Official Title: A Phase 3, Double-Blind, Randomized, Vehicle-Controlled, Efficacy and Safety Study of Ruxolitinib Cream Followed by a Long-Term (Safety Extension Period in Children (Ages ≥ 2 Years to < 12 Years) With Atopic Dermatitis

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Statistical Analysis Plan

INCB 18424-305

Topical Ruxolitinib Evaluation in Atopic Dermatitis Study 3 (TRuE-AD3)

A Phase 3, Double-Blind, Randomized, Vehicle-Controlled, Efficacy and Safety Study of Ruxolitinib Cream Followed by a Long-Term Safety Extension Period in Children (Ages ≥ 2 Years to < 12 Years) With Atopic Dermatitis

Product:	**Ruxolitinib Cream**
IND Number	[redacted]
EudraCT Number:	**2021-000489-14**
Phase of Study:	**3**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 6 dated 22 FEB 2023**
CRF Approval Date:	**10 JAN 2023**
SAP Version:	**Original**
SAP Author:	[redacted] [redacted]**, Biostatistics**
Date of Plan:	**02 JUN 2023**

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
ANC	absolute neutrophil count
AD	atopic dermatitis
AE	adverse event
ANOVA	analysis of variance
ASR	application site reaction
BID	twice daily
BSA	body surface area
[redacted]	[redacted]
CI	confidence interval
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
[redacted]	[redacted]
EASI	Eczema Area and Severity Index
[redacted]	[redacted]
EASI75	≥ 75% improvement in EASI score
[redacted]	[redacted]
eCRF	electronic case report form
EOT	end of treatment
[redacted]	[redacted]
ET	early termination
FDA	Food and Drug Administration
[redacted]	[redacted]
IGA	Investigator's Global Assessment
IGA-TS	Investigator's Global Assessment Treatment Success (IGA score of 0 or 1 with ≥ 2-grade improvement from baseline)
ITT	intent-to-treat
LTS	long-term safety
MedDRA	Medical Dictionary for Regulatory Activities
MI	multiple imputation
MMRM	mixed-model repeated measures
NRI	nonresponder imputation
NRS	numerical rating scale
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Abbreviation	Term
ANC	absolute neutrophil count
[redacted]	[redacted]
PP	per protocol
[redacted]	[redacted]
PT	preferred term
[redacted]	[redacted]
SAP	Statistical Analysis Plan
SOC	system organ class
TCI	topical calcineurin inhibitor
TCS	topical corticosteroid
TEAE	treatment-emergent adverse event
WHO	World Health Organization
[redacted]	[redacted]
VC	vehicle-controlled

1. INTRODUCTION

Study INCB 18424-305 is a randomized, double-blind, vehicle-controlled study with an LTS period in pediatric participants aged ≥ 2 to < 12 years with AD eligible for topical therapy. This Phase 3 study will be conducted at roughly 60 sites in the United States and Canada. Approximately 315 participants will be randomized 2:2:1 to blinded treatment with either ruxolitinib 1.5% cream BID, ruxolitinib 0.75% cream BID, or vehicle cream BID; stratification will be by baseline IGA score and age. Enrollment will be capped such that no more than approximately 25% of randomized participants have a baseline IGA score of 2. At least 40% of the overall study population will consist of children aged ≥ 2 to 6 years. In this trial, participants will apply blinded study treatment for 8 weeks followed by a randomized 44-week LTS extension period. In the LTS period, participants initially randomized to vehicle cream will apply either ruxolitinib 0.75% or 1.5% cream BID; this will replicate the design of the earlier pivotal studies (INCB 18424-303 and INCB 18424-304) in adolescents and adults with AD.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCB 18424-305 Protocol. The Department of Biostatistics or designee will execute the scope of this plan [redacted].

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 18424-305 Protocol Amendment 6 dated 22 FEB 2023 and CRFs approved 10 JAN 2023. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To establish the efficacy of ruxolitinib cream in participants with AD.	Proportion of participants who achieve IGA-TS at Week 8.
Key Secondary	
To further assess the treatment effects of ruxolitinib cream.	• Proportion of participants with a ≥ 4-point improvement in Itch NRS score from baseline to Week 8. • Proportion of participants with a ≥ 4-point improvement in Itch NRS score from baseline to Day 7 (Week 1). • Proportion of participants with a ≥ 4-point improvement in Itch NRS score from baseline to Day 3.
Secondary	
To evaluate the safety and tolerability of ruxolitinib cream.	The type, frequency, and severity of AEs and changes from baseline in physical examinations, vital signs, height, weight, and laboratory data for hematology and serum chemistry.
To further evaluate the efficacy of ruxolitinib cream.	• Proportion of participants who achieve IGA-TS at Weeks 2 and 4. • Proportion of participants with a ≥ 4-point improvement in Itch NRS score from baseline to Weeks 2 and 4. • Proportion of participants who achieve EASI75 at Weeks 2, 4, and 8. • Time to achieve Itch NRS score improvement of at least 2 or 4 points.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

3. STUDY DESIGN

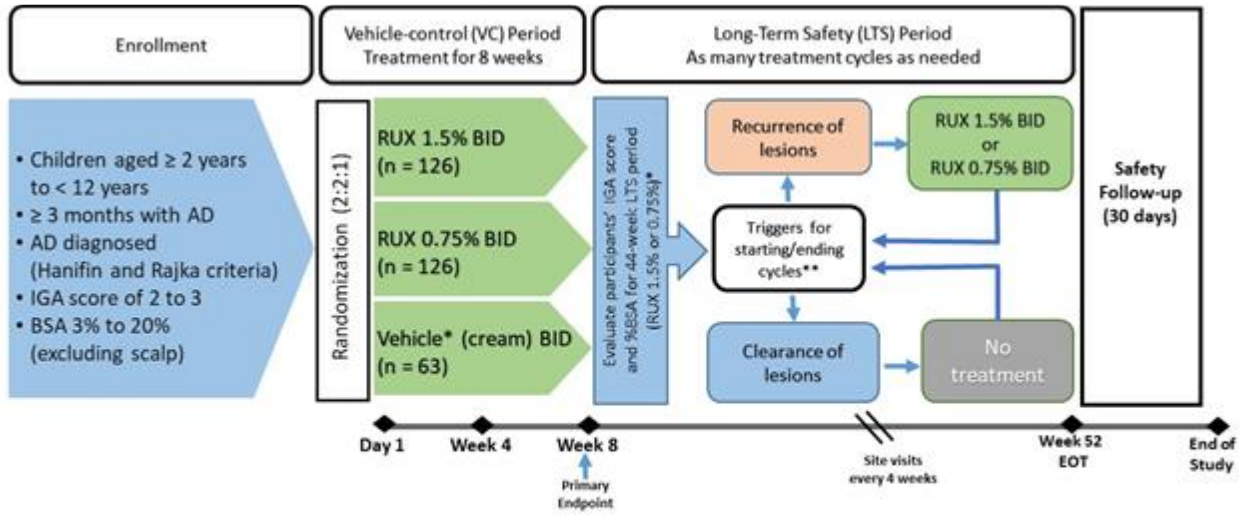
This is a randomized, double-blind, VC study with an LTS period in pediatric participants aged ≥ 2 to < 12 years with AD eligible for topical therapy. For participants who meet all study inclusion criteria and none of the exclusion criteria, study drug will be assigned at the Day 1/baseline visit. Participants will be randomized 2:2:1 to blinded treatment with either ruxolitinib 0.75% cream BID, ruxolitinib 1.5% cream BID, or vehicle cream BID, with stratification by baseline IGA score and age. Enrollment will be capped, such that no more than approximately 25% of randomized participants have a baseline IGA score of 2. At least 40% of the overall study population will consist of children aged ≥ 2 to 6 years.

Participants who complete Week 8 assessments with no additional safety concerns will continue into the 44-week LTS period with the same treatment regimen, except those initially randomized to vehicle cream who will be rerandomized (1:1) in a blinded manner to 1 of the 2 active treatment groups (ruxolitinib 0.75% or 1.5% cream BID). The IGA score required for participants to enter the LTS period is 0 to 4, and participants must have a %BSA in the range of 0% to 20% (excluding the scalp).

Following the end of treatment (Week 52/EOT or ET), all participants will have a safety follow-up visit 30 days later (or 30 days after the last application of study treatment if the Week 52/EOT or ET visit was not performed); this visit will evaluate the safety and duration of response (refer to Protocol Amendment 6).

Figure 1 presents the study design schema.

Figure 1: Study Design Schema



* *At Week 8 (LTS baseline), participants initially on vehicle during the VC period will be rerandomized to either ruxolitinib 1.5% or 0.75% cream BID. Participants initially randomized to either ruxolitinib 0.75% or 1.5% BID will continue their treatment through the LTS period.*

** *Treatment is ceased 3 days after clearing of AD lesions. Treatment is restarted if AD lesions recur. There is no limit on the number of treatment cycles during the 44-week LTS.*

3.1. Randomization

In the VC period, the IRT system will assign approximately 315 participants in a 2:2:1 ratio to ruxolitinib 1.5% cream BID, ruxolitinib 0.75% cream BID, or vehicle cream BID, respectively. Additionally, participants will be stratified by baseline IGA score (2 or 3) and age (2-6 years or 7 to < 12 years).

Participants who complete Week 8 assessments with no safety concerns will continue into the 44-week LTS period with the same treatment regimen, except that those initially randomized to vehicle cream who will be rerandomized (1:1) in a blinded manner to 1 of the 2 active treatment groups (ruxolitinib 0.75% or 1.5% cream BID).

3.2. Control of Type I Error

For the primary and key secondary analyses, an overall 2-sided Type I error of 0.05 will be used.

A graphical procedure with gatekeeping testing strategy for the primary and key secondary analyses will be implemented. The underlying procedure is derived using the methodology developed by Bretz et al (2009). The method will guarantee a strong control of the family-wise error rate.

