Official Title:	**Topical Ruxolitinib Evaluation in Vitiligo Study 2 (TRuE-V2): A Phase 3, Double-Blind, Randomized, Vehicle-Controlled, Efficacy and Safety Study of Ruxolitinib Cream Followed by an Extension Period in Participants With Vitiligo**
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Statistical Analysis Plan

INCB 18424-306/307

Topical **Ru**xolitinib **E**valuation in **V**itiligo Study **1/2**
(TRuE-V1/2)

A Phase 3, Double-Blind, Randomized, Vehicle-Controlled, Efficacy and Safety Study of Ruxolitinib Cream Followed by an Extension Period in Participants With Vitiligo

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SAP Author:	[redacted] [redacted] **Biostatistics**
Date of Plan:	**09 MAR 2021**

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

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LIST OF ABBREVIATIONS

Abbreviations	Definition
AE	adverse event
ANCOVA	analysis of covariance
ASR	application site reaction
BID	twice daily
BMI	Body Mass Index
BSA	body surface area
CDLQI	Children's Dermatology Life Quality Index
CI	confidence interval
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
DBP	diastolic blood pressure
DLQI	Dermatology Life Quality Index
eCRF	electronic case report form
FAS	Full Analysis Set
F-BSA	facial body surface area
F-PaGIC-V	facial assessment of Patient Global Impression of Change-Vitiligo
F-PhGVA	facial assessment of Physician Global Vitiligo Assessment
F-VASI	Face Vitiligo Area Scoring Index
F-VASI25/50/75/90	≥ 25%/50%/ 75%/ 90% improvement from baseline in Face Vitiligo Area Scoring Index score
HADS	Hospital Anxiety and Depression Scale
MedDRA	Medical Dictionary for Regulatory Activities
MI	multiple imputation
MMRM	mixed-effect model repeat measurement
NCI	National Cancer Institute
NRI	nonresponder imputation
Pa-GIC-V	Patient Global Impression of Change-Vitiligo
PD	pharmacodynamic
PhGVA	Physician Global Vitiligo Assessment
PK	pharmacokinetics
PP	per protocol

Abbreviations	Definition
PT	preferred term
SAP	Statistical Analysis Plan
SBP	systolic blood pressure
SOC	system organ class
T-BSA	total body surface area
TE	treatment-extension
TEAE	treatment-emergent adverse event
T-PaGIC-V	total body assessment of Patient Global Impression of Change-Vitiligo
T-PhGVA	total body assessment of Physician Global Vitiligo Assessment
TSQM	Treatment Satisfaction Questionnaire for Medication
T-VASI	total body Vitiligo Area Scoring Index
T-VASI25/50/75/90	≥ 25%/50%/ 75%/ 90% improvement in total body Vitiligo Area Scoring Index
VASI	Vitiligo Area Scoring Index
VitiQoL	Vitiligo-specific quality of life
VNS	Vitiligo Noticeability Scale
WHO-5	World Health Organization-Five Well-Being Index

1. INTRODUCTION

INCB 18424-306 is a randomized, vehicle-controlled study in adolescent and adult participants (age ≥ 12 years) with nonsegmental vitiligo who have depigmented area including ≥ 0.5% BSA on the face, ≥ 0.5 F-VASI, ≥ 3% BSA on nonfacial areas, ≥ 3 T-VASI, and for whom total body involved vitiligo area (facial and nonfacial) does not exceed 10% BSA. Approximately 300 participants will be randomized 2:1 to receive initial study treatment (ruxolitinib cream 1.5% BID:vehicle; applied to depigmented vitiligo areas on the face and body up to 10% total BSA) for 24 weeks. Participants will be stratified by region (North America or Europe) and skin type (Fitzpatrick scale Type I and II vs Type III, IV, V, and VI). Adolescents (≥ 12 to < 18 years) will make up at least 10% of the study population, and no more than 50% of participants will be > 40 years old.

After completion of the Week 24 assessments, participants will be offered the opportunity to receive an additional 28 weeks of treatment extension with ruxolitinib cream 1.5% BID. To be eligible for the treatment extension, participants must have completed the baseline and Week 24 visit assessments, be compliant with study procedures, and not have any safety issues. The total treated area should not exceed 10% BSA (facial and nonfacial).

Participants who successfully complete the 52-week treatment in this study may be eligible to participate in a separate extension study to evaluate durability of effect and maintenance regimens.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the study Protocol. The scope of this plan will be executed by the Department of Biostatistics or designee, and the analyses of PK will be executed by the Department of Clinical Pharmacokinetics or designee.

Another Phase 3 study, INCB 18424-307, has the identical study design as INCB 18424-306. This SAP applies to both INCB 18424-306 and INCB 18424-307 studies.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 18424-306 and -307 Protocol Amendment 3-US-CA dated 13 MAR 2020, INCB 18424-306 CRF approved 04 JUN 2020, and INCB 18424-307 CRF approved 05 JUN 2020. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and CRF versions.

2.2. Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To evaluate the efficacy of ruxolitinib cream in participants with vitiligo.	• Proportion of participants achieving F-VASI75 at Week 24.
Key Secondary	
To further assess the efficacy of ruxolitinib cream.	• Proportion of participants achieving F-VASI50 at Week 24. • Proportion of participants achieving F-VASI90 at Week 24. • Proportion of participants achieving T-VASI50 at Week 24. • Proportion of participants achieving a VNS of "4 – A lot less noticeable" or "5 – No longer noticeable" at Week 24. • Percentage change from baseline in F-BSA at Week 24.
Secondary	
To evaluate the safety and tolerability of ruxolitinib cream.	• The frequency and severity of AEs; physical examinations; vital signs; and laboratory data for hematology and serum chemistry.
To further assess the efficacy of ruxolitinib cream.	• Proportion of participants achieving F-VASI25/50/75/90 during the treatment period (double-blind and treatment extension periods). • Percentage change from baseline in F-VASI during the treatment period (double-blind and treatment extension periods). • Percentage change from baseline in F-BSA during the treatment period (double-blind and treatment extension periods). • Percentage change from baseline in T-VASI during the treatment period (double-blind and treatment extension periods). • Percentage change from baseline in T-BSA during the treatment period (double-blind and treatment extension periods). • Proportion of participants achieving T-VASI25/50/75/90 during the treatment period (double-blind and treatment extension periods). • Proportion of participants in each category of VNS during the treatment period (double-blind and treatment extension periods). • Change from baseline in DLQI (or CDLQI) during the treatment period (double-blind and treatment extension periods).
To evaluate the ruxolitinib PK in plasma after treatment of ruxolitinib cream.	• Population-based (trough) plasma concentrations of ruxolitinib at Weeks 4, 24, and 40.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Exploratory	
To further assess the efficacy of ruxolitinib cream.	• Proportion of participants achieving an F-PhGVA of clear (0) or almost clear (1) during the treatment period (double-blind and treatment extension periods). • Proportion of participants achieving a T-PhGVA of clear (0) or almost clear (1) during the treatment period (double-blind and treatment extension periods). • Proportion of participants in each F-PhGVA category during the treatment period (double-blind and treatment extension periods). • Proportion of participants in each T-PhGVA category during the treatment period (double-blind and treatment extension periods). • Proportion of participants who report F-PaGIC-V of very much improved or much improved during the treatment period (double-blind and treatment extension periods). • Proportion of participants in each F-PaGIC-V category during the treatment period (double-blind and treatment extension periods). • Proportion of participants who report T-PaGIC-V of very much improved or much improved during the treatment period (double-blind and treatment extension periods). • Proportion of participants in each T-PaGIC-V category during the treatment period (double-blind and treatment extension periods). • Proportion of participant in each category for the color-matching question during the treatment period (double-blind and treatment extension periods).
To determine the participants' quality of life.	• Change from baseline in WHO-5 during the treatment period (double-blind and treatment extension periods). • Actual measurements in TSQM during the treatment period (double-blind and treatment extension periods). • Change from baseline in VitiQoL during the treatment period (double-blind and treatment extension periods). • Change from baseline in HADS during the treatment period (double-blind and treatment extension periods).
To evaluate translational biomarkers in the blood of participants treated with ruxolitinib cream.	• Change from baseline in the expression of select biomarkers in peripheral blood at Weeks 12, 24, 40, and 52.

