VETF by Visit in the Open-Label Period	Open-label evaluable		
2.10 PaGIC-V				
2.2.10.1		Summary of PaGIC-V by Visit in the Open-Label Period	Open-label evaluable	
[redacted]				
Safety				
3.1 Study Drug Exposure				
3.2.1.1	Summary of Drug Compliance in the Open-Label Period	Safety	X	
3.2.1.2	Summary of Study Drug Exposure in the Open-Label Period	Safety	X	
3.2 Adverse Events				
3.2.2.1	Overall Summary of Treatment-Emergent Adverse Events in the Open-Label Period	Safety	X	
3.2.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	

Table No.	Title	Population	Standard	In-Text
3.2.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the Open-Label Period	Safety	X	

3.2.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity in the Open-Label Period	Safety	X	
3.2.2.5	Summary of Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.2.2.6	Summary of Treatment-Related Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the Open-Label Period	Safety	X	
3.2.2.7	Summary of Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity in the Open-Label Period	Safety	X	
3.2.2.8	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.2.2.9	Summary of Grade 3 or 4 Treatment-Related TreatmentEmergent Adverse Events by MedDRA Preferred Term in the Open-Label Period	Safety	X	
3.2.2.10	Summary of Treatment-Emergent Adverse Events Leading to Death by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.2.2.11	Summary of Treatment-Emergent SAEs by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.2.2.12	Summary of Treatment-Emergent SAEs by MedDRA Preferred Term in Descending Order of Frequency in the Open-Label Period	Safety	X	
3.2.2.13	Summary of Treatment-Related SAEs by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.2.2.14	Summary of TEAEs Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.2.2.15	Summary of TEAEs Leading to Discontinuation of Treatment by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.2.2.16[a]	Summary of Nonserious TEAEs by MedDRA System Organ Class and Preferred Term in the Open-Label Period	Safety	X	
3.3 Laboratory				
3.2.3.1	Summary of Laboratory Values in the Open-Label Period - Hematology	Safety	X	
3.2.3.2	Summary of Laboratory Values in the Open-Label Period - Chemistry	Safety	X	
Table No.	**Title**	**Population**	**Standard**	**In-Text**
3.4 Vital Signs				

3.2.4.1	Summary of Systolic Blood Pressure in the Open-Label Period	Safety	X	
3.2.4.2	Summary of Diastolic Blood Pressure in the Open-Label Period	Safety	X	
3.2.4.3	Summary of Pulse in the Open-Label Period	Safety	X	
3.2.4.4	Summary of Respiratory Rate in the Open-Label Period	Safety	X	
3.2.4.5	Summary of Body Temperature in the Open-Label Period	Safety	X	
3.2.4.6	Summary of Weight in the Open-Label Period	Safety	X	

[a] Non-SAE table will be generated for the study with the express purpose of clinical trial results posting.

Figures

		Period/Population	
Figure No.	**Title**	**DB Period**	**Open-Label Period**
Efficacy			
2.x.1.1	Proportion of Subjects Achieving F-VASI50 Response by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.1.1.2	Proportion of Subjects Achieving a F-VASI50 Response by Visit and Treatment Group	PP	
2.x.1.3	F-VASI Score by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.x.1.4	Mean Change From Baseline in F-VASI Score by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.x.1.5	Percentage Change From Baseline in F-VASI Score by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.1.1.6	Kaplan–Meier Curve of Time to F-VASI50 Response	ITT	
2.x.2.1	Proportion of Subjects Achieving T-VASI50 Response Score by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.x.2.2	T-VASI Score by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.x.2.3	Mean Change From Baseline in T-VASI Score by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label Evaluable
2.x.2.4	Percentage Change From Baseline in T-VASI Score by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.1.2.5	Kaplan-Meier Curve of Time to T-VASI50 Response	ITT	

Figure No.	Title	Period/Population	
		DB Period	Open-Label Period
2.x.3.1	Proportion of Subjects Achieving F-PhGVA Response by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.1.3.2	Kaplan-Meier Curve of Time to F-PhGVA Response	ITT	
2.x.4.1	Proportion of Subjects Achieving T-PhGVA Response by Visit and Treatment Group	x = 1 ITT	x = 2 Open-label evaluable
2.1.4.2	Kaplan-Meier Curve of Time to T-PhGVA Response	ITT	
2.x.10.1	Proportion of Subjects Achieving PaGIC-V Response	x = 1 ITT	x = 2 Open-label evaluable
2.1.10.2	Kaplan-Meier Curve of Time to PaGIC-V Response	ITT	
Laboratory			
3.x.3.1.y[b]	Box-and-Whisker Plot of Selected Laboratory Hematology Values[d] by Visit	x = 1 ITT	x = 2 Open-label evaluable
3.x.3.2.y[c]	Box-and-Whisker Plot of Selected Laboratory Values[e] by Study Visit	x = 1 ITT	x = 2 Open-label evaluable

[b,c] y = 1, 2, 3, etc, where each y corresponds to an applicable test.
[d,e] "Selected Laboratory Hematology/Chemistry Values" should be replaced by the name of an applicable test.

Listings

Listing No.	Title
Demographic and Baseline Characteristics	
1.1.1	Subject Enrollment and Disposition Status
1.1.2	Subject Inclusion and Exclusion Criteria Violations
1.1.3	Protocol Deviations and Violations
1.2.1	Demographics
1.2.2	Baseline Characteristics
1.3	Medical History
1.4.1	Prior and Concomitant Medications
1.4.2	Prior and Concomitant Medications for Vitiligo
1.5	Study Drug Compliance
Efficacy	
2.1.1	F-VASI Score
2.1.2	Time to F-VASI50 Response

2.2	T-VASI Score
2.2	Time to T-VASI50 Response
2.3	F-PhGVA Score
Listing No.	**Title**
2.3	Time to F-PhGVA Response
2.4	T-PhGVA Score
2.4	Time to T-PhGVA Response
2.5	F-PaGVA Score
2.6	T-PaGVA Score
2.7	F-BSA
2.8	T-BSA
2.9	VETF Score
2.10.1	PaGIC-V
2.10.2	Time to PaGIC-V Response
[redacted]	[redacted]
Adverse Events and Exposure	
3.1	Study Drug Administration
3.2.1	Adverse Events
3.2.2	Adverse Events Leading to Discontinuation
3.2.3	Serious Adverse Events
3.2.4	Adverse Events Leading to Death
3.2.5	Treatment-Related Adverse Events
3.2.6	Adverse Events Leading to Dose Interruption
3.2.7	Adverse Events Requiring Concomitant Medications
Laboratory Data	
3.3.1	Clinical Laboratory Values – Hematology
3.3.2	Clinical Laboratory Values – Serum Chemistry
3.3.4	Abnormal Clinical Laboratory Values – Hematology
3.3.5	Abnormal Clinical Laboratory Values – Serum Chemistry
[redacted]	[redacted]
3.3.7	Central Laboratory Collection Times
Vital Signs	
3.4.1	Vital Signs
3.4.2	Abnormal Vital Sign Values
3.4.3	Alert Vital Sign Values
ECG	

3.5	Abnormal ECG Values

Signature Manifest

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