In Step 1, 2 families of 4 elementary hypotheses tests at Week 8 are grouped according to treatment comparison between each ruxolitinib cream group and the vehicle cream group, where

- Family 1 (1.5% BID vs vehicle):
  - H11: proportion of participants who achieve IGA-TS
  - H12: proportion of participants with a ≥ 4-grade improvement in Itch NRS score over baseline
- Family 2 (0.75% BID vs vehicle):
  - H21: proportion of participants who achieve IGA-TS
  - H22: proportion of participants with a ≥ 4-grade improvement in Itch NRS score over baseline

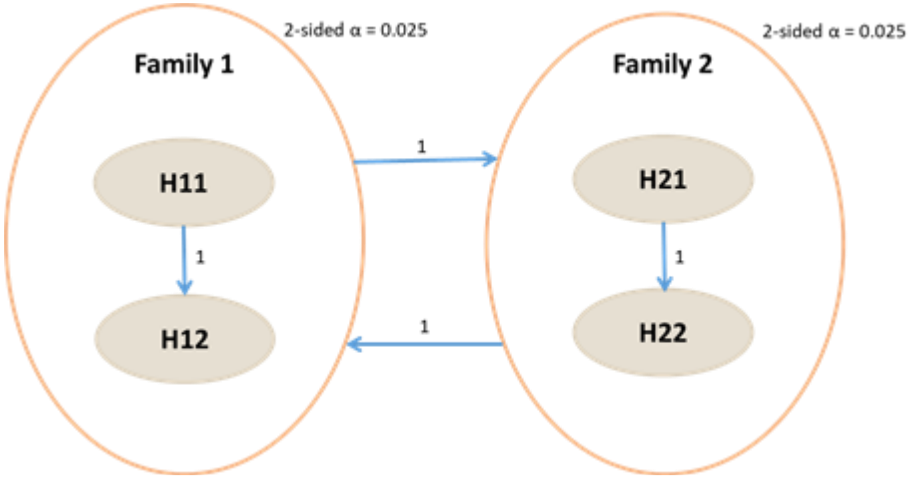
Step 2 has 2 families of 4 hypotheses tests:

- Family 3 (1.5% BID vs vehicle and 0.75% BID vs vehicle on Day 7 Itch NRS):
  - H13: proportion of participants with a ≥ 4-grade improvement in Itch NRS score over baseline to Day 7 (Week 1) between 1.5% BID and vehicle
  - H23: proportion of participants with a ≥ 4-grade improvement in Itch NRS score over baseline to Day 7 (Week 1) between 0.75% BID and vehicle
- Family 4 (1.5% BID vs vehicle and 0.75% BID vs vehicle on Day 3 Itch NRS):
  - H14: proportion of participants with a ≥ 4-grade improvement in Itch NRS score over baseline to Day 3 between 1.5% BID and vehicle
  - H24: proportion of participants with a ≥ 4-grade improvement in Itch NRS score over baseline to Day 3 between 0.75% BID and vehicle

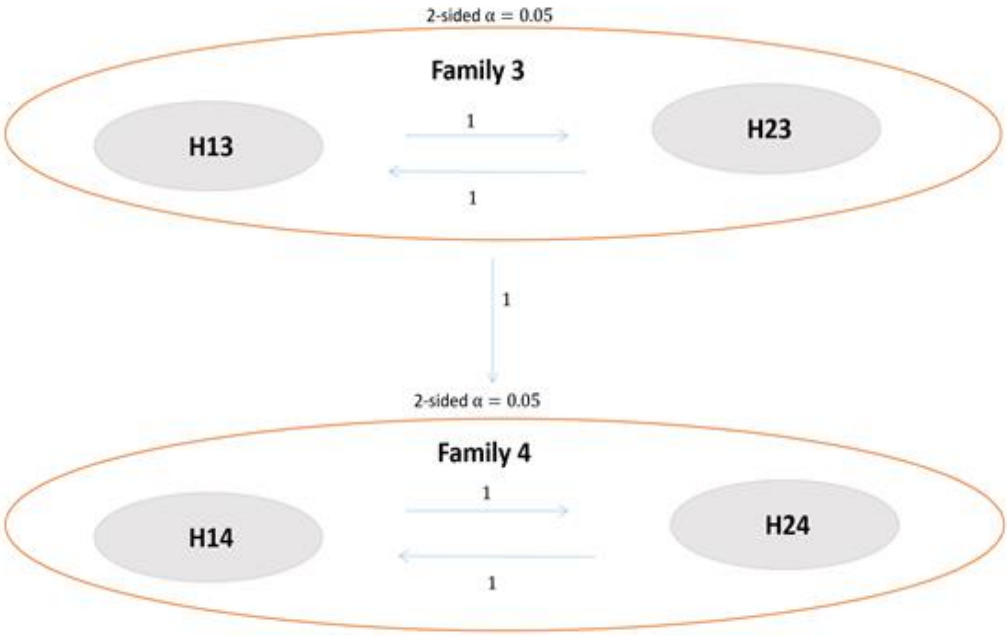
To control the overall Type I error rate, 2-sided $\alpha = 0.05$, the Bonferroni's method will be used. In Step 1, within Family 1 and 2, the endpoints are tested in a fixed sequence at a Bonferronized 2-sided $\alpha = 0.025$ level. The key secondary endpoint will be tested only if the associated primary endpoint is rejected. For any treatment strength, if the 2 related null hypotheses can be rejected, then the fixed sequence for the other treatment strength can be conducted at the 2-sided $\alpha = 0.05$ level. If all null hypotheses in Family 1 and 2 are rejected, in Step 2, the endpoints in Family 3 (H13 and H23) will be tested using Bonferroni-Hochberg's procedure with overall 2-sided $\alpha = 0.05$ level. If both hypotheses in Family 3 are rejected, the endpoints in Family 4 (H14 and H24) will be tested similarly using Bonferroni-Hochberg's procedure with overall 2-sided $\alpha = 0.05$ level. The approach is visualized in Figure 2.

Figure 2: Control of Overall Type I Error Rate

Step 1:



Step 2:



3.3. Sample Size Considerations

Approximately 315 participants will be randomized 2:2:1 to blinded treatment with either ruxolitinib 1.5% cream BID, ruxolitinib 0.75% cream BID, or vehicle cream BID. The sample size calculation is based on the Fisher exact test for the primary efficacy endpoint. Based on the results from the 2 pivotal studies in adolescents and adults with AD (INCB 18424-303 and INCB 18424-304), the response rate of IGA-TS at Week 8 is assumed to be 51% and 47% for the active arms (ie, 1.5% BID and 0.75% BID, respectively) versus 14% for placebo.

Using a 2-sided alpha of 0.025, the sample size will have > 95% power to detect a difference between each of the 2 active treatment groups versus the vehicle. In addition to providing adequate power for efficacy variables, the sample size is determined to provide a large database for safety evaluations.

3.4. Schedule of Assessments

Refer to Protocol Amendment 6 dated 22 FEB 2023 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

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 the VC 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 LTS period, baseline for LTS 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 the VC period.
- For safety evaluation, for participants who cross over from vehicle to ruxolitinib cream, baseline is the last nonmissing measurement obtained before or on the day of first application of ruxolitinib cream in the LTS period; for participants on ruxolitinib cream in both periods, baseline is the last nonmissing measurement obtained before or on the day of first application of study treatment in the VC 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. Last Available Value

The last available value is the last nonmissing measurement obtained after starting ruxolitinib cream or vehicle cream and within 30 days after the last application of ruxolitinib cream or vehicle cream, or before the first application of ruxolitinib cream in the next period, whichever is earlier.

4.1.5. Handling of Missing and Incomplete Data

In general, values for missing dates will not be handled unless methods for handling missing dates are specified in this section or relevant sections. The original reported dates collected on the eCRF should be used in all relevant listings. The following rules will be used for handling partial dates for analyses requiring dates.

For response endpoints, all nonresponders, as well as all participants who are missing postbaseline values at Week 8, will be defined as nonresponders for the NRI analysis.

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. The 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 will be calculated as follows:

Body mass index (kg/m^2) = (weight [kg] / (height [m])^2

4.2.2. Prior and Concomitant Therapy

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

Concomitant therapy is defined as any nonstudy therapy 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 therapy could also be classified as "both prior and concomitant therapy" if the end date is on or after the first application of study treatment. In the listing, it will be indicated whether a therapy is prior only, concomitant only, or both prior and concomitant.

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

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.1 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, first quartile, third 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-blinded, VC study followed by a LTS extension period. Data will be summarized based on treatment regimen that was assigned (ITT) or that the participant actually applied (safety).

During the VC period, the treatment groups will be 1.5% BID, 0.75% BID, and vehicle.

For the LTS period, the treatment groups will be 1.5% BID, 0.75% BID, vehicle to 1.5% BID, and vehicle to 0.75% BID.

5.3. Analysis Populations

5.3.1. Intent-to-Treat Population

All participants who are randomized to the study 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 study treatment the participant might apply during their participation in the study.

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

5.3.2. Per Protocol Population

Participants in the ITT population who are considered to be sufficiently compliant with the Protocol compose the PP population, which is defined for supportive sensitivity analyses for the primary endpoint in the VC 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.

[redacted]

[redacted]

5.3.5. Long-Term Safety Evaluable Population

All participants who applied study drug at least once during the LTS period will constitute the LTS evaluable population. All efficacy and safety analyses for the LTS period will be conducted with the LTS evaluable population.

[redacted]

[redacted]

[redacted]

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 and listed for the ITT population during the VC period and the LTS evaluable population during the LTS period: age, age group, sex, race, ethnicity, weight, height, and body mass index.

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics summarized and listed for the ITT population during the VC period include, but are not limited to the following:

- Time since first onset of AD
- Prior history of asthma (no/yes)
- Prior allergies (food, environmental) (no/yes)
- History of contact dermatitis (no/yes)
- Common complications of AD
- Time since onset of current AD episode
- Prior therapy for AD given in the past 30 days (no/yes)
- Total %BSA involvement in current AD episode
- Facial and/or neck involvement (no/yes) during past episodes
- Number of AD episodes/flare-ups over the last 12 months
- Average duration of episodes/flare-ups over the last 12 months
- Baseline IGA score (2, 3)
- Baseline EASI score
- Baseline Itch NRS score
- [redacted]

6.1.3. Prior Therapies for Atopic Dermatitis

Prior therapies for AD, including medication and other types of therapies during the 12 months prior to the screening visit, will be coded using the WHO Drug Dictionary and summarized and listed by treatment group for the ITT population. The type of treatment and reason for discontinuation will be summarized as well. Prior therapies for AD in the past 30 days will be summarized in a similar way.