3. STUDY DESIGN

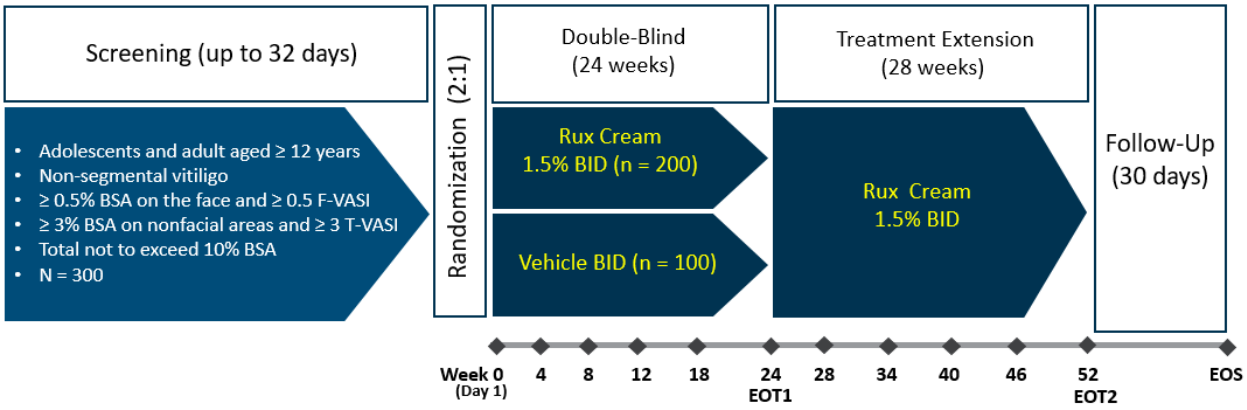
INCB 18424-306 and -307 are randomized, vehicle-controlled studies in adolescent and adult participants (age ≥ 12 years) with nonsegmental vitiligo who have depigmented area including ≥ 0.5% BSA on the face, ≥ 0.5 F-VASI, ≥ 3% BSA on nonfacial areas, ≥ 3 T-VASI, and for whom total body involved vitiligo area (facial and nonfacial) does not exceed 10% BSA. Approximately 300 participants will be randomized 2:1 to receive initial study treatment (ruxolitinib cream 1.5% BID:vehicle) for 24 weeks. Participants will be stratified by region (North America or Europe) and skin type (Fitzpatrick scale Type I and II vs Type III, IV, V, and VI). Adolescents (≥ 12 to < 18 years) will make up at least 10% of the study population, and no more than 50% of participants will be > 40 years old.

After completion of the Week 24 assessments, participants will be offered the opportunity to receive an additional 28 weeks of treatment extension with ruxolitinib cream 1.5% BID. To be eligible for the treatment extension, participants must have completed the baseline and Week 24 visit assessments, be compliant with study procedures, and not have any safety issues. The total treated area should not exceed 10% BSA (facial and nonfacial).

Participants who successfully complete the 52-week treatment in this study may be eligible to participate in a separate extension study to evaluate durability of effect and maintenance regimens.

The study schema is shown below in Figure 1. All participants will have follow-up assessments 30 (+ 7) days after the last application of study drug.

Figure 1: Study Design Schema



3.1. Randomization

Approximately 300 participants will be randomized 2:1 to receive initial study treatment (ruxolitinib cream 1.5% BID:vehicle) for 24 weeks. Participants will be stratified by skin type (Fitzpatrick scale Type I and II vs Type III, IV, V, and VI) and region (North America or Europe).

3.2. Control of Type I Error

The gatekeeping testing strategy for the primary and key secondary analyses will be implemented to control the overall Type I error rate, 2-sided $\alpha = 0.05$. These endpoints will be tested in a fixed sequence at 2-sided $\alpha = 0.05$ level in the following order:

- Proportion of participants achieving F-VASI75 at Week 24
- Proportion of participants achieving F-VASI50 at Week 24
- Proportion of participants achieving F-VASI90 at Week 24
- Proportion of participants achieving T-VASI50 at Week 24
- Vitiligo – VNS Response at Week 24
- Percentage change from baseline in F-BSA at Week 24

The endpoint will be tested only if the primary endpoint (and the secondary endpoints in previous steps) are rejected.

3.3. Sample Size Considerations

Approximately 300 participants will be randomized 2:1 to ruxolitinib cream 1.5% BID or vehicle and stratified by baseline skin type (Fitzpatrick scale Type I and II vs Type III, IV, V, and VI) and region (North America or Europe). The sample size is calculated to provide sufficient power (> 85%) to detect a difference between the 1.5% BID with the vehicle in primary and key secondary endpoints. The powers for different endpoints are provided in Table 2. The Fisher's exact test with a 2-sided alpha of 0.05 is used to provide a conservative evaluation of statistical power, and it is accurate when there is a small expected number of responders in the vehicle group.

Table 2: Powering for Primary and Key Secondary Endpoints

Endpoints	Response Rates in Ruxolitinib 1.5% BID[a]	Response Rates in Vehicle[a]	Power[b]
F-VASI75 at Week 24	20%	5%	95%
F-VASI50 at Week 24	30%	10%	95%
F-VASI90 at Week 24	10%	1%	88%
T-VASI50 at Week 24	10%	1%	88%
Vitiligo - VNS Response at Week 24	10%	1%	88%

[a] Based on the results from a Phase 2, randomized, dose-ranging study (INCB18424-211).
[b] Based on the Fisher's exact test with a 2-sided alpha of 0.05.

3.4. Schedule of Assessments

Refer to Protocol Amendment 3-US-CA dated 13 MAR 2020 for a full description of all study procedures and assessment schedules (Protocol Tables 3 and 4) for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date that the first application of ruxolitinib cream or vehicle cream is administered to the participants in the specific period.

For randomized participants not treated with any study drug, Day 1 is defined as the day of randomization.

4.1.2. Study Day

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

Day # = (visit/reporting date – Day 1 date + 1).

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

Day # = (visit/reporting date – Day 1 date).

A study day of −1 indicates 1 day before Day 1.

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before or on the day of first application of ruxolitinib cream or vehicle cream for double-blind period.

For randomized participants not treated with any study drug, baseline is defined as the last nonmissing assessment before or on the day of randomization for all parameters.

For participants who continue in the treatment extension period, baseline is defined as follows:

- For efficacy evaluation, baseline is the last nonmissing measurement obtained before or on the day of first application of study treatment in double-blind period;
- For safety evaluation, for participants who cross over from vehicle group to ruxolitinib cream, the baseline is the last nonmissing measurement obtained before or on the day of first application of ruxolitinib cream in the extension period; for participants who applies ruxolitinib cream in both periods, baseline is the last nonmissing measurement obtained before or on the day of first application of study treatment in double-blind period.

When scheduled assessments and unscheduled assessments occur on the same day and time of the assessment or time of first application is not available, use the following convention to determine baseline:

- If both a scheduled and an unscheduled visit are available on the day of the first application and the time is missing, use the scheduled assessment as baseline.
- If all scheduled assessments are missing on the day of the first application and an unscheduled assessment is available, use the unscheduled assessment as baseline.

4.1.4. Handling of Missing and Incomplete Data

For response endpoints, including F-VASI75, F-VASI50, F-VASI90, T-VASI50, and VNS 4 or 5 as listed in the primary and key secondary endpoints, all participants who are missing postbaseline values, will be handled using MI under the missing-at-random assumption.

For continuous endpoints, any participant who is missing postbaseline values may have missing data handled using MMRM or MI under the missing-at-random assumption. MMRM model implicitly adjusts for missing data through a variance-covariance structure.

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

4.2. Variable Definitions

4.2.1. Body Mass Index

Body mass index (BMI) will be calculated as follows:

$$\text{BMI } (kg/m^2) = [\text{weight } (kg)] / [\text{height } (m)]^2.$$

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first application of study treatment.

Concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first application of study treatment and is ongoing throughout the study or ends on/after the date of first application of study treatment.
- On/after the date of first application of study treatment 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 the first application of study treatment. 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.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; Version 9.1 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, maximum, 1st quartile, 3rd quartile, and 95% CI. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

This is a randomized, double-blind, vehicle-controlled study followed by a treatment extension period. Data will be summarized based on treatment regimen that was assigned (FAS) or that the participant actually applied (safety).

During the double-blind (DB) period, the treatment groups will be ruxolitinib cream 1.5% BID and vehicle cream.

During the treatment extension period, the treatment groups will be ruxolitinib cream 1.5% BID and vehicle to ruxolitinib cream 1.5% BID.

5.3. Analysis Populations

5.3.1. Full Analysis Set

All participants who are randomized and have baseline and any postbaseline assessments constitute the FAS. Treatment groups for this population will be defined according to the treatment assignment at the time of randomization regardless of the actual study treatment the participant might apply during his/her participation in the study. Those participants who have only study baseline, but not any postbaseline assessment are not included in the FAS.

The FAS will be used for the summary of analyses of demographics, baseline characteristics, participant disposition, and all efficacy data.

5.3.2. Per Protocol Population

Participants in the FAS population who are considered to be sufficiently compliant with the Protocol compose the PP population, which is defined for supportive sensitivity analyses for primary efficacy endpoint in the double-blind period. Participants with important protocol deviations, as defined in Section 6.3, will be excluded from the PP population.

5.3.3. Safety Population

All randomized participants who applied ruxolitinib cream or vehicle cream at least once will constitute the safety population. Treatment groups for this population will be determined according to the actual treatment the participant applied on Day 1 regardless of assigned study treatment.

All safety analyses will be conducted using the safety population.

5.3.4. Treatment-Extension Evaluable Population

Participants who applied at least 1 application of ruxolitinib cream in treatment extension period will constitute the TE evaluable population.

5.3.5. Pharmacokinetic/Pharmacodynamic Evaluable Population

The PK/PD evaluable population will include all participants who applied ruxolitinib cream at least once and provided at least 1 postdose plasma sample (1 PK/PD measurement) that complies with the instruction in the Protocol. Participants in whom it is not possible to obtain a blood sample for PK/PD from an area of the body that was not treated with (exposed to) study drug (eg, due to difficulties of technical/ procedural nature) will not be included in the PK/PD evaluable population because of the material risk of the contamination of such a sample with study drug from the skin through which a needle is passed. The study pharmacokineticist will review data listings of study drug application and sample records to identify participants to be excluded from PK data analyses. The study research investigator will review data listings of PD data and sample records to identify participants to be excluded from analyses of PD data.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

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

6.1.1. Demographics

The following demographics will be summarized for the FAS and Safety population during the DB period and the TE evaluable population in the TE period: age, age group, sex, race, ethnicity, region, weight, height, and BMI.

6.1.2. Baseline Disease Characteristics

Baseline disease characteristics summarized for the FAS and Safety population include but are not limited to the following:

- Time since initial diagnosis of vitiligo
- Vitiligo diagnosed in childhood (No/Yes [age]: 0-5 years, 6-11 years, 12-17 years)
- Disease status (stable/progressive)
- Skin type (type I/II/III/IV/V/VI)
- Other autoimmune disorders
- Prior therapy given for vitiligo (predefined systemic treatments, phototherapy, and surgical procedures)
- History of acne vulgaris (No/Yes)

- Currently have acne vulgaris on the face (No/Yes)
- Vitiligo in genital area (No/Yes)
- Baseline F-VASI
- Baseline T-VASI
- Baseline F-BSA involvement (% of the total body)
- Baseline T-BSA involvement (% of the total body)

6.1.3. Prior Therapy for Vitiligo

Prior medication information for vitiligo will be used to identify other non-predefined medication received by participants before enrollment into the study. Prior medications for vitiligo will be summarized by treatment group.

6.1.4. Medical History

For participants in the safety population during the DB period, medical history will be summarized by assigned treatment group. This summary will include the number and percentage of participants with medical history for each body SOC/PT as documented in the eCRF.

6.2. Disposition of Participants

The number and percentage of participants who were randomized, treated, and completed the DB period and of participants who discontinued the treatment or withdrew from the study during the DB period with a primary reason for discontinuation will be summarized for both the FAS and safety population during the DB period.

The number and percentage of participants who completed the TE period and discontinued treatment or withdrew from the study during the TE period with a primary reason for discontinuation will be summarized for the TE evaluable population in the TE period.

6.3. Protocol Deviations

In general, the following are important protocol deviations that may significantly affect the primary and gated secondary analyses:

- Missing primary endpoint on F-VASI;
- Compliance < 60% based on the application numbers.

Participants with 1 or more such deviations will be excluded from the PP population. In addition, protocol deviations related to inclusion/exclusion criteria, discontinuation criteria, and use of excluded concomitant medications will be reviewed. Decisions as to whether any of these deviations warrant exclusion from the PP population will be made before breaking the blind.

6.4. Exposure

For participants in the safety population during the DB period and participants in the TE evaluable population during the TE period, descriptive statistics will be provided by treatment group for duration of treatment, average daily dose, and total dose. Summary for overall

exposure including DB and TE periods will be provided for participants continually using 1.5% BID. Duration of treatment with ruxolitinib cream or vehicle cream is defined as the number of days from Day 1 to the last record of ruxolitinib cream or vehicle cream application in the specific period.

6.5. Study Drug Compliance

Overall compliance (%) for the application of ruxolitinib cream or vehicle cream during the DB and treatment extension periods will be calculated for all participants in the safety population as follows:

> Overall application compliance (%) = 100 × [total number of nonmissing applications] / [total number of intended applications]

where the total number of nonmissing applications is the total number of applications that the participant actually applied in each period during the study. The total number of intended applications is the number of planned applications minus the number of interrupted applications.

6.6. Prior and Concomitant Medication

For participants in the safety population during the DB period, prior medications and concomitant medications will be coded using the WHO Drug Dictionary and summarized as number and percentage of participants with prior and concomitant medications by WHO drug class and WHO drug term. For participants in the treatment extension period (ie, the TE evaluable population), only concomitant medications will be summarized.

Prior and concomitant medications will be summarized by treatment group as well as listed.

7. EFFICACY

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

7.1. General Considerations

For all continuous variables, both the actual value and change and/or percentage from baseline (if available) will be analyzed.

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

7.2. Efficacy Measures

7.2.1. Body Surface Area

Total % BSA (includes facial and nonfacial areas) depigmented by vitiligo will be estimated at each visit. Body surface area assessment will be performed by the Palmar Method. Body surface area should be estimated to the nearest 0.1%. The approximate size of the participant's entire palmar surface (ie, the palm plus 5 digits) should be considered as 1% BSA, and the approximate size of the participant's thumb should be considered as 0.1% BSA.

7.2.2. Vitiligo Area Scoring Index

Areas affected by depigmentation due to vitiligo will be assessed using the VASI. It 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.

Facial VASI (F-VASI) is measured by percentage of vitiligo involvement (% of BSA) and the degree of depigmentation. The percentage of BSA (hand unit) vitiligo involvement is estimated by the investigator using the Palmar Method. Hand unit is based on participant's hand size. Investigator uses his/her hand to mimic the participant's hand size to evaluate percentage of BSA vitiligo involvement. The degree of depigmentation for each vitiligo involvement site is 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 F-VASI is then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each site on the face and summing the values of all sites together (possible range 0-3).

[redacted]

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

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

The body is divided into the following 6 separate and mutually exclusive sites: 1) head/neck, 2) hands, 3) upper extremities (excluding hands), 4) trunk, 5) lower extremities (excluding feet), and 6) feet. The percentage of vitiligo involvement is estimated in hand units (% of BSA) by the same investigator during the entire course of the study. Hand unit is based on participant's hand size. The investigator uses his/her hand to mimic the participant's hand size to evaluate % BSA vitiligo involvement. The degree of depigmentation for each body site is determined and estimated to the nearest of the following percentages: 0%, 10%, 25%, 50%, 75%, 90%, or 100%. The T-VASI is then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each body site and summing the values of all body sites together (Hamzavi et al 2004).

The categorical variable F-VASI25 will be equal to 1 for percentage improvement from baseline in F-VASI of ≥ 25% and will be equal to 0 for percentage improvement of < 25%. F-VASI50/75/90 and T-VASI25/50/75/90 are defined with the same pattern.

7.2.3. Physician's Global Vitiligo Assessment (Facial)

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 (F-PhGVA).

Table 3: Facial Physician's Global Vitiligo Assessment Scale

Score	Severity	Description
0	Clear	No signs of vitiligo or complete/near complete repigmentation
1	Almost Clear	Mostly pigmented areas with small depigmented or difficult to repigment areas (eg, philtrum, nares, corners of eyes, perioral skin)
2	Mild Disease	Modest areas of depigmentation (not more than half of facial skin) with approximately 50% pigmentation within vitiligo areas or significant perifollicular pattern present
3	Moderate Disease	Large areas of depigmented vitiligo areas (more than half of facial skin); significant depigmentation within vitiligo areas
4	Severe Disease	Extensive areas of vitiligo to complete depigmentation on face

An F-PhGVA of clear (0) or almost clear (1) can be interpreted as F-PhGVA response.