6.1.4. Medical History

For participants in the ITT population during the VC period, medical history will be summarized and listed by assigned treatment groups. This summary will include the number and percentage of participants with medical history for each body system/organ class as documented in the eCRF.

6.2. Disposition of Participants

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

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

6.3. Protocol Deviations

In general, the following are important protocol deviations that may significantly affect the primary analysis:

- Missing data for the primary endpoint
- Overall application compliance < 80% during the VC period
- Did not apply any study cream in the VC period
- IGA assessment 14 days out of the target visit date at Week 8 (Day 57 ±7)

Participants with any of the deviations listed above will be excluded from the PP population. Additionally, important protocol deviations, such as those related to inclusion/exclusion criteria, discontinuation criteria, and the use of prohibited concomitant medications, will be reviewed. Decisions as to whether any of these deviations warrant exclusion from the PP population will be made prior to unblinding.

Protocol deviations will be summarized and listed by treatment groups in the VC and LTS periods separately.

6.4. Exposure

For participants in the safety population during the VC period and in the LTS evaluable population in the LTS period, descriptive statistics will be provided (ie, by treatment group for the duration of treatment, the average daily amount of cream applied [g], and the total amount of cream applied [g]). 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

For participants in the safety population, overall compliance (%) for the application of ruxolitinib cream or vehicle cream during the VC period will be calculated for all participants 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 during the study and the total number of intended applications is the number of planned applications minus the number of interrupted applications. Overall compliance will be summarized and listed for the safety population during the VC period.

6.6. Prior and Concomitant Therapies

For participants in the ITT population during the VC period, prior and concomitant therapies will be coded using the WHO Drug Dictionary and summarized as number and percentage of participants with prior and concomitant therapies by WHO drug class and WHO drug term.

For participants in the LTS period, only concomitant therapies will be summarized. Concomitant therapies for AD will also be summarized by treatment groups in the VC and LTS periods.

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 safety follow-up period, if the data are available.

7.2. Analysis of the Primary Efficacy Parameters

7.2.1. Primary Efficacy Measures

7.2.1.1. Investigator's Global Assessment

The IGA is an overall eczema severity rating on a 0 to 4 scale that will be assessed during site visits. The grades for the IGA are shown in Table 2.

Table 2: Investigator's Global Assessment

Grade	Severity	Status
0	Clear	No erythema or induration/papulation, no oozing/crusting; there may be minor residual discoloration.
1	Almost clear	There may be trace faint pink erythema, with almost no induration/papulation, and no oozing/crusting.
2	Mild	There may be faint pink erythema, with mild induration/papulation and no oozing/crusting.
3	Moderate	There may be pink-red erythema with moderate induration/papulation and there may be some oozing/crusting.
4	Severe	There may be deep or bright red erythema with severe induration/papulation and with oozing/crusting.

Source: FDA 2012.

The IGA-TS is defined as an IGA score of 0 or 1 with ≥ 2-grade improvement from baseline.

7.2.2. Primary Efficacy Analyses

The primary analysis will be based on the ITT population in the VC period. The primary alternative hypothesis (superiority of ruxolitinib 1.5% BID or 0.75% BID compared with vehicle) will be tested using logistic regression. This model will include the treatment group (1.5% BID, 0.75% BID, and vehicle) and stratification factors (baseline IGA score and age). The unadjusted p-values between each treatment group versus vehicle will be calculated based on the Wald test, which will be compared with the procedure defined in Section 3.2. Exact logistic regression (Mehta and Patel 1995) will be used for all of the comparisons if any of the dose levels have an expected cell count < 5.

The odds ratio and 95% CI at Week 8 for the response rates (ruxolitinib cream/vehicle) will be computed for the above model. Additionally, the difference in IGA-TS response rates (ruxolitinib cream − vehicle) at Week 8 will be computed. The 95% CI for the difference will be computed based on a large-sample normal approximation with continuity correction.

All nonresponders during the VC period, as well as all participants missing the Week 8 assessment and who discontinue study treatment at any time before Week 8, or discontinue from the study for any reason, will be defined as nonresponders for the nonresponder imputation analysis.

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

7.2.3. Subgroup Analyses for the Primary Endpoint

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

- Baseline IGA score (2, 3)
- Baseline EASI score (≤ 7, > 7)
- Age (2 to 6 years, 7 to < 12 years)
- Sex (male, female)
- Race
- Country (United States or Canada)
- Prior TCS therapy (yes/no)
- Prior TCI therapy (yes/no)
- Prior systemic therapy (yes/no)
- Prior AD therapy (yes/no)

7.2.4. Sensitivity and Supportive Analyses for the Primary Endpoint

7.2.4.1. Longitudinal Logistic Regression With Repeated Measures

To adjust for the dependence underlying the hierarchical multilevel data structure (visit, participant, and site), a longitudinal logistic regression with repeated measures will be applied. The 3 level structures in the model are

- Level 1: visit
- Level 2: participant
- Level 3: site,

where visits are nested within participants and participants are further nested within sites.

The binary response (IGA-TS) of each participant at Weeks 2, 4, and 8 will be included as the dependent variable. Treatment (1.5% BID, 0.75% BID, and vehicle BID), randomization stratification factors (baseline IGA score and age), visit, and treatment-by-visit interaction will

be included as fixed effects. Site level intercept and participant nested in site level intercept will be included as random effects. The within-participant and within-site errors will be modeled by an unstructured variance-covariance matrix. The Kenward-Roger approximation will be used to estimate denominator degrees of freedom for this model.

7.2.4.2. Multiple Imputation

Multiple imputation with missing-at-random assumption will be used as an alternative method to handle missing data. A full conditional specification method (van Buuren 2007) that assumes the existence of a joint distribution for all variables will be used to impute the IGA score. A regression model including treatment group, stratification factor age group, and baseline and scheduled postbaseline IGA scores up to Week 8 will be specified for the fully conditional specification method. The imputation will be repeated 40 times to generate corresponding complete datasets in order to reflect the uncertainty around the true values. The primary endpoint binary response will be derived for each of the imputed datasets per the definition in Section 7.2.1.1 and the logistic regression described in Section 7.2.2 will be applied. The results will then be combined for the inference using Rubin's rule.

The following sample SAS code will be used for the MI:

```
proc mi data=mi_wide seed=18424305 nimpute=40 out=impute_IGA;
  class trt01p agestrata;
     var trt01p agestrata avalBASELINE avalWEEK2 avalWEEK4   avalWEEK8;
     fcs REGPMM nbiter=30;
run;
```

7.2.4.3. Last Observation Carried Forward

For participants who are missing postbaseline values, the last observed nonmissing value will be used to fill in missing values at Week 8. The proposed logistic regression described in Section 7.2.2 will then be applied to the imputed dataset.

7.2.4.4. Tipping Point Analysis

A tipping point sensitivity analysis will be conducted to examine the potential effects of missing data. The missing binary IGA-TS response in each treatment group at Week 8 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 active treatment groups are nonresponders and all the missing participants in the 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 chi-square test. If there are N missing responses in the 1.5% BID arm and Mmissing responses in the vehicle arm, the following process will be used to determine the tipping point and a similar process will be implemented for the 0.75% BID arm versus the vehicle arm:

- Missing responses in the 1.5% BID arm will be imputed with a range of values from 0 to N.
- Missing responses in the vehicle arm will be imputed with a range of values from 0 to M.

- Treatment comparisons between the 1.5% BID arm and the vehicle arm will be analyzed in each of the (N + 1) × (M + 1) imputed datasets using a chi-square test, which will result in a (N + 1) × (M + 1) table; columns will represent the number of responses imputed for the 1.5% BID arm and rows will represent the number of responses imputed for the vehicle arm. A separate table will be generated to compare the 0.75% BID arm with the vehicle arm following the same process.

7.3. Analysis of the Key Secondary Efficacy Parameters

7.3.1. Key Secondary Efficacy Measures

7.3.1.1. Itch Numerical Rating Scale Score

The Itch NRS is a once-daily patient-reported measure of itch intensity assessed using an 11-point scale (0 = no itch to 10 = worst imaginable itch). Participants aged 6 years or older will be asked to record their highest (worst) level of itch in the evening over the 24-hour recall period.

The Itch NRS score for baseline will be determined by averaging the 7 daily NRS scores directly before Day 1 (Day –7 to Day –1) for all the by-visit summaries. The by-visit Itch NRS score for postbaseline visits will be determined by averaging the 7 daily NRS scores directly before the visit day. If 4 or more daily scores are missing (out of the 7), the Itch NRS score at the visit will be set to missing. For all daily itch related analyses, including time to achieve Itch NRS score improvement of at least 2 or 4 points analyses, baseline will be defined as the last available Itch NRS score during the week prior to Day 1 (Day −7 to Day −1).

The proportion of participants with a clinically relevant change in itch, defined as a ≥ 4-point improvement in by-visit or daily Itch NRS score from baseline, will be summarized by treatment group for participants with baseline Itch NRS score ≥ 4.

7.3.2. Key Secondary Efficacy Analysis

Key secondary efficacy analyses will be conducted in the ITT population in the VC period. If the primary objective is achieved, the statistical comparisons for key secondary endpoints will be tested with the procedures specified in Section 3.2.

The same nonresponder imputation method as specified in the primary analysis will be used to handle missing Week 8 itch data, and the logistic regression described in Section 7.2.2 will be applied to compare each ruxolitinib cream group and the vehicle cream group for the key secondary endpoint of ≥ 4-point improvement in Itch NRS score response at Week 8.

For the key secondary endpoints of Itch NRS score responses on Day 7 (Week 1) and Day 3, all participants who are missing Day 7 and/or Day 3 daily Itch NRS scores will be imputed using multiple imputation by fully conditional specification method. The variables to be included in the imputation regression model are treatment group, stratification factor, baseline itch score, and postbaseline daily itch score on Day 1 to Day 7. The corresponding binary response on Day 7 and Day 3 will be derived for each of the imputed datasets per the definition in Section 7.3.1.1. The logistic regression specified in Section 7.2.2 will be applied to each imputed dataset and then the results will be combined for the inference using Rubin's rule.