7.2.4. Physician's Global Vitiligo Assessment (Total Body)

The severity of total body vitiligo will be assessed by the physician using the PhGVA, which has a 5-point scale (Table 4). Response will be reported for total body (T-PhGVA).

Table 4: Total Body Physician's Global Vitiligo Assessment Scale

Score	Severity	Description
0	Clear	No signs of vitiligo or complete/near complete repigmentation
1	Almost Clear	Mostly pigmented areas with small depigmented or difficult to repigment areas (eg, hands, feet, philtrum, nares, corners of eyes, perioral skin)
2	Mild Disease	Modest areas of depigmentation with approximately 50% pigmentation within vitiligo areas or significant perifollicular pattern present
3	Moderate Disease	Large areas of depigmented vitiligo areas; significant depigmentation within vitiligo areas
4	Severe Disease	Extensive areas of vitiligo with complete depigmentation

An T-PhGVA of clear (0) or almost clear (1) can be interpreted as T-PhGVA response.

7.2.5. Patient-Reported Outcomes

Patient-reported outcomes and quality of life will be assessed using the following tools:

- VNS (Section 7.2.5.1)
- Color-matching question (Section 7.2.5.2)
- F-PaGIC-V (Section 7.2.5.3)
- T-PaGIC-V (Section 7.2.5.4)
- DLQI or CDLQI (Section 7.2.5.5)
- WHO-5 (Section 7.2.5.6)
- TSQM (Section 7.2.5.7)

- VitiQoL (Section 7.2.5.8)
- HADS (Section 7.2.5.9)

7.2.5.1. Vitiligo Noticeability Scale

The VNS is a patient-reported measure of vitiligo treatment success, which has a 5-point scale (Batchelor et al 2016). The baseline facial photograph will be shown to the participants for reference, and a mirror will be provided for the participants to assess the vitiligo on their face. The participant will be asked to respond to the following query:

> Compared with before treatment, how noticeable is the vitiligo now? Responses: (1) More noticeable, (2) As noticeable, (3) Slightly less noticeable, (4) A lot less noticeable, and (5) No longer noticeable.

VNS scores of 4 or 5 can be interpreted as representing treatment success.

7.2.5.2. Color-Matching Question

The baseline photograph and current participants' facial image (participants will be provided a mirror) will be shown to the participant for reference, and the participant will be asked to respond to the following query:

> At this point of your treatment, how well does your skin color match between your face treated vitiligo skin and face normal skin? Responses: (1) Excellent, (2) Very good, (3) Good, (4) Poor, and (5) Very poor.

7.2.5.3. Patient Global Impression of Change-Vitiligo (Facial)

The F-PaGIC-V is an assessment of improvement by the participant. It is a 7-point scale comparing the vitiligo areas at baseline with the participant's treated areas of facial vitiligo at the study visit. Response will be reported for face (F-PaGIC-V). The baseline photograph and current participants' facial image (participants will be provided a mirror) will be shown to the participant for reference. The participant will be asked to respond to the following query:

> Since the start of the treatment you've received in this study, your vitiligo on your face 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.

F-PaGIC-V scores of 1 or 2 can be interpreted as representing treatment success.

7.2.5.4. Patient Global Impression of Change-Vitiligo (Total Body)

The T-PaGIC-V is an assessment of improvement by the participant. It is a 7-point scale comparing the vitiligo areas at baseline with the participant's treated areas of total body vitiligo at the study visit. Response will be reported for total body (T-PaGIC-V). The participant will be asked to respond to the following query:

> Since the start of the treatment you've received in this study, your vitiligo on your total body 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.

T-PaGIC-V scores of 1 or 2 can be interpreted as representing treatment success.

7.2.5.5. Dermatology Life Quality Index

The DLQI (Finlay and Khan 1994) is a simple 10-question validated questionnaire for use in participants aged 16 years and over to measure how much the skin problem has affected the participant over the previous 7 days.

The scoring of each question is as follows: Very much = 3; A lot = 2; A little = 1; Not at all = 0; Not relevant = 0; Question 7, "Prevented work or studying" = 3.

The following imputation will be applied for incorrectly completed questionnaires:

- If 1 question is left unanswered, this is scored 0 and the scores are summed and expressed as usual out of a maximum of 30.
- If 2 or more questions are left unanswered, the questionnaire is not scored.
- If Question 7 is answered "yes," this is scored 3. If Question 7 is answered "no," but then either "a lot" or "a little" is ticked, this is then scored 2 or 1. If "Not relevant" is ticked, the score for Question 7 is 0. If it is answered "no," but the second half is left incomplete, the score will remain 0.
- If 2 or more response options are ticked, the response option with the highest score should be recorded.
- If there is a response between 2 tick boxes, the lower of the 2 score options should be recorded.
- For DLQI 6 subscales, if the answer to 1 question in a subscale is missing, that subscale should not be scored.

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

The meaning of total DLQI scores can be categorized as follows:

- 0 to 1 = No effect
- 2 to 5 = Small effect
- 6 to 10 = Moderate effect
- 11 to 20 = Very large effect
- 21 to 30 = Extremely large effect

A change from baseline in DLQI and CDLQI score of at least 4 points is considered clinically important (Basra et al 2015, Waters et al 2010).

The questionnaire is also analyzed under 6 subscales as follows:

- Symptoms and feelings (Questions 1 and 2)
- Daily activities (Questions 3 and 4)
- Leisure (Questions 5 and 6)
- Work and school (Question 7)

- Personal relations (Questions 8 and 9)
- Treatment (Question 10)

CDLQI (Lewis-Jones and Finlay 1995) is the youth/children's version of the DLQI and will be completed by adolescents aged ≥ 12 years to < 16 years. The scoring of each question is Very much = 3; Quite a lot = 2; Only a little = 1; Not at all = 0; Question unanswered = 0; Question 7: "Prevented school" = 3. The CDLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

The questionnaire is also analyzed under 6 subscales as follows:

- Symptoms and feelings (Questions 1 and 2)
- Leisure (Questions 4, 5, and 6)
- School or holidays (Question 7)
- Personal relationships (Questions 3 and 8)
- Sleep (Question 9)
- Treatment (Question 10)

The severity banding for CDLQI scores is as follows:

- 0 to 1 = No effect on child's life
- 2 to 6 = Small effect
- 7 to 12 = Moderate effect
- 13 to 18 = Very large effect
- 19 to 30 = Extremely large effect

The following imputation will be applied for incorrectly completed questionnaires for CDLQI:

1. If 1 question is left unanswered, this is scored 0, and the scores are summed and expressed as usual out of a maximum of 30.
2. If 2 or more questions are left unanswered, the questionnaire is not scored.
3. If both parts of Question 7 are completed, the higher of the 2 scores should be counted.

7.2.5.6. WHO-5

The WHO-5 is a validated, self-administered, 5-item questionnaire designed to assess mental well-being over the past 2 weeks, which can be used as an outcome measure for the wanted and unwanted effects of treatments (WHO Collaborating Center for Mental Health, Topp et al 2015). The questionnaire consists of 5 statements, which respondents rate according to the following scale: 0 = At no time; 1 = Some of the time; 2 = Less than half of the time; 3 = More than half of the time; 4 = Most of the time; 5 = All of the time.

The raw score is calculated by totaling the figures of the 5 answers for a range of 0 to 25, with 0 representing the worst possible and 25 representing the best possible quality of life. A score below 13 indicates poor well-being. No imputation will be performed for missing values.

7.2.5.7. Treatment Satisfaction Questionnaire for Medication

TSQM (Bharmal et al 2009) is a validated 9-item questionnaire that measures a participant's satisfaction with medication taken in a clinical study using a recall period of the past 2 to 3 weeks or since the medication was last used. The TSQM comprises 3 subscales that assess the patient's perception of medication effectiveness, convenience, and global satisfaction. The effectiveness subscale assesses the patient's satisfaction with the ability of the medication to treat the condition and relieve symptoms and the length of time it takes for the medication to start working. The convenience subscale addresses the convenience of administration and ease of planning and following a schedule. The global satisfaction subscale gauges a patient's confidence that the medication is a good thing and that the advantages of taking it outweigh the disadvantages. Each TSQM subscale consists of 3 items, with responses measured on a Likert scale ranging from 1 (low) to 7 (high). Subscale scores were transformed to a range from 0 to 100, with higher scores indicating greater satisfaction.