The following sample SAS code will be used for the MI:

```
proc mi data=mi_wide seed=18424 nimpute=30 out=impute_itch;
    class trt01p strat1 strat2;
    var trt01p strat1 strat2 base avald1 avald2 avald3 avald4 avald5
avald6 avald7;
     fcs regpmm nbiter=30;

run;
```

7.4. Analysis of Secondary Efficacy Parameters

7.4.1. Secondary Efficacy Measures

7.4.1.1. Eczema Area and Severity Index Score

Atopic dermatitis will be assessed using the EASI scoring system, which is a validated scoring system that grades the physical signs of AD to provide a measure of AD severity (ranging from 0 to 72).

The weight of the body regions for the EASI scoring is based on age (< 8 years or ≥ 8 years):

- For participants 8 years of age or older: head/neck (H) = 0.1, upper limbs (UL) = 0.2, trunk (T) = 0.3, and lower limbs (LL) = 0.4
- For participants 7 years or younger: head/neck (H) = 0.2, upper limbs (UL) = 0.2, trunk (T) = 0.3, and lower limbs (LL) = 0.3

Each of the 4 body regions is assessed separately for erythema (E), induration/papulation/edema (I), excoriations (Ex), and lichenification (L) for an average degree of severity of each sign in each region with 0 = none, 1 = mild, 2 = moderate, and 3 = severe, with half-steps allowed.

The disease severity strata for the EASI are as follows: 0 = clear; 0.1 to 1.0 = almost clear; 1.1 to 7.0 = mild; 7.1 to 21.0 = moderate; 21.1 to 50.0 = severe; and 50.1 to 72.0 = very severe.

The categorical variable EASI75 to indicate the EASI responder will be set to 1 for percentage improvement from baseline in EASI score of 75% or greater and will be equal to 0 for percentage improvement of less than 75%. [redacted]

7.4.2. Secondary Efficacy Analysis

All secondary efficacy analyses will be conducted based on the ITT population in the VC period.

7.4.2.1. Categorical Efficacy Endpoints

For the following categorical parameters, summary statistics including sample size, frequency, and percentages will be presented by visit:

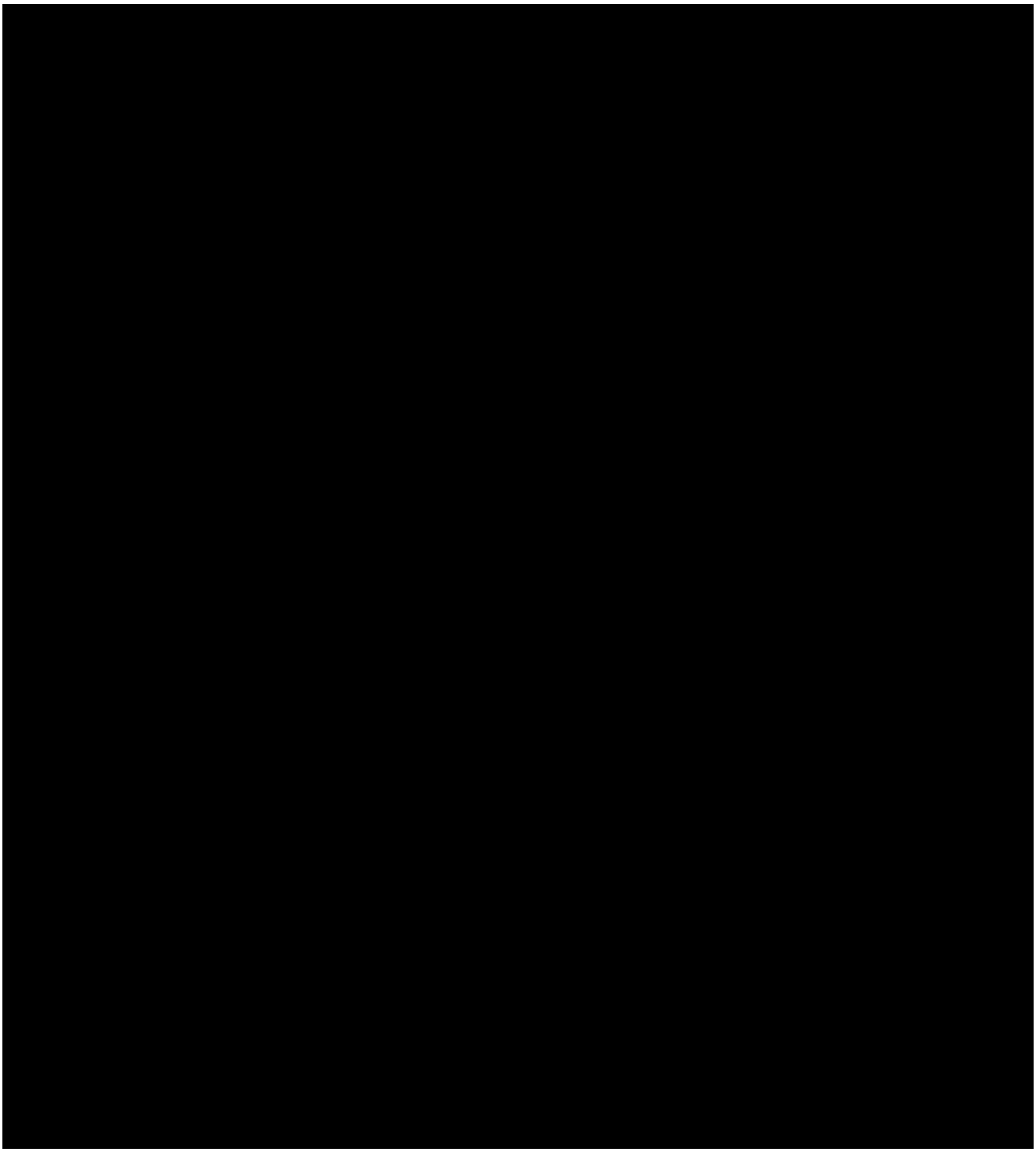
- Proportion of participants achieving an IGA-TS
- Proportion of participants with a ≥ 4-point improvement in Itch NRS score
- Proportion of participants achieving EASI75

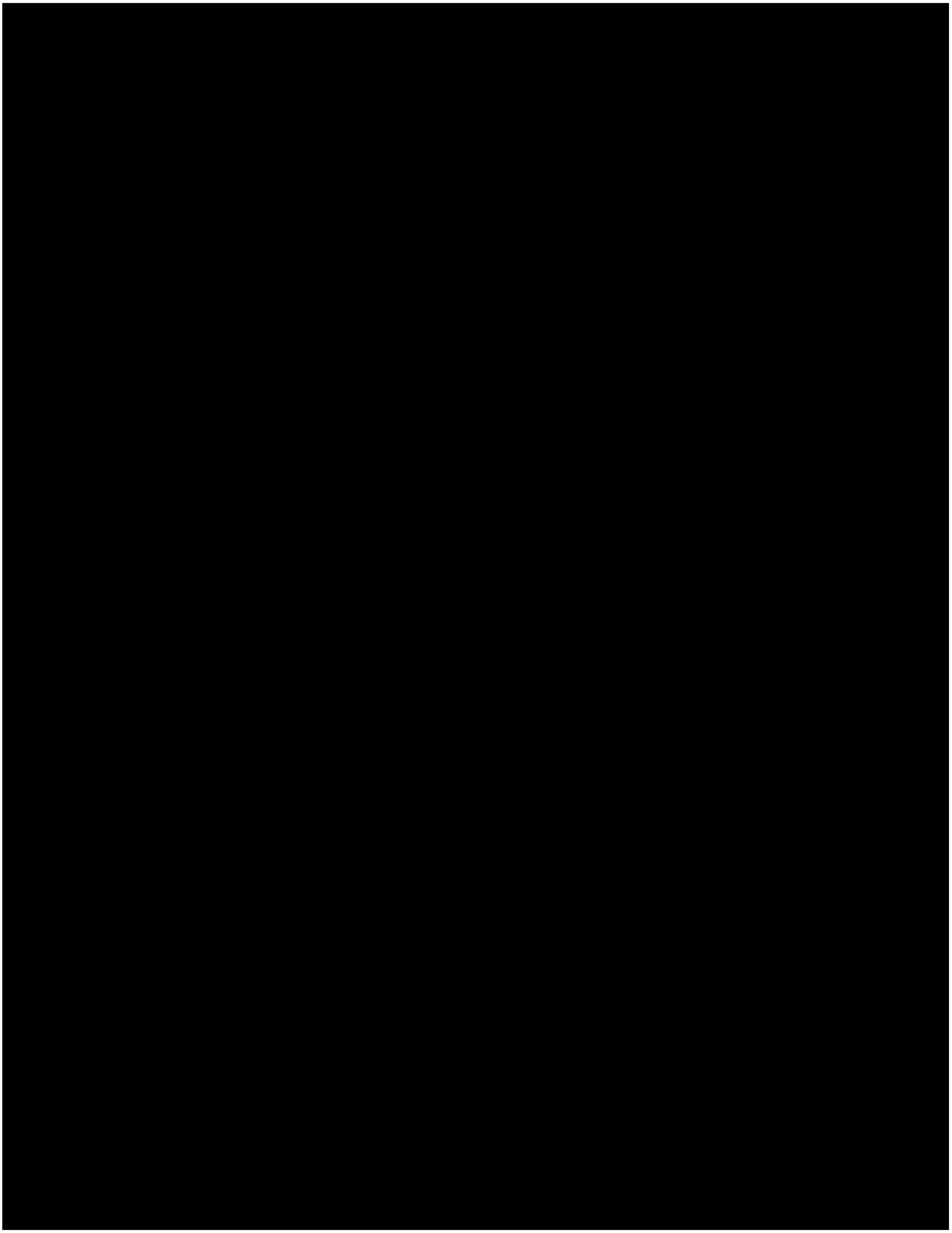
A logistic regression model with treatment and stratification factors as covariates will be fit at Week 8. The p-values between each ruxolitinib group versus vehicle will be calculated based on the Wald test. Exact logistic regression will be used for all of the comparisons if any of the dose levels have an expected cell count < 5. The NRI will be used to impute postbaseline missing values for binary outcomes based on IGA, Itch NRS, and EASI scores.

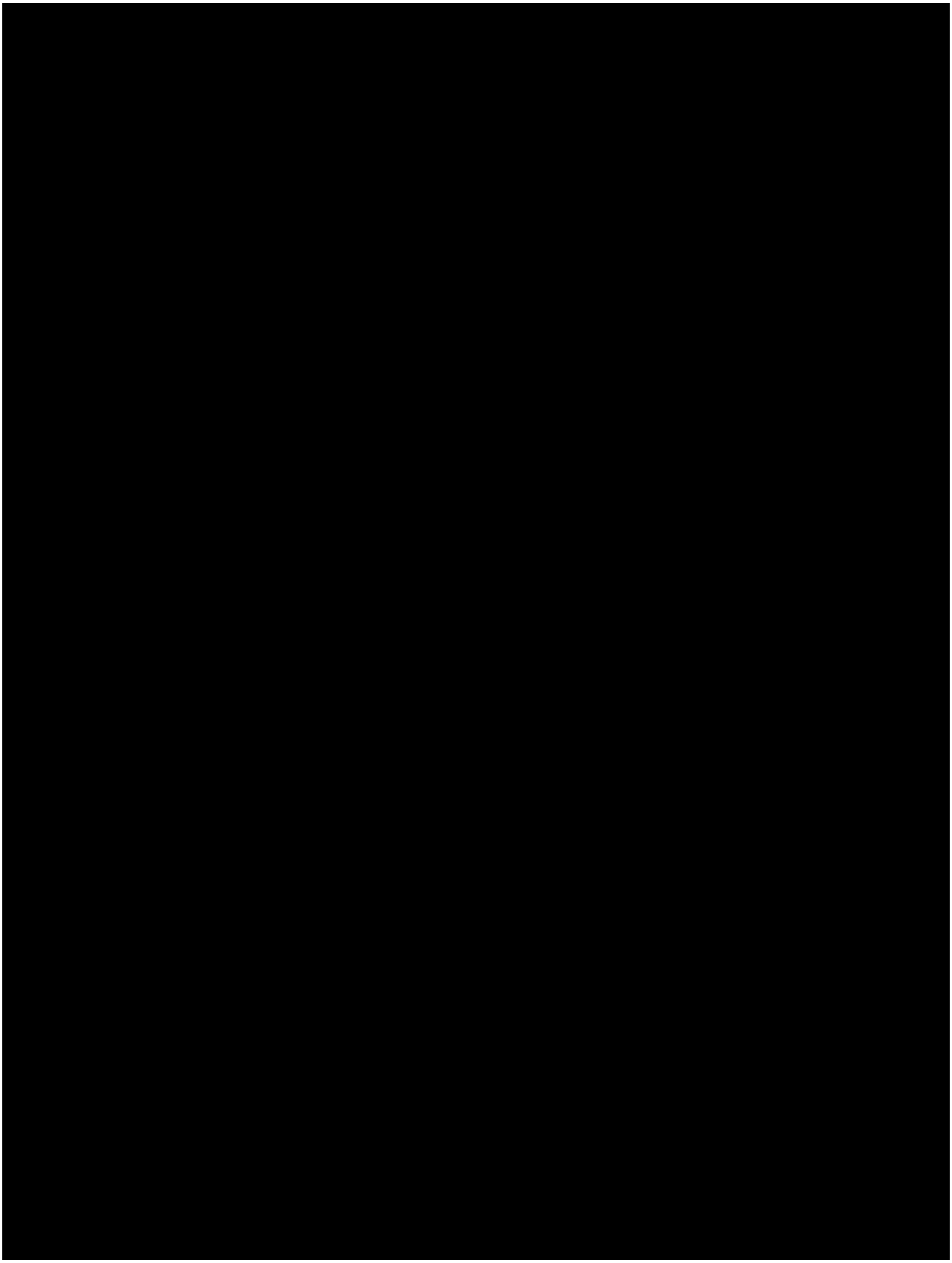
7.4.2.2. Time-to-Event Efficacy Endpoints

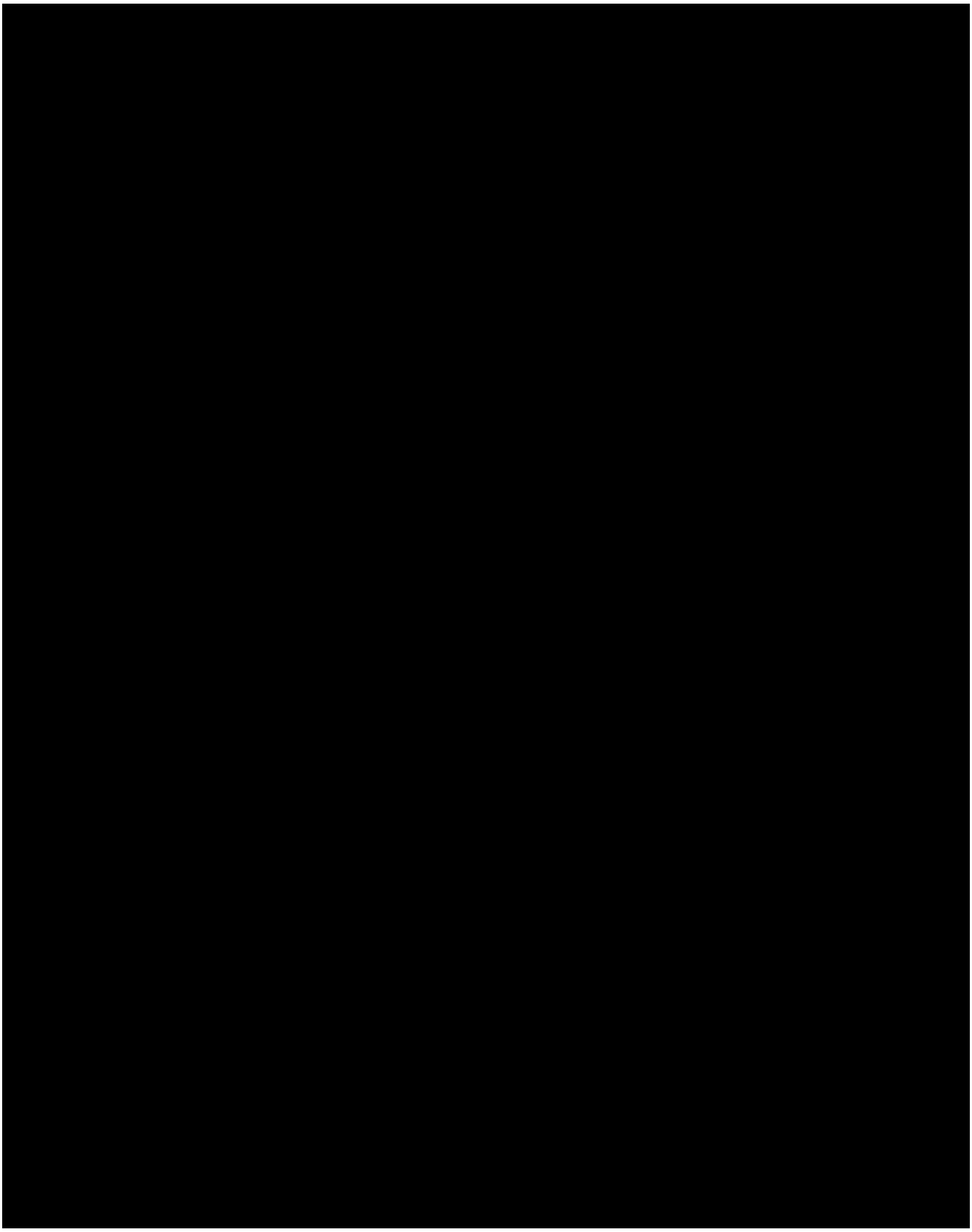
For the time to achieve Itch NRS score improvement of at least 2 or 4 points, a log-rank test stratified by randomization stratification factors will be used for between-treatment group comparisons. The hazard ratio and its 95% CI will be estimated based on the stratified Cox regression model using Efron's method accounting for ties. Kaplan-Meier curves will be presented by treatment group. The number of participants, number of events, and number of censoring will be summarized by treatment group. The Kaplan-Meier estimate of median time will be presented with its 95% CI. The 95% CI will be calculated using the method by Brookmeyer and Crowley (1982).