Scale scoring algorithm (Atkinson et al 2005) is as follows:

- Effectiveness: [Item 1 + Item 2 +Item 3 − 3] /18 ×100.
- Convenience: [Item 4 + Item 5 + Item 6 − 3] /18× 100.
- If one item in Effectiveness or convenience is missing, the algorithm will be

  [(Sum of nonmissing items) – 2] / 12 × 100.
- Global satisfaction:
  - First recode Item 9_recode = (Item 9 − 1) × 4 / 6 + 1.
  - Then: [Item 7 + Item 8 + Item 9_recode − 3] / 12 × 100.
- If 1 item in overall satisfaction is missing, the algorithm will be

  [(Sum of nonmissing items) – 2] /8 × 100.

No imputation will be performed for any subscale with missing items ≥ 2.

7.2.5.8. Vitiligo-Specific Health-Related Quality-of-Life Instrument

VitiQoL is a 15-item quality-of-life assessment that asks participants to rate various aspects of their condition during the past month. Each item is scored on a 0 ("not at all") to 6 ("all of the time") continuous bipolar scale (Lilly et al 2013).

Scores are pooled and reported for each of the following 3 domains:

- Participation limitation (Item 3, 4, 6, 9, 10, 11, and 14);
- Stigma (Item 1, 2, 5, 7, and 15);
- Behaviors (Item 8, 12, and 13).

A total score ranging from 0 (better) to 90 (worse) will be also provided.

No imputation will be performed for missing values.

7.2.5.9. Hospital Anxiety and Depression Scale

HADS is a 14-item questionnaire that assesses the levels of anxiety and depression that a person is currently experiencing (Zigmond and Snaith 1983). There are 7 questions each for measuring anxiety and for measuring depression, with 4 possible responses to each question (responses are scored as 0, 1, 2, or 3). Separate total scores are calculated for anxiety and depression, each total score being the sum of the 7 questions. If 4 or more scores are missing (out of the 7) for anxiety or depression, the total score will be set to missing; otherwise, the total score will be the average score of the nonmissing items multiplied by 7.

7.3. Analysis of the Primary Efficacy Parameter

The primary efficacy endpoint is F-VASI75 at Week 24.

7.3.1. Primary Efficacy Analyses

The primary analysis will be based on the FAS population. The primary alternative hypothesis (superiority of ruxolitinib 1.5% BID compared with vehicle) will be tested using exact logistic regression (Mehta and Patel 1995). This model will include the treatment group (1.5% BID and vehicle) and stratification factors (skin type and region). The unadjusted p-values between each treatment group versus vehicle will be compared with the procedure defined in Section 3.2.

Odds ratio in response rates (ruxolitinib cream vs vehicle) at Week 24 will also be computed. All participants who are missing the F-VASI assessment at a given visit in the DB period will be handled using MI under the missing-at-random assumption. Rescue therapy is not allowed in the studies. Any participant who received rescue therapy will be considered as a protocol violation and will be imputed as a nonresponder. The numerical values for F-VASI will not be included in the MI model or other sensitivity analyses.

For MI, a fully conditional specification method (van Buuren 2007) that assumes the existence of a joint distribution for all variables will be used to impute F-VASI score. A regression model including treatment group, stratification factors, and baseline and postbaseline F-VASI scores up to Week 24 will be specified for the fully conditional specification method. The randomization seed will set to be 18424306 for Study INCB 18424-306 and 18424307 for Study INCB 18424-307. The imputation will be repeated 10 times to generate corresponding complete datasets, in order to reflect the uncertainty around the true value. After the missing values have been imputed, the binary variable F-VASI75 response will be derived. The exact logistic regression will be applied to each imputed dataset, and then the results will be combined for the inference.

The following is example SAS code for MI:

```
proc mi data=mi_wide seed=18424306 nimpute=10 out=impute_fvasi;
    class trt01p strat1 strat2;
    var trt01p strat1 strat2 avalBASELINE avalWEEK4 avalWEEK8
    avalWEEK12 avalWEEK18 avalWEEK24;
    fcs;
run;
```

The following is example SAS code for exact logistic regression:

```
proc logistic data=fvasi75_mi exactonly;
    class trt01p (ref='VEHICLE CREAM') strat1 strat2/param=ref;
    model resp (event='Y') = trt01p strat1 strat2/covb;
    exact trt01p/estimate=both;
    by _Imputation_;

run;
```

The primary endpoint will also be examined for the PP population using the same model as the primary analysis.

7.3.2. Subgroup Analyses for Primary Efficacy Endpoint

Subgroup analysis will be performed based on the following participant characteristics and baseline variables for those participants whose data are available:

- Skin type (Fitzpatrick scale Type I and II vs Type III, IV, V, VI)
- Age (12 to 17, ≥ 18 to 64, ≥ 65 years; ≤ 40, > 40 years)
- Region (North America, Europe)
- Sex (Male, Female)
- Race
- F-BSA (<1.5, ≥1.5)

7.3.3. Sensitivity and Supportive Analyses for Primary Endpoint

7.3.3.1. Nonresponder Imputation

Nonresponder imputation will be used as an alternative method to handle missing data. All participants who do not respond, as well as all participants who are missing postbaseline values, will be defined as nonresponders for the NRI analysis.

7.3.3.2. Last Observation Carried Forward

For the participants who are missing postbaseline values, the last observed nonmissing postbaseline value will be used to fill in missing values at Week 24. Then the proposed exact logistic regression described in Section 7.3.1 will also applied to the imputed dataset.

7.3.3.3. Tipping Point Analysis

A tipping point sensitivity analysis will be conducted to examine the potential effects of missing data. The missing F-VASI75 response at Week 24 in each treatment group will be replaced by a range of values from the most conservative case to the most aggressive case. The most conservative case is that all the missing participants in 1.5% BID group are nonresponders and all the missing participants in vehicle group are responders, while the most aggressive case is the other way around. For each scenario, between-treatment comparisons will be performed using a Fisher's exact test.

7.4. Analysis of the Key Secondary Efficacy Parameters

If the primary objective is achieved, the statistical hypotheses for the following key secondary endpoints will be tested in a fixed sequence in the following order:

- F-VASI50 at Week 24
- F-VASI90 at Week 24
- T-VASI50 at Week 24
- Vitiligo – VNS Response at Week 24
- Percentage change from baseline in F-BSA at Week 24.

Key secondary efficacy analyses at Week 24 will be conducted in the FAS population. The statistical comparisons for binary outcomes (F-VASI50/90, T-VASI50, and VNS response) will be analyzed using the similar method as specified in the primary analysis.

For F-BSA, the missing values at Week 24 will be imputed using the MI method specified in the primary analysis. Then the derived percentage change from baseline in F-BSA at Week 24 will be analyzed using an ANCOVA model with treatment group, stratification factors, and baseline value as covariates. A test for superiority between ruxolitinib cream 1.5% BID and vehicle cream will be performed using the least squares mean estimate of the percentage change from baseline in F-BSA at Week 24 from the ANCOVA model. Superiority will be established if the p-value of the difference (ruxolitinib cream 1.5% BID minus vehicle) is < 0.05.

7.5. Analysis of Other Secondary Efficacy Parameters

7.5.1. Other Secondary Efficacy Analysis

All other secondary efficacy analyses will be conducted based on the FAS population during the treatment period (double-blind and treatment extension periods).

7.5.1.1. Continuous Efficacy Endpoints

By-visit summary statistics for the following continuous measurements, including actual measurement, change from baseline, and percentage change from baseline, will be presented:

- F-VASI/T-VASI
- F-BSA/T-BSA
- DLQI (or CDLQI) Total score and Subscores

Summary statistics, including sample size, mean, median, standard deviation, minimum, maximum, first quartile, third quartile, and 95% CI, will be presented by visits. A mixed-effect model with repeated measurements may be fit for the comparisons between 1.5% BID cream group and vehicle cream group.

7.5.1.2. Categorical Efficacy Endpoints

For the following categorical parameters, summary statistics, including sample size, frequency, and percentages, will be presented by visit. Similar exact logistic regression models as specified in the primary and key secondary analysis will be used if applicable.