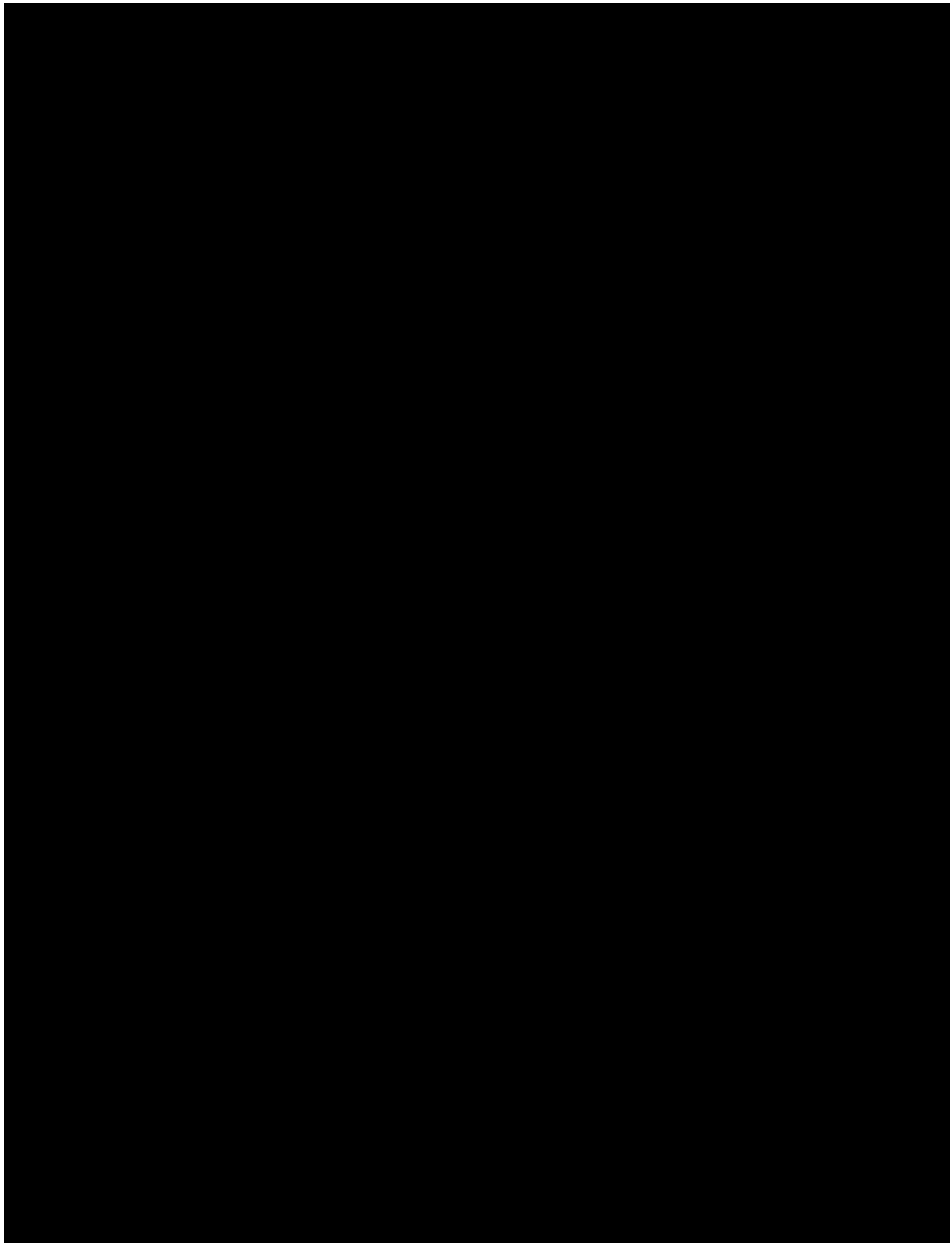
[redacted]











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9. SAFETY AND TOLERABILITY

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

9.1. General Considerations

The analyses in this section will be provided for the safety population in the VC period and for the LTS evaluable population in the LTS period. Cumulative TEAEs across the treatment periods (VC and LTS periods) will be summarized. 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.

9.2. Adverse Events

9.2.1. 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 after 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 administration.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE v5. The CTCAE (Grade 1 to 5) 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 treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered treatment-related. The incidence of AEs and treatment-related AEs will be tabulated. In addition, 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 also be provided for the safety population, including cumulative TEAEs and cumulative ASRs.

9.2.2. Adverse Event Summaries

An overall summary of AEs by treatment group will include the following:

- Number (%) of participants reporting any TEAEs
- 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 in part of the treated areas because of TEAEs
- Number (%) of participants who temporarily interrupted study drug in all of the treated areas because of TEAEs
- Number (%) of participants who temporarily interrupted study drug in any of the treated areas 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 Grade 3 or higher TEAEs by SOC and PT
- Summary of Grade 3 or higher TEAEs 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 in any of the treated areas by SOC and PT
- Summary of TEAEs leading to dose interruption of study drug in part of the treated areas by SOC and PT

- Summary of TEAEs leading to dose interruption of study drug in all of the treated areas by SOC and PT
- Summary of TEAEs leading to discontinuation of study drug by SOC and PT

Subgroup analysis for TEAEs by age categories will also be provided.

Adverse events of interest will be summarized in the following categories:

- Cytopenias
  - Anemia
  - Thrombocytopenia
  - Neutropenia
- Herpes zoster
- Viral skin infections
- Nonmelanoma skin neoplasms
- Liver function test elevations
- Malignancies
- Major Adverse Cardiovascular Events
- Venous and arterial thromboembolic events
- Thrombocytosis and elevated mean platelet volume

9.3. Clinical Laboratory Tests

9.3.1. 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 administration 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.

9.3.2. 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 numerical 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 nonmissing laboratory 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.

Test results will be summarized and listed 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 the VC period, as well as the LTS period for the LTS evaluable population. Shift tables will be presented to show change in CTCAE grade from baseline to worst grade postbaseline as well. The denominator for the percentage calculation will use the number of participants in the baseline category.

Subgroup analysis for laboratory results by age categories will also be provided.

9.4. Body Weight and Height

Values at each scheduled visit, change, and percentage change from baseline for body weight and height will be summarized descriptively and listed.

9.5. 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 3 and Table 4. 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 from baseline > 25%. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 3: Criteria for Clinically Notable Vital Sign Abnormalities for Ages ≥ 7 to < 12 Years

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 120 mm Hg	< 97 mm Hg
Diastolic blood pressure	> 80 mm Hg	< 57 mm Hg
Pulse	> 118 bpm	< 75 bpm
Temperature	> 38.0°C	< 35.5°C
Respiratory rate	> 25 breaths/min	< 18 breaths/min

Table 4: Criteria for Clinically Notable Vital Sign Abnormalities for Ages ≥ 2 to < 7 Years

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 112 mm Hg	< 89 mm Hg
Diastolic blood pressure	> 72 mm Hg	< 46 mm Hg
Pulse	> 120 bpm	< 80 bpm
Temperature	> 38.0°C	< 35.5°C
Respiratory rate	> 28 breaths/min	< 20 breaths/min

10. PLANNED ANALYSES

No formal interim analysis is planned for this study. There are 2 formal planned analyses.

- The primary analysis will occur after the primary database lock, when all participants have completed the VC period. The sponsor will be unblinded after the primary database lock; however, investigators and participants will remain blinded to the individual study treatment assignment.
- The final analysis will occur when all participants have completed or withdrawn from the study.

11. 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	02 JUN 2023

11.1. Changes to Protocol-Defined Analyses

Not applicable.

11.2. Changes to the Statistical Analysis Plan

Not applicable.

12. REFERENCES

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.

[redacted].

[redacted]

Food and Drug Administration. Draft guidance on pimecrolimus. March 2012.

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

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

[redacted].

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APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the Clinical Study Report. Shells are provided in a separate document for tables that are not in the most current Standard Safety Tables.

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

Tables

Table No.	Title	Population	Standard
Baseline Demographic and Characteristic			
1.1.1	Analysis Populations	All	X
1.1.2.1	Summary of Participant Disposition in the VC Period	ITT	X
1.1.2.2	Summary of Participant Disposition in the LTS Period	LTS Evaluable	X
1.1.3	Summary of Number of Participants Enrolled by Country and Site	ITT	X
1.1.4.1	Summary of Protocol Deviations During the VC Period	ITT	X
1.1.4.2	Summary of Protocol Deviations During the LTS Period	LTS Evaluable	X
1.2.1	Summary of Demographics and Baseline Characteristics in the VC Period	ITT	X
1.2.2	Summary of Demographics and Baseline Characteristics in the LTS Period	LTS Evaluable	X
1.3	Summary of Baseline Disease Characteristics	ITT	X
1.4.1	Summary of Prior Non-AD Medications	ITT	X
1.4.2.1	Summary of Prior Therapies for Atopic Dermatitis During the Past 12 Months	ITT	X
1.4.2.2	Summary of Prior Therapies for Atopic Dermatitis During the Past 12 Months by Therapy Type and Discontinuation Reason	ITT	X
1.4.2.3	Summary of Prior Therapies for Atopic Dermatitis During the Past 30 Days	ITT	X
1.4.2.4	Summary of Prior Therapies for Atopic Dermatitis During the Past 30 Days by Therapy Type and Discontinuation Reason	ITT	X
1.4.3.1	Summary of Non-AD Concomitant Medications During the VC Period	ITT	X
1.4.3.2	Summary of Non-AD Concomitant Medications During the LTS Period	LTS Evaluable	X
1.4.3.3	Summary of Concomitant Therapies for AD During the VC Period	ITT	X
1.4.3.4	Summary of Concomitant Therapies for AD During the LTS Period	LTS Evaluable	X
1.5	Summary of General Medical History	ITT	X
1.6.1	Summary of Participants With Assessments Affected by the COVID-19 Pandemic in the VC Period	ITT	X
1.6.2	Summary of Participants With Assessments Affected by the COVID-19 Pandemic in the LTS Period	LTS Evaluable	X

Table No.	Title	Population	Standard
Efficacy			
IGA			
2.1.1	Summary and Analysis of Participants Achieving IGA-TS in the VC Period	ITT	
2.1.2	Summary and Sensitivity Analysis of Participants Achieving IGA-TS at Week 8 by Tipping Point Analysis	ITT	
2.1.3	Summary and Analysis of Participants Achieving IGA-TS in the VC Period	PP	
2.1.4	Summary and Analysis of Participants Achieving IGA-TS by Baseline IGA Score in the VC Period	ITT	
2.1.5	Summary and Analysis of Participants Achieving IGA-TS by Baseline EASI Score in the VC Period	ITT	
2.1.6	Summary and Analysis of Participants Achieving IGA-TS by Country in the VC Period	ITT	
2.1.7	Summary and Analysis of Participants Achieving IGA-TS by Age Group in the VC Period	ITT	
2.1.8	Summary and Analysis of Participants Achieving IGA-TS by Sex in the VC Period	ITT	
2.1.9	Summary and Analysis of Participants Achieving IGA-TS by Race in the VC Period	ITT	
2.1.10	Summary and Analysis of Participants Achieving IGA-TS by Any Prior TCS Therapy in the VC Period	ITT	
2.1.11	Summary and Analysis of Participants Achieving IGA-TS by Any Prior TCI Therapy in the VC Period	ITT	
2.1.12	Summary and Analysis of Participants Achieving IGA-TS by Any Prior Systemic Therapy in the VC Period	ITT	
2.1.13	Summary and Analysis of Participants Achieving IGA-TS by Any Prior AD Therapy in the VC Period	ITT	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
2.1.15.1	Summary of Participants in Each Category of IGA Score in the VC Period	ITT	
2.1.15.2	Summary of Participants in Each Category of IGA Score in the LTS Period	LTS Evaluable	
EASI			
2.2.1	Summary and Analysis of Participants Achieving EASI75 in the VC Period	ITT	
[redacted]			

Table No.	Title	Population	Standard
2.2.5.1	Summary of Participants in Each Category of EASI Score in the VC Period	ITT	
Itch NRS Score			
2.3.1	Summary and Analysis of Participants Achieving ≥ 4-Point Improvement in Itch NRS Score in the VC Period by Visit	ITT with baseline Itch NRS Score ≥ 4	
[redacted]			
2.3.3	Summary and Analysis of Time to ≥ 2-Point Improvement in Itch NRS Score in the VC Period	ITT with daily baseline Itch NRS Score ≥ 2	
2.3.4	Summary and Analysis of Time to ≥ 4-Point Improvement in Itch NRS Score in the VC Period	ITT with daily baseline Itch NRS Score ≥ 4	
[redacted]			
2.3.6	Summary and Analysis of Participants Achieving ≥ 4-Point Improvement in Itch NRS Score from Day 1 to Day 7	ITT with daily baseline Itch NRS Score ≥ 4	

[redacted]

Table No.	Title	Population	Standard
[redacted]			

Table No.	Title	Population	Standard
[redacted]			
Exposure, Adverse Events, Laboratory, and Vital Signs			
Exposure			
3.1.1.1	Summary of Exposure During the VC Period	Safety	X
3.1.1.2	Summary of Exposure During the LTS Period	LTS Evaluable	X
3.1.1.3	Summary of Exposure From Baseline to Week 52	Safety	X
3.1.2	Summary of Study Drug Compliance During the VC Period	Safety	X
Adverse Events			
3.2.1.1.1	Overall Summary of Treatment-Emergent Adverse Events in the VC Period	Safety	X
3.2.1.1.2	Overall Summary of Treatment-Emergent Adverse Events by Age Group in the VC Period	Safety	X
3.2.1.1.3	Overall Summary of Treatment-Emergent Adverse Events in the LTS Period	LTS Evaluable	X
3.2.1.1.4	Overall Summary of Treatment-Emergent Adverse Events for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.2.1.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X

Table No.	Title	Population	Standard
3.2.2.1.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.2.1.3	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.2.1.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.3.1.1	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the VC Period	Safety	X
3.2.3.1.2	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency by Age Group in the VC Period	Safety	X
3.2.3.1.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the LTS Period	LTS Evaluable	X
3.2.3.1.4	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.3.2.1	Summary of Treatment-Emergent Adverse Events in ≥ 1% of Participants in Any Treatment Group by MedDRA Preferred Term in Decreasing Order of Frequency in the VC Period	Safety	X
3.2.3.2.2	Summary of Treatment-Emergent Adverse Events in ≥ 1% of Participants in any Treatment Group by MedDRA Preferred Term in Decreasing Order of Frequency by Age Group in the VC Period	Safety	X
3.2.3.2.3	Summary of Treatment-Emergent Adverse Events in ≥ 1% of Participants in Any Treatment Group by MedDRA Preferred Term in Decreasing Order of Frequency in the LTS Period	LTS Evaluable	X
3.2.3.2.4	Summary of Treatment-Emergent Adverse Events in ≥ 1% of Participants by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.3.3.1	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency in the VC Period	Safety	X
3.2.3.3.2	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency by Age Group in the VC Period	Safety	X
3.2.3.3.3	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency in the LTS Period	LTS Evaluable	X
3.2.3.3.4	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X

Table No.	Title	Population	Standard
3.2.4.1.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.4.1.2	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.4.1.3	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.4.2.2	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.5.1.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the VC Period	Safety	X
3.2.5.1.2	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency by Age Group in the VC Period	Safety	X
3.2.5.1.3	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the LTS Period	LTS Evaluable	X
3.2.5.1.4	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.6.1.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.6.1.2	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.6.1.3	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.6.1.4	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.7.1.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the VC Period	Safety	X
3.2.7.1.2	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency by Age Group in the VC Period	Safety	X
3.2.7.1.3	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the LTS Period	LTS Evaluable	X

Table No.	Title	Population	Standard
3.2.7.1.4	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.8.1.1	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.8.1.2	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.8.1.3	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.8.1.4	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.9.1.1	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the VC Period	Safety	X
3.2.9.1.2	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency by Age Group in the VC Period	Safety	X
3.2.9.1.3	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the LTS Period	LTS Evaluable	X
3.2.9.1.4	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.10.1.1	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.10.1.2	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.10.1.3	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.10.1.4	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.11.1.1	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X

Table No.	Title	Population	Standard
3.2.11.1.2	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.11.1.3	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.11.1.4	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.12.1.1	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.12.1.2	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.12.1.3	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.12.1.4	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.13.1.1	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Any of the Treated Areas by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.13.1.2	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Any of the Treated Areas by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.13.1.3	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Any of the Treated Areas by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.13.1.4	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Any of the Treated Areas by MedDRA System Organ Class and Preferred Term for Participants who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.13.2.1	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Part of the Treated Areas by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.13.2.2	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Part of the Treated Areas by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.13.2.3	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Part of the Treated Areas by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X

Table No.	Title	Population	Standard
3.2.13.2.4	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in Part of the Treated Areas by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.13.3.1	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in All of the Treated Areas by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.13.3.2	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in All of the Treated Areas by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.13.3.3	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in All of the Treated Areas by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.13.3.4	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption in All of the Treated Areas by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.14.1.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term in the VC Period	Safety	X
3.2.14.1.2	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term by Age Group in the VC Period	Safety	X
3.2.14.1.3	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term in the LTS Period	LTS Evaluable	X
3.2.14.1.4	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.15.1.1	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA System Organ Class and Preferred Term in the VC period	Safety	X
3.2.15.1.2	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA System Organ Class and Preferred Term by Age Group in the VC period	Safety	X
3.2.15.1.3	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA System Organ Class and Preferred Term in the LTS period	LTS Evaluable	X
3.2.15.1.4	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA System Organ Class and Preferred Term for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
3.2.16.1.1	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA Preferred Term in Decreasing Order of Frequency in the VC period	Safety	X

Table No.	Title	Population	Standard
3.2.16.1.2	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA Preferred Term in Decreasing Order of Frequency by Age Group in the VC period	Safety	X
3.2.16.1.3	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA Preferred Term in Decreasing Order of Frequency in the LTS period	LTS Evaluable	X
3.2.16.1.4	Summary of Treatment-Emergent Adverse Events of Interest by MedDRA Preferred Term in Decreasing Order of Frequency for Participants Who Applied Ruxolitinib Cream Throughout the Study (Baseline to Week 52)	Safety	X
Laboratory			
3.3.1.1.1	Summary of Laboratory Values – Hematology in the VC Period	Safety	X
3.3.1.1.2	Summary of Laboratory Values – Hematology by Age Group in the VC Period	Safety	X
3.3.1.1.3	Summary of Laboratory Values – Hematology in the LTS Period	LTS Evaluable	X
3.3.2.1.1	Summary of Laboratory Values – Chemistry in the VC Period	Safety	X
3.3.2.1.2	Summary of Laboratory Values – Chemistry by Age Group in the VC Period	Safety	X
3.3.2.1.3	Summary of Laboratory Values – Chemistry in the LTS Period	LTS Evaluable	X
3.3.3.1	Shift Summary of Hematology Laboratory Values in CTCAE Grade – To the Worst Abnormal Value in the VC Period	Safety	X
3.3.3.2	Shift Summary of Hematology Laboratory Values in CTCAE Grade – To the Worst Abnormal Value in the VC Period by Age Group	Safety	X
3.3.3.3	Shift Summary of Hematology Laboratory Values in CTCAE Grade – To the Worst Abnormal Value in the LTS Period	LTS Evaluable	X
3.3.4.1	Shift Summary of Chemistry Laboratory Values in CTCAE Grade – To the Worst Abnormal Value in the VC Period	Safety	X
3.3.4.2	Shift Summary of Chemistry Laboratory Values in CTCAE Grade – To the Worst Abnormal Value in the VC Period by Age Group	Safety	X
3.3.4.3	Shift Summary of Chemistry Laboratory Values in CTCAE Grade – To the Worst Abnormal Value in the LTS Period	LTS Evaluable	X
3.3.5.1	Shift Summary of Hematology Values – To the Worst Abnormal Value in the VC Period	Safety	X
3.3.5.2	Shift Summary of Hematology Values – To the Worst Abnormal Value in the VC Period by Age Group	Safety	X
3.3.5.3	Shift Summary of Hematology Values – To the Worst Abnormal Value in the LTS Period	LTS Evaluable	X
3.3.6.1	Shift Summary of Chemistry Values – To the Worst Abnormal Value in the VC Period	Safety	X
3.3.6.2	Shift Summary of Chemistry Values – To the Worst Abnormal Value in the VC Period by Age Group	Safety	X
3.3.6.3	Shift Summary of Chemistry Values – To the Worst Abnormal Value in the LTS Period	LTS Evaluable	X

Table No.	Title	Population	Standard
Body Weight and Height			
3.4.1.1	Summary of Body Weight and Height in the VC Period	Safety	X
3.4.1.2	Summary of Body Weight and Height in the LTS Period	LTS Evaluable	X
Vital Signs			
3.5.1.1	Summary of Systolic Blood Pressure in the VC Period	Safety	X
3.5.1.2	Summary of Systolic Blood Pressure in the LTS Period	LTS Evaluable	X
3.5.2.1	Summary of Diastolic Blood Pressure in the VC Period	Safety	X
3.5.2.2	Summary of Diastolic Blood Pressure in the LTS Period	LTS Evaluable	X
3.5.3.1	Summary of Pulse in the VC Period	Safety	X
3.5.3.2	Summary of Pulse in the LTS Period	LTS Evaluable	X
3.5.4.1	Summary of Respiratory Rate in the VC Period	Safety	X
3.5.4.2	Summary of Respiratory Rate in the LTS Period	LTS Evaluable	X
3.5.5.1	Summary of Body Temperature in the VC Period	Safety	X
3.5.5.2	Summary of Body Temperature in the LTS Period	LTS Evaluable	X