- Proportion of participants achieving F-VASI25/50/75/90
- Proportion of participants achieving T-VASI25/50/75/90
- Proportion of participants in each category of VNS

Secondary endpoint analyses at Week 52 on VASI (eg, F-VASI25/50/75/90 and T-VASI25/50/75/90) will be performed in the FAS population with the following methods:

- For participants randomized in the vehicle group, VASI score at Week 52 in treatment extension period will be imputed using linear extrapolation method based on their data up to Week 24. For participants who discontinue the study drug before Week 24 due to any reason, all missing values of VASI will be imputed using the MI until Week 24 before the extrapolation.
- For participants randomized in the 1.5% BID group, VASI scores at Week 52 will be used for comparison. If the VASI score at Week 52 is missing, the value will be imputed using the MI method based on the data from Day 1 to Week 52.

In each scenario of missing value imputation, the binary outcomes on responses, VASI25/50/75/90, will be derived based on the imputed values. The statistical comparisons for these endpoints will be analyzed using the similar method as specified in the primary analysis.

7.6. Analysis of Exploratory Efficacy Parameters

7.6.1. Exploratory Efficacy Analysis

Similar to the secondary efficacy endpoints, all exploratory efficacy analyses will be conducted based on the FAS population during the treatment period (double-blind and treatment extension periods.

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

- WHO-5 Total Score
- TSQM Subscales (Effectiveness, Convenience, Overall satisfaction)
- VitiQoL Total scales and Subscales
- HADS Anxiety and Depression scores

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

- F-PhGVA and T-PhGVA
- F-PaGIC-V and T-PaGIC-V
- Color-matching question

- Proportion of participants achieving T-PhGVA response
- Proportion of participants achieving F-PhGVA response
- Proportion of participants achieving F-PaGIC-V response
- Proportion of participants achieving T-PaGIC-V response

7.7. Pharmacokinetic Analyses

Trough plasma concentrations of ruxolitinib at all study visits will be summarized using descriptive statistics by treatment group.

7.8. Pharmacodynamic Analyses

Biomarkers from serum samples will be summarized by descriptive statistics by treatment group. The purpose of these analyses will be to retrospectively evaluate changes in disease related biomarkers (eg, CXCL9, CXCL10, IL-15, IFN-gamma) at baseline before drug administration and at Weeks 12, 24, 40, and 52.

7.9. Pharmacokinetic/Pharmacodynamic Analyses

A basic linear or Emax model may be evaluated to characterize changes in disease related biomarkers (eg, CXCL9, CXCL10, IL-15, IFN-gamma) from baseline and as a function of plasma ruxolitinib steady-state exposures (C_{min}).

8. SAFETY AND TOLERABILITY

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

8.1. General Considerations

The analyses in this section will be provided for the safety population in the DB period and the TE evaluable population in TE period. Cumulative TEAEs across the treatment periods (DB and TE period) will be summarized. In addition, summaries of exposure-adjusted TEAEs will be provided based on the actual treatment received.

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 participants.

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 and within 30 days of the last dose of study drug. For participants who cross over treatments, the first application date is period-specific, and the end date is 30 days after the last application date in this period, or the first application date in the next period, whichever comes first. 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 v5.0 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 treatment-related AEs will be tabulated. Serious AEs 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.

Application site reactions are AEs that occur at the site of drug application. A summary of ASRs will be provided. Exposure-adjusted summaries will be provided for the safety population including cumulative TEAEs.

8.2.2. Adverse Event Summaries

An overall summary of AEs by treatment group will include:

- Number (%) of participants reporting any TEAEs
- Number (%) of participants reporting any ASRs
- Number (%) of participants reporting any serious TEAEs
- Number (%) of participants reporting any Grade 3 or higher TEAEs
- Number (%) of participants reporting any treatment-related TEAEs
- Number (%) of participants who temporarily interrupted study drug because of TEAEs
- Number (%) of participants who permanently discontinued study drug because of TEAEs
- Number (%) of participants who had a fatal TEAE

The following summaries will be produced by MedDRA term (if 2 or fewer participants 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 ≥ 1% in any treatment group by PT in decreasing order of frequency

- Summary of ASRs by PT in decreasing order of frequency
- Summary of exposure-adjusted incidence rates of TEAEs by PT in decreasing order of frequency
- Summary of Grade 3 or higher AEs by SOC and PT
- Summary of Grade 3 or higher AEs by PT in decreasing order of frequency
- Summary of serious TEAEs by SOC and PT
- Summary of serious TEAEs by PT in decreasing order of frequency
- Summary of treatment-related TEAEs by SOC and PT
- Summary of treatment-related TEAEs by PT in decreasing order of frequency
- Summary of Grade 3 or higher treatment-related TEAEs by SOC and PT
- Summary of treatment-related serious TEAEs by SOC and PT
- Summary of TEAEs with a fatal outcome by SOC and PT
- Summary of TEAEs leading to dose interruption of study drug by SOC and PT
- Summary of TEAEs leading to discontinuation of study drug 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, and non-numeric test values will be tabulated when necessary.

The baseline value will be determined using the last nonmissing value collected before the first application, prioritizing scheduled assessments for baseline identification over unscheduled visits. The last record before application in the highest priority 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 and serum chemistry, will be performed at the Protocol-specified visits. 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. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units.

When there are multiple laboratory nonmissing values for a participant's particular test within a visit window, the laboratory value with the smallest laboratory sequence number will be used in by-visit summaries.

For test results that will be summarized with available normal ranges, the number and percentage of participants with the laboratory values being low (but never high), normal, high (but never low), and both low and high will be calculated for each test. This shift summary will be produced for each test for the safety population in DB and TE periods. Shift tables will also be presented showing change in CTCAE grade from baseline to worst grade postbaseline. The denominator for the percentage calculation will use the number of participants in the baseline category.

8.4. Vital Signs

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

Criteria for clinically notable vital sign abnormalities are defined in Table 5, Table 6, and Table 7. The abnormal values for participants 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 > 25%. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 5: Criteria for Clinically Notable Vital Sign Abnormalities for 12 to 15 Years Old

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 131 mmHg	< 110 mmHg
Diastolic blood pressure	> 83 mmHg	< 64 mmHg
Pulse	> 100 bpm	< 60 bpm
Temperature	> 38.0ºC	< 35.5ºC
Respiratory rate	> 20 breaths/min	< 8 breaths/min

Table 6: Criteria for Clinically Notable Vital Sign Abnormalities for 16 to 17 Years Old

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 120 mmHg	< 90 mmHg
Diastolic blood pressure	> 85 mmHg	< 50 mmHg
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38.0ºC	< 35.5ºC
Respiratory rate	> 20 breaths/min	< 8 breaths/min

Table 7: Criteria for Clinically Notable Vital Sign Abnormalities for ≥ 18 Years Old

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 155 mmHg	< 85 mmHg
Diastolic blood pressure	> 100 mmHg	< 40 mmHg
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38ºC	< 35.5ºC
Respiratory rate	> 20 breaths/min	< 8 breaths/min

9. PLANNED ANALYSES

No formal interim analysis is planned in this study.

The primary analysis will occur after the primary database lock, when all participants have completed the vehicle-controlled, double-blind treatment period. Sponsors will be unblinded, while investigators and participants will still be blinded to the study treatment after the primary database lock.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 8.

Table 8: Statistical Analysis Plan Versions

SAP Version	Date
Original	09 MAR 2020

10.1. Changes to Protocol-Defined Analyses

- The FAS will be used to replace ITT in evaluation of the efficacy during DB period. The participants with only baseline but not any postbaseline assessments are excluded from the FAS. Those participants are not considered to be able to contribute to the efficacy analysis because of missing data in postbaseline visits.
- Multiple imputation will be used to replace the NRI to handle missing values in the analysis for primary and key secondary endpoints. Multiple imputation is able to provide unbiased estimates of the parameters under MAR.
- DLQI/CDLQI have been moved from exploratory endpoints to secondary endpoints.

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

Atkinson MJ, Kumar R, Cappelleri JC, Hass SL. Hierarchical construct validity of the Treatment Satisfaction Questionnaire for Medication (TSQM Version II) among outpatient pharmacy consumers. Value Health 2005;8:S9-S24.

Basra MK, Salek MS, Camilleri L, Sturkey R, Finlay AY. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. Dermatology 2015;230:27-33.

Batchelor JM, Tan W, Tour S, Yong A, Montgomery AA, Thomas KS. Validation of the Vitiligo Noticeability Scale: a patient-reported outcome measure of vitiligo treatment success. Br J Dermatol 2016;174:386-394.

Bharmal M, Payne K, Atkinson MJ, Desrosiers MP, Morisky DE, Gemmen E. Validation of an abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9) among patients on antihypertensive medications. Health Qual Life Outcomes 2009;7:36.