Figures

Figure No.	Title	Population
IGA		
4.1.1	Proportion of Participants Achieving IGA-TS in the VC Period	ITT
4.1.1.1	Proportion of Participants Achieving IGA-TS by Baseline IGA Score in the VC Period	ITT
4.1.1.2	Proportion of Participants Achieving IGA-TS by Baseline EASI Score in the VC Period	ITT
4.1.1.3	Proportion of Participants Achieving IGA-TS by Country in the VC Period	ITT
4.1.1.4	Proportion of Participants Achieving IGA-TS by Age Group in the VC Period	ITT
4.1.1.5	Proportion of Participants Achieving IGA-TS by Sex in the VC Period	ITT
4.1.1.6	Proportion of Participants Achieving IGA-TS by Race in the VC Period	ITT
4.1.1.7	Proportion of Participants Achieving IGA-TS by Prior TCS Therapy in the VC Period	ITT
4.1.1.8	Proportion of Participants Achieving IGA-TS by Prior TCI Therapy in the VC Period	ITT
4.1.1.9	Proportion of Participants Achieving IGA-TS by Prior Systemic Therapy in the VC Period	ITT
4.1.1.10	Proportion of Participants Achieving IGA-TS by Prior AD Therapy in the VC Period	ITT
4.1.1.11	Forest Plot of Response Rate Difference in Achieving IGA-TS at Week 8: 1.5% BID Versus Vehicle	ITT
4.1.1.12	Forest Plot of Response Rate Difference in Achieving IGA-TS at Week 8: 0.75% BID Versus Vehicle	ITT
[redacted]		
EASI		
[redacted]		

Figure No.	Title	Population
4.2.2	Proportion of Participants Achieving EASI75 in the VC Period	ITT
[redacted]		
Itch NRS		
4.3.1.1	Proportion of Participants Achieving ≥ 4-Point Improvement in Itch NRS Score in the VC Period	ITT with baseline Itch NRS score ≥ 4
4.3.1.2	Proportion of Participants Achieving ≥ 2-Point Improvement in Itch NRS Score in the VC Period	ITT with baseline Itch NRS score ≥ 2
4.3.2.1	Mean and Standard Error Plot of Itch NRS Score by Visit in the VC Period	ITT with age ≥ 6 years
[redacted]		
4.3.3	Kaplan-Meier Curve of the Time to ≥ 2-Point Improvement in Itch NRS Score in the VC Period	ITT with daily baseline Itch NRS score ≥ 2
4.3.4	Kaplan-Meier Curve of the Time to ≥ 4-Point Improvement in Itch NRS Score in the VC Period	ITT with daily baseline Itch NRS score ≥ 4
[redacted]		
4.3.6	Proportion of Participants Achieving ≥ 4-Point Improvement in Itch NRS Score from Day 1 to Day 7	ITT with daily baseline Itch NRS score ≥ 4
[redacted]		

Figure No.	Title	Population
[redacted]		

Figure No.	Title	Population
[redacted]		
Laboratory		
4.13.1.1.1	Box Plot of Hemoglobin (g/L) by Visit in the VC Period	Safety
4.13.1.1.2	Box Plot of Hemoglobin (g/L) by Visit in the VC Period by Age Group	Safety
4.13.1.2.1	Box Plot of Change From Baseline in Hemoglobin (g/L) by Visit in the VC Period	Safety
4.13.1.2.2	Box Plot of Change From Baseline in Hemoglobin (g/L) by Visit in the VC Period by Age Group	Safety
4.13.1.3.1	Box Plot of Percentage Change From Baseline in Hemoglobin (g/L) by Visit in the VC Period	Safety
4.13.1.3.2	Box Plot of Percentage Change From Baseline in Hemoglobin (g/L) by Visit in the VC Period by Age Group	Safety
4.13.2.1.1	Box Plot of Platelets (10^9/L) by Visit in the VC Period	Safety
4.13.2.1.2	Box Plot of Platelets (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.2.2.1	Box Plot of Change From Baseline in Platelets (10^9/L) by Visit in the VC Period	Safety
4.13.2.2.2	Box Plot of Change From Baseline in Platelets (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.2.3.1	Box Plot of Percentage Change From Baseline in Platelets (10^9/L) by Visit in the VC Period	Safety
4.13.2.3.2	Box Plot of Percentage Change From Baseline in Platelets (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.3.1.1	Box Plot of Neutrophils (10^9/L) by Visit in the VC Period	Safety
4.13.3.1.2	Box Plot of Neutrophils (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.3.2.1	Box Plot of Change From Baseline in Neutrophils (10^9/L) by Visit in the VC Period	Safety
4.13.3.2.2	Box Plot of Change From Baseline in Neutrophils (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.3.3.1	Box Plot of Percentage Change From Baseline in Neutrophils (10^9/L) by Visit in the VC Period	Safety
4.13.3.3.2	Box Plot of Percentage Change From Baseline in Neutrophils (10^9/L) by Visit in the VC Period by Age Group	Safety

Figure No.	Title	Population
4.13.4.1.1	Box Plot of Leukocytes (10^9/L) by Visit in the VC Period	Safety
4.13.4.1.2	Box Plot of Leukocytes (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.4.2.1	Box Plot of Change From Baseline in Leukocytes (10^9/L) by Visit in the VC Period	Safety
4.13.4.2.2	Box Plot of Change From Baseline in Leukocytes (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.4.3.1	Box Plot of Percentage Change From Baseline in Leukocytes (10^9/L) by Visit in the VC Period	Safety
4.13.4.3.2	Box Plot of Percentage Change From Baseline in Leukocytes (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.5.1.1	Box Plot of Lymphocytes (10^9/L) by Visit in the VC Period	Safety
4.13.5.1.2	Box Plot of Lymphocytes (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.5.2.1	Box Plot of Change From Baseline in Lymphocytes (10^9/L) by Visit in the VC Period	Safety
4.13.5.2.2	Box Plot of Change From Baseline in Lymphocytes (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.5.3.1	Box Plot of Percentage Change From Baseline in Lymphocytes (10^9/L) by Visit in the VC Period	Safety
4.13.5.3.2	Box Plot of Percentage Change From Baseline in Lymphocytes (10^9/L) by Visit in the VC Period by Age Group	Safety
4.13.6.1.1	Box Plot of Erythrocytes (10^12/L) by Visit in the VC Period	Safety
4.13.6.1.2	Box Plot of Erythrocytes (10^12/L) by Visit in the VC Period by Age Group	Safety
4.13.6.2.1	Box Plot of Change From Baseline in Erythrocytes (10^12/L) by Visit in the VC Period	Safety
4.13.6.2.2	Box Plot of Change From Baseline in Erythrocytes (10^12/L) by Visit in the VC Period by Age Group	Safety
4.13.6.3.1	Box Plot of Percentage Change From Baseline in Erythrocytes (10^12/L) by Visit in the VC Period	Safety
4.13.6.3.2	Box Plot of Percentage Change From Baseline in Erythrocytes (10^12/L) by Visit in the VC Period by Age Group	Safety
4.13.7.1.1	Box Plot of Reticulocytes/Erythrocytes (%) by Visit in the VC Period	Safety
4.13.7.1.2	Box Plot of Reticulocytes/Erythrocytes (%) by Visit in the VC Period by Age Group	Safety
4.13.7.2.1	Box Plot of Change From Baseline in Reticulocytes/Erythrocytes (%) by Visit in the VC Period	Safety
4.13.7.2.2	Box Plot of Change From Baseline in Reticulocytes/Erythrocytes (%) by Visit in the VC Period by Age Group	Safety
4.13.7.3.1	Box Plot of Percentage Change From Baseline in Reticulocytes/Erythrocytes (%) by Visit in the VC Period	Safety
4.13.7.3.2	Box Plot of Percentage Change From Baseline in Reticulocytes/Erythrocytes (%) by Visit in the VC Period by Age Group	Safety

Listings

Listing No.	Title
Baseline Demographic and Characteristic	
2.1.1.1	Participant Enrollment and Disposition Status in the VC Period
2.1.1.2	Participant Enrollment and Disposition Status in the LTS Period
2.1.2	Participant Inclusion and Exclusion Criteria Violations
2.1.3	Participants Who Discontinued Treatment or Discontinued From the Study Due to COVID-19
2.1.4	Participants With Assessments Affected by the COVID-19 Pandemic
2.2	Protocol Deviations
2.3	Analysis Populations
2.4.1	Demographic Characteristics
2.4.2	Baseline Disease Characteristics
2.4.3	Prior and Concomitant Medications
2.4.4	Prior Medications for Atopic Dermatitis
2.4.5	Medical History
2.5.1	Study Drug Exposure and Compliance in the VC Period
2.5.2	Study Drug Exposure in the LTS Period
2.5.3	Study Drug Exposure from Baseline to Week 52
Efficacy	
2.6.1	IGA Score
2.6.2.1	EASI Individual Scores
2.6.2.2	EASI Total Score
2.6.3.1	Itch NRS Daily Score
[redacted]	[redacted]
2.6.3.3	Time to Itch Response

[redacted]

Listing No.	Title
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
2.7.5	Adverse Events With a Fatal Outcome
2.7.6	Adverse Events Leading to Interruption of Study Drug
2.7.7	Grade 3 or Higher Adverse Events
2.7.8	Application Site Reactions
2.7.9	Adverse Events of Interest
Laboratory Data	
2.8.1	Clinical Laboratory Values – Hematology
2.8.2	Clinical Laboratory Values – Serum Chemistry
2.8.3	Abnormal Clinical Laboratory Values – Hematology
2.8.4	Abnormal Clinical Laboratory Values – Serum Chemistry
Body Weight and Height	
2.9.1	Body Weight and Height
Vital Signs	
2.10.1	Vital Signs
2.10.2	Abnormal Vital Sign Values
2.10.3	Alert Vital Sign Values