Bretz F, Maurer W, Brannath W, Posch M. A graphical approach to sequentially rejective multiple test procedures. Stat Med 2009;28:586-604.

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics 1982;38:29-41.

Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-216.

Hamzavi I, Jain H, McLean D, Shapiro J, Zeng H, Lui H. Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: the Vitiligo Area Scoring Index. Arch Dermatol 2004;140:677-683.

Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. Br J Dermatol 1995;132:942-949.

Lilly E, Lu PD, Borovicka JH, et al. Development and validation of a vitiligo-specific quality-of-life instrument (VitiQoL). J Am Acad Dermatol 2013;69:e11-18.

Mehta CR, Patel NR. Exact logistic regression: theory and examples. Stat Med 1995;14:2143-2160.

Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. PharmacoEconomics 1993;4:353-365.

Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York, NY: John Wiley & Sons;1987.

Topp CW, Østergaard SD, Søndergaard S, Bech P. The WHO-5 Well-Being Index: a systematic review of the literature. Psychother Psychosom 2015;84:167-176.

University of Nottingham. Harmonising Outcome Measures for Eczema (HOME).

van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res 2007;16:219-242.

Waters A, Sandhu D, Beattie P, Ezughah F, Lewis-Jones S. Severity stratification of Children's Dermatology Life Quality Index (CDLQI) scores. Br J Dermatol 2010;163(suppl 1):121.

WHO Collaborating Center for Mental Health, Psychiatric Research Unit. The WHO-5 website.

Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-370.

APPENDIX A. PLANNED TABLES AND FIGURES

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 current version. Shells are provided for nonstandard tables. In-text tables are identical in structure and content as appendix tables, but follow a Rich Text Format.

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

Tables

Table No.	Title	Population
Demographics and Disposition		
1.1.1	Analysis Populations	All
1.1.2.1	Summary of Participant Disposition in Double-Blind Period	Safety/FAS
1.1.2.2	Summary of Participant Disposition in Treatment Extension Period	TE
1.1.3	Summary of Number of Participants Enrolled by Country and Site	Safety
1.1.4.1	Summary of Protocol Deviations in Double-Blind Period	Safety
1.1.4.2	Summary of Protocol Deviations in Treatment Extension Period	TE
1.2.1	Summary of Demographics and Baseline Characteristics	Safety/FAS
1.2.2	Summary of Demographics and Baseline Characteristics	TE
1.3	Summary of Baseline Disease Characteristics	Safety/FAS
1.4.1	Summary of Prior Therapy for Vitiligo	Safety
1.4.2	Summary of Prior Medications	Safety
1.4.3.1	Summary of Concomitant Medications in Double-Blind Period	Safety
1.4.3.2	Summary of Concomitant Medications in Treatment Extension Period	TE
1.5	Summary of General Medical History	Safety
1.6	Summary of Participants With Assessments Not Done Due to COVID-19 Pandemic	Safety
Efficacy		
F-VASI / T-VASI		
2.1.1	Summary and Analysis of Participants Achieving F-VASI75 During the Treatment Period	FAS
2.1.1.2	Summary and Analysis of Participants Achieving F-VASI75 During the Treatment Period	PP
2.1.1.3	Summary and Analysis of Participants Achieving F-VASI75 by Skin Type During the Treatment Period	FAS
2.1.1.4	Summary and Analysis of Participants Achieving F-VASI75 by Age Group During the Treatment Period	FAS
2.1.1.5	Summary and Analysis of Participants Achieving F-VASI75 by Region During the Treatment Period	FAS
2.1.1.6	Summary and Analysis of Participants Achieving F-VASI75 by Sex During the Treatment Period	FAS
2.1.1.7	Summary and Analysis of Participants Achieving F-VASI75 by Race During the Treatment Period	FAS
2.1.1.8	Summary and Analysis of Participants Achieving F-VASI75 at Week 24 by F-BSA	FAS

Table No.	Title	Population
2.1.1.9	Summary and Analysis of Participants Achieving F-VASI75 at Week 24 by Tipping Point Analysis	FAS
2.1.2	Summary and Analysis of Participants Achieving F-VASI25 During the Treatment Period	FAS
2.1.3	Summary and Analysis of Participants Achieving F-VASI50 During the Treatment Period	FAS
2.1.4	Summary and Analysis of Participants Achieving F-VASI90 During the Treatment Period	FAS
2.1.5	Summary and Analysis of F-VASI During the Treatment Period	FAS
2.2.1	Summary and Analysis of Participants Achieving T-VASI25 During the Treatment Period	FAS
2.2.2	Summary and Analysis of Participants Achieving T-VASI50 During the Treatment Period	FAS
2.2.3	Summary and Analysis of Participants Achieving T-VASI75 During the Treatment Period	FAS
2.2.4	Summary and Analysis of Participants Achieving T-VASI90 During the Treatment Period	FAS
2.2.5	Summary and Analysis of T-VASI During the Treatment Period	FAS
F-BSA/T-BSA		
2.3.1	Summary and Analysis of F-BSA During the Treatment Period	FAS
2.3.2	Summary and Analysis of T-BSA During the Treatment Period	FAS
VNS		
2.4.1	Summary and Analysis of Participants Achieving VNS Scores of 4 or 5 During the Treatment Period	FAS
2.4.2	Summary of Participants in Each Category of VNS Scores During the Treatment Period	FAS
F-PhGVA/T-PhGVA		
2.5.1	Summary and Analysis of Participants Achieving an F-PhGVA of Clear or Almost Clear During Treatment Period	FAS
2.5.2	Summary of Participants in Each Category of F-PhGVA Scores During Treatment Period	FAS
2.6.1	Summary and Analysis of Participants Achieving an T-PhGVA of Clear or Almost Clear During Treatment Period	FAS
2.6.2	Summary of Participants in Each Category of T-PhGVA Scores During Treatment Period	FAS
F-PaGIC-V/T-PaGIC-V		
2.7.1	Summary and Analysis of Participants Who Report F-PaGIC-V of Very Much Improved or Much Improved During Treatment Period	FAS
2.7.2	Summary of Participants in Each Category of F-PaGIC-V Scores During Treatment Period	FAS
2.8.1	Summary and Analysis of Participants Who Report T-PaGIC-V of Very Much Improved or Much Improved During Treatment Period	FAS
2.8.2	Summary of Participants in Each Category of T-PaGIC-V Scores During Treatment Period	FAS
All Other Efficacy Parameters		
2.9.1	Summary of Participants in Each Category of Color-Matching Question During the Treatment Period	FAS
2.9.2	Summary of DLQI During Treatment Period	FAS

Table No.	Title	Population
2.9.3	Summary of CDLQI During Treatment Period	FAS
2.9.4	Summary of WHO-5 During Treatment Period	FAS
2.9.5	Summary of TSQM During Treatment Period	FAS
2.9.6	Summary of VitiQoL During Treatment Period	FAS
2.9.7	Summary of HADS During Treatment Period	FAS
Exposure & Compliance		
3.1.1.1	Summary of Exposure in Double-Blind Period	Safety
3.1.1.2	Summary of Exposure in Treatment Extension Period	TE
3.1.1.3	Summary of Exposure in During Treatment Period	Safety
3.1.2.1	Summary of Study Drug Compliance in Double-Blind Period	Safety
3.1.2.2	Summary of Study Drug Compliance in Treatment Extension Period	TE
3.1.2.3	Summary of Study Drug Compliance in During Treatment Period	Safety
Adverse Events		
3.2.1.1.X	Overall Summary of Treatment-Emergent Adverse Events	Safety
3.2.1.1.Y	Overall Summary of Exposure-Adjusted Treatment-Emergent Adverse Events	Safety
3.2.2.1.X	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.3.1.X	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.3.1.1.X	Summary of Treatment-Emergent Adverse Events ≥ 1% in Any Treatment Group by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.3.1.2.X	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.3.1.Y	Summary of Treatment-Emergent Adverse Events With Vehicle Group by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	Safety
3.2.3.1.1.Y	Summary of Treatment-Emergent Adverse Events ≥ 1% in any Treatment Group With Vehicle Group by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	Safety
3.2.3.1.2.Y	Summary of Application Site Reactions With Vehicle Group by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	Safety
3.2.3.1.3.Y	Summary of Exposure-Adjusted Incidence Rates of Treatment-Emergent Adverse Events With Vehicle Group by MedDRA Preferred Terms in Decreasing Order of Frequency During the Treatment Period	Safety
3.2.3.1.4.Y	Summary of Exposure-Adjusted Incidence Rates of Treatment-Emergent Adverse Events ≥ 1% in Any Treatment Group With Vehicle Group by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	Safety
3.2.3.1.5.Y	Summary of Exposure-Adjusted Incidence Rates of Application Site Reactions With Vehicle Group by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	Safety
3.2.4.1.X	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.4.2.X	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.5.1.X	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.5.2.X	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety

Table No.	Title	Population
3.2.6.1.X	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.6.2.X	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.7.1.X	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.8.1.X	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.9.1.X	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Safety
3.2.10.1.X	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety
3.2.11.1.X	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term	Safety
Laboratory Values and Vital Signs		
3.3.1.X	Summary of Laboratory Values – Hematology	Safety
3.3.3.X	Shift Summary of Hematology Laboratory Values in CTC Grade – To the Worst Abnormal Value	Safety
3.3.4.X	Summary of Laboratory Values – Chemistry	Safety
3.3.6.X	Shift Summary of Chemistry Laboratory Values in CTC Grade – To the Worst Abnormal Value	Safety
3.4.1.X	Summary of Systolic Blood Pressure	Safety
3.4.2.X	Summary of Diastolic Blood Pressure	Safety
3.4.3.X	Summary of Pulse	Safety
3.4.4.X	Summary of Respiration Rate	Safety
3.4.5.X	Summary of Body Temperature	Safety

Note: For AE tables ending with "X", separate tables will be provided for the double-blind period, treatment extension period, and the treatment period (double-blind and treatment extension periods).
Note: For AE tables ending with "Y", tables will be provided for the treatment period (double-blind and treatment extension periods). For participants who cross over, he/she should be included in both treatment groups.
Note: For Laboratory Values/Vital Sign tables ending with "X", separate tables will be provided for the double-blind period and treatment extension period.

Figure

Figure No.	Title	Population
4.1.1	Proportion of Participants Achieving F-VASI75 During Treatment Period	FAS
4.1.2	Proportion of Participants Achieving F-VASI25 During Treatment Period	FAS
4.1.3	Proportion of Participants Achieving F-VASI50 During Treatment Period	FAS
4.1.4	Proportion of Participants Achieving F-VASI90 During Treatment Period	FAS
4.1.6	Mean and Standard Error Plot of F-VASI During Treatment Period	FAS
4.1.7	Mean and Standard Error Plot of Change From Baseline in F-VASI During Treatment Period	FAS
4.1.8	Mean and Standard Error Plot of Percent Change From Baseline in F-VASI During Treatment Period	FAS
4.1.9	Forest Plot of Response Rate Difference in Achieving F-VASI75 at Week 24	FAS
4.2.1	Proportion of Participants Achieving T-VASI75 During Treatment Period	FAS
4.2.2	Proportion of Participants Achieving T-VASI25 During Treatment Period	FAS

Figure No.	Title	Population
4.2.3	Proportion of Participants Achieving T-VASI50 During Treatment Period	FAS
4.2.4	Proportion of Participants Achieving T-VASI90 During Treatment Period	FAS
4.2.6	Mean and Standard Error Plot of T-VASI During Treatment Period	FAS
4.2.7	Mean and Standard Error Plot of Change From Baseline in T-VASI During Treatment Period	FAS
4.2.8	Mean and Standard Error Plot of Percent Change From Baseline in T-VASI During Treatment Period	FAS
4.3.1	Mean and Standard Error Plot of F-BSA During Treatment Period	FAS
4.3.2	Mean and Standard Error Plot of Change From Baseline in F-BSA During Treatment Period	FAS
4.3.3	Mean and Standard Error Plot of Percent Change From Baseline in F-BSA During Treatment Period	FAS
4.4.1	Mean and Standard Error Plot of T-BSA During Treatment Period	FAS
4.4.2	Mean and Standard Error Plot of Change From Baseline in T-BSA During Treatment Period	FAS
4.4.3	Mean and Standard Error Plot of Percent Change From Baseline in T-BSA During Treatment Period	FAS
4.5	Proportion of Participants Achieving VNS scores of 4 or 5 During the Treatment Period	FAS
4.6	Proportion of Participants Achieving an F PhGVA of Clear or Almost Clear During Treatment Period	FAS
4.7	Proportion of Participants Achieving an T-PhGVA of Clear or Almost Clear During Treatment Period	FAS
4.8	Proportion of Participants who Report F PaGIC V of Very Much Improved or Much Improved During Treatment Period	FAS
4.9	Proportion of Participants who Report T-PaGIC-V of Very Much Improved or Much Improved During Treatment Period	FAS
4.10.1	Mean and Standard Error Plot of DLQI During Treatment Period	FAS
4.10.2	Mean and Standard Error Plot of Change From Baseline in DLQI During Treatment Period	FAS
4.10.3	Mean and Standard Error Plot of Percent Change From Baseline in DLQI During Treatment Period	FAS
4.11.1	Mean and Standard Error Plot of CDLQI During Treatment Period	FAS
4.11.2	Mean and Standard Error Plot of Change From Baseline in CDLQI During Treatment Period	FAS
4.11.3	Mean and Standard Error Plot of Percent Change From Baseline in CDLQI During Treatment Period	FAS
4.12.1	Mean and Standard Error Plot of WHO-5 During Treatment Period	FAS
4.12.2	Mean and Standard Error Plot of Change From Baseline in WHO-5 During Treatment Period	FAS
4.12.3	Mean and Standard Error Plot of Percent Change From Baseline in WHO-5 During Treatment Period	FAS
4.13.1	Mean and Standard Error Plot of TSQM During Treatment Period	FAS
4.14.1	Mean and Standard Error Plot of VitiQoL During Treatment Period	FAS
4.14.2	Mean and Standard Error Plot of Change From Baseline in VitiQoL During Treatment Period	FAS
4.14.3	Mean and Standard Error Plot of Percent Change From Baseline in VitiQoL During Treatment Period	FAS

Figure No.	Title	Population
4.15.1	Mean and Standard Error Plot of HADS During Treatment Period	FAS
4.15.2	Mean and Standard Error Plot of Change From Baseline in HADS During Treatment Period	FAS
4.15.3	Mean and Standard Error Plot of Percent Change From Baseline in HADS During Treatment Period	FAS

Listings

Listing No.	Title
Demographic and Baseline Characteristics	
2.1.1	Participant Enrollment and Disposition Status
2.1.2	Participant Inclusion and Exclusion Criteria Violations
2.1.3	Participants Who Discontinued Treatment or Discontinued From Study Due to COVID-19
2.1.4	Participants With Assessments Not Done Due to COVID-19 Pandemic
2.2.1	Protocol Deviations and Violations
2.3	Analysis Populations
2.4.1	Demographic Characteristics
2.4.2	Baseline Disease Characteristics
2.4.3	Medical History
2.4.4	Prior and Concomitant Medications
2.4.5	Prior Medications for Vitiligo
2.5.1	Study Drug Exposure and Compliance
Efficacy	
2.6.1	F-VASI Score
2.6.2	T-VASI Score
2.6.3	F-BSA
2.6.4	T-BSA
2.6.5	VNS Score
2.6.6	F-PhGVA Score
2.6.7	T-PhGVA Score
2.6.8	F-PaGIC-V Score
2.6.9	T-PaGIC-V Score
2.6.10	Color-matching Questions
2.6.11	DLQI Score
2.6.12	CDLQI Score
2.6.13	TSQM Score
2.6.14	HADS
2.6.15	WHO-5
2.6.16	VitiQoL Score
2.6.17	Participants With F-VASI Assessments Not Done Due to COVID-19 Pandemic
Adverse Events	
2.7.1	Adverse Events
2.7.2	Adverse Events Leading to Study Drug Discontinuation
2.7.3	Serious Adverse Events
2.7.4	Treatment-Related Adverse Events

Listing No.	Title
2.7.5	Adverse Events With a Fatal Outcome
2.7.6	Adverse Events Leading to Interruption of Study Drug
2.7.8	Grade 3 or Higher Adverse Events
2.7.9	Application Site Reactions
Laboratory Data	
2.8.1.1	Clinical Laboratory Values – Hematology
2.8.1.2	Clinical Laboratory Values – Chemistry
2.8.1.3	Abnormal Clinical Laboratory Values – Hematology
2.8.1.4	Abnormal Clinical Laboratory Values – Chemistry
Vital Signs	
2.8.2.1	Vital Signs
2.8.2.2	Abnormal Vital Sign Values
2.8.2.3	Alert Vital Sign